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**Getting Started**

Welcome to the CIBMTR Forms Instruction Manual. The Table of Contents on the left side of the screen is for navigational purposes; if you are on a mobile device you may find the Table on Contents on the top of the page.

**General Instructions** provides useful general background information for successfully completing forms.

**2804/2814: CRID Assignment and Indication** provides explanatory text used to generate a CIBMTR Research ID (CRID) and report the indication.

**Transplant Essential Data (TED) Manuals** provides explanatory text for each question found on the TED forms.

**Comprehensive Baseline & Follow-up Forms Manuals** provides explanatory text for each question on the Baseline, Follow-up, IDMs, HLA, and Infusion forms.

**Comprehensive Disease Specific Manuals** provides explanatory text and additional information for disease indications requiring CIBMTR reporting.

**Cellular Therapy Manuals** provides explanatory text for completing pre-infusion, infusion, and post-infusion forms

**Infection & Miscellaneous Manuals** provides explanatory text for manuals such as the Hepatitis Serology, VOD / SOS, and Myelofibrosis CMS Study forms.

**Appendices** provide additional information beyond the scope of the other manuals.

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
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<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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<tr>
<td>3/19/19</td>
<td><strong>2450: Post-TED</strong></td>
<td>Add</td>
<td>Added the following red warning box instruction (in red below) below question 75 to clarify when to use the CCR option in the Disease</td>
</tr>
<tr>
<td>Date</td>
<td>Document Section/Question</td>
<td>Action</td>
<td>Details</td>
</tr>
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</tr>
<tr>
<td>2/27/19</td>
<td>Assessment at the Time of Best Response to HCT section of the Post-TED (2450) form</td>
<td>Add</td>
<td>Continued Complete Remission (CCR) should be reported for all patients who were already in CR at the start of the preparative regimen.</td>
</tr>
<tr>
<td>2/27/19</td>
<td>2116: PCD Post-HCT</td>
<td>Add</td>
<td>Added (in red below) additional instruction for question 61: However, bisphosphonate therapy (e.g., Zometa) should not be reported as planned therapy since it is universally administered to myeloma patients. Additionally, supportive care such as Denosumab (e.g., Prolia) should not be reported as planned therapy.</td>
</tr>
<tr>
<td>2/27/19</td>
<td>2402: Disease Classification</td>
<td>Add</td>
<td>Added (in red below) additional instruction for question 277: Question 277: Was a PET (or combination PET / CT) scan performed? (at last evaluation prior to the start of the preparative regimen / infusion) Report “Yes” and go to question 278 if a PET scan was performed within three months prior to the start of the preparative regimen / infusion. Combination PET / CT may also be reported, but a CT scan alone should not be captured here. Centers may report a PET scan performed during the most recent line of therapy so long as it is the most recent scan and was done within noted period. Report “No” and go to question 283 if a PET scan was not performed within this period.</td>
</tr>
<tr>
<td>2/27/19</td>
<td>Appendix J: Reporting Comorbidities</td>
<td>Remove</td>
<td>Removed (struck out below) incorrect instruction for reporting Cerebrovascular disease comorbidities: Any history of:  - Transient ischemic attack  - Cerebrovascular accident / stroke  - Subarachnoid hemorrhage: do not include subdural, epidural, or intraparenchymal hemorrhage</td>
</tr>
<tr>
<td>2/27/19</td>
<td>2402: Disease Classification</td>
<td>Add</td>
<td>Added (in red below) additional instruction for question 165: Indicate the number of times the recipient has been in the disease phase reported in question 163.</td>
</tr>
<tr>
<td>2/27/19</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Add</td>
<td>Added additional instruction (in red below) regarding T-Cell depletion under questions 73-95: T-Cell depletion: T-cell depletion removes some or all of the T cells in an effort to minimize GVHD. Methods of T-cell depletion include antibody affinity column, antibody-coated plates, antibody-coated plates and soybean lectin, antibody + toxin, immunomagnetic beads, CD34 affinity column plus sheep red blood cell resetting, and T-cell receptor alpha / beta depletion.</td>
</tr>
</tbody>
</table>
| 2/27/19    | 2400: Pre-TED             | Modify   | Modified (removed text is struck out below, updated text is in red) the instructions for question 52 on where to report cellular therapy product data for products that are not intended to achieve hematopoietic engraftment. If infusions of additional cells (not intended to produce engraftment) were given prior to the HCT being reported (i.e., prior to clinical day 0), the cells must be reported as a product on the Pre-TED Form (Form 2400, question 51) and on a separate Cellular Therapy Infusion Product Form (Form 4006 4003). If the additional cells were infused post-HCT, for any reason other
than a subsequent HCT, they should be reported as a DCI on the appropriate follow-up form. Reporting the additional cells (given pre-HCT and not intended to produce engraftment) on the Form 4006 4003 is the only mechanism the CIBMTR has in place to collect this data and ensure that the quality assurance data is reported to cord blood banks, if applicable.

<table>
<thead>
<tr>
<th>Date</th>
<th>Form / Manual</th>
<th>Action</th>
<th>Notes</th>
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<tbody>
<tr>
<td>2/27/19</td>
<td>2556: Myelofibrosis Pre-HCT Data and 2557: Myelofibrosis Post-HCT Data</td>
<td>Remove</td>
<td>Removed text referencing the CMS study for Myelofibrosis. The 2556 and 2557 are required for all patients with Myelofibrosis, not just patients enrolled in the CMS study. The titles of the forms have already been changed to remove CMS study from the title.</td>
</tr>
</tbody>
</table>
| 2/1/2019   | Cellular Therapy Manuals               | Modify  | Added clarification (in red below): What cellular therapies to report and when:  
   1. **Cellular therapy given in context of HCT (e.g. co-infusion, DLI/DCI):** When a cellular therapy is given in context of a transplant, such as a co-infusion with an HCT or a DLI/DCI post-HCT, these infusions need to be reported to the CIBMTR. This includes both autologous and allogeneic products, such as cell stored prior to an allogeneic HCT used for treatment of graft failure.  
   2. **Cellular therapy given with a prior HCT (e.g. CAR T-cell therapy for treatment of relapse):** When a cellular therapy (e.g. CAR T-cell therapy) is given and there is a prior HCT, reporting these infusions are voluntary at this time.  
   3. **Stand-alone cellular therapy (no prior HCT) (e.g. CAR T-cells):** reporting these infusions are voluntary at this time*.  
*Reporting of commercial products infusions (i.e. Kymriah, Yescarta) is strongly encouraged. |
| 1/24/2019  | 4100: Cellular Therapy Essential Data Follow-up | Modify  | Added examples (in red below) in question 33 on when to use “previously reported” option:  
If a new malignancy is reported, please complete the Subsequent Neoplasms Form 3500 to answer questions specific to the new malignancy. The option of ‘Previously reported’ should only be used if the same new...|
A malignancy instance has already been reported on a F3500. See examples below. If there is a question regarding use of this option, please contact your CIBMTR CRC.

Example 1. Recipient develops a new malignancy at day +68. It is reported at the time the 100-day form 4100 is completed. Question 33 should be answered as ‘yes’ and the form 3500 should be completed to report all new malignancy information.

Example 2. Recipient develops a new malignancy at day +68 and had received a commercial CAR-T product. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The form 3500 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. No other new malignancy develops during the 100-day reporting period. When the 100-day form 4100 is completed, question 33 should be answered as ‘previously reported’.

Example 3. Recipient develops a new malignancy at day +68 and had received a commercial CAR-T product. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The form 3500 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. Another new malignancy develops at day +100. It is decided to report the 2nd new malignancy on the 100-day form 4100 since it is due. Question 33 should be answered as ‘yes’ to create another form 3500.

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<tr>
<td>1/17/2019</td>
<td>Modify</td>
<td>Added (in red below) clarification on how hypogammaglobulinemia is documented: Report the date (YYYY-MM-DD) in question 126 when the hypogammaglobulinemia was documented by either a physician/health care provider or determined by lab results. If the hypogammaglobulinemia continues from a prior reporting period, report the original diagnosis date as the onset date and override the error. Example 1. The recipient developed hypogammaglobulinemia at day +22 which was reported on the 4100 day 100 form. The lab results continue to show IgG levels &lt; 600 mg/dl during the 6 month reporting period. Report the original diagnosis date on the 4100 6 month form and override the error.</td>
</tr>
<tr>
<td>1/17/2019</td>
<td>Remove</td>
<td>Removed the following blue note box instruction (struck out below) for questions 250 to 252 functional status. Functional status should be reported for every indication. These questions are for malignant disease indications or relapsed, persistent, or progressive disease only.</td>
</tr>
</tbody>
</table>
Manual Reference Diagram

Questions 41-42: Indication for cellular therapy

- From the list provided, specify the disease classification for which the patient will be receiving cellular therapy. Examples include:
  - Autoimmune disease: Crohn’s disease, ulcerative colitis, diabetes mellitus type I, rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis
  - Cardiovascular and peripheral vascular disease: acute myocardial infarction, chronic coronary artery disease (ischemic, cardiomyopathy), heart failure (non-ischemic etiology), limb ischemia, thromboangiitis obliterans
  - Musculoskeletal disease: avascular necrosis of femoral head, osteoarthritis, osteonecrosis, impotence, traumatic joint injury
  - Neurologic disease: acute cerebral vascular ischemia, amyotrophic lateral sclerosis, Parkinson’s disease, spinal cord injury, cerebral palsy, congenital hydrocephalus, multiple sclerosis, myasthenia gravis

Report any other indication for cellular therapy for regenerative medicine under “other disease” and specify in question 42.

Question 43: Is this the first application of cellular therapy for this indication?

Indicate “yes” if the planned therapy will be the first cellular therapy for regenerative medicine for this recipient. If the recipient has previously received cellular therapy (for regenerative medicine) for the same indication, indicate “no”.

Feedback

Post your comment on this topic.

Was this helpful?

Provide questions, comments, concerns about the manual to CIBMTR. Submitted questions, comments, concerns will not be published.

Click to enlarge
Providing Feedback

For each manual section, an opportunity to provide feedback is offered at the bottom of the page. Select “Was this helpful?” with “yes” and “no” options; note that identifying information is not attached to your vote. To add a specific comment, it will be necessary to include your name and email address in order to respond to your question or concern. Comments made by centers will never be posted to the manual, but will be delivered directly to the manual team.

⚠️ The comments feature states “Please do not use this for support questions. For customer support, please contact us here.” If you have a question, comment, or concern about a manual section itself, please use the comment box. If you have a question about using the manual website or a problem with the manual website, please use the “contact us here” link, so that we may answer your questions more quickly.
Historical Manual Updates

January 2019
February 2019
March 2019

Updates made during the current calendar year are included below. For updates prior to 2019, click on the subtopic corresponding to the year of interest. If you need to reference an archived manual section for a retired form, please refer to the Retired Forms Manuals webpage.

March 2019

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<td>3/19/19</td>
<td>2450: Post-TED</td>
<td>Add</td>
<td>Added the following red warning box instruction (in red below) below question 75 to clarify when to use the CCR option in the Disease Assessment at the Time of Best Response to HCT section of the Post-TED (2450) form: Continued Complete Remission (CCR) should be reported for all patients who were already in CR at the start of the preparative regimen.</td>
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February 2019

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<td>2116: PCD Post-HCT</td>
<td>Add</td>
<td>Added (in red below) additional instruction for question 61: However, bisphosphonate therapy (e.g., Zometa) should not be reported as planned therapy since it is universally administered to myeloma patients. Additionally, supportive care such as Denosumab (e.g., Prolia) should not be reported as planned therapy.</td>
</tr>
<tr>
<td>2/27/19</td>
<td>2402: Disease</td>
<td>Add</td>
<td>Added (in red below) additional instruction for question 277: Question 277: Was a PET (or combination PET / CT) scan performed?</td>
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<td>Section/Change</td>
<td>Action</td>
<td>Description</td>
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<tr>
<td>2/27/19</td>
<td>Classification</td>
<td></td>
<td><em>(at last evaluation prior to the start of the preparative regimen / infusion)</em>&lt;br&gt;Report “Yes” and go to question 278 if a PET scan was performed within three months prior to the start of the preparative regimen / infusion.&lt;br&gt;Combination PET / CT may also be reported, but a CT scan alone should not be captured here. Centers may report a PET scan performed during the most recent line of therapy so long as it is the most recent scan and was done within noted period. Report “No” and go to question 283 if a PET scan was not performed within this period.</td>
</tr>
<tr>
<td>2/27/19</td>
<td>Appendix J: Reporting Comorbidities</td>
<td>Remove</td>
<td>Removed (struck out below) incorrect instruction for reporting Cerebrovascular disease comorbidities:&lt;br&gt;&lt;br&gt;Any history of:&lt;br&gt;• Transient ischemic attack&lt;br&gt;• Cerebrovascular accident / stroke&lt;br&gt;• Subarachnoid, hemorrhage: do not include subdural, epidural, or intraparenchymal hemorrhage</td>
</tr>
<tr>
<td>2/27/19</td>
<td>2402: Disease Classification</td>
<td>Add</td>
<td>Added (in red below) additional instruction for question 165:&lt;br&gt;&lt;br&gt;<em>Indicate the number of times the recipient has been in the disease phase reported in question 163.</em></td>
</tr>
<tr>
<td>2/27/19</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Add</td>
<td>Added additional instruction (in red below) regarding T-Cell depletion under questions 73-95:&lt;br&gt;&lt;br&gt;<em>T-Cell depletion:</em> T-cell depletion removes some or all of the T cells in an effort to minimize GVHD. Methods of T-cell depletion include antibody affinity column, antibody-coated plates, antibody-coated plates and soybean lectin, antibody + toxin, immunomagnetic beads, CD34 affinity column plus sheep red blood cell resetting, and T-cell receptor alpha / beta depletion.</td>
</tr>
<tr>
<td>2/27/19</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Modified (removed text is struck out below, updated text is in red) the instructions for question 52 on where to report cellular therapy product data for products that are not intended to achieve hematopoietic engrainment. If infusions of additional cells (not intended to produce engraftment) were given prior to the HCT being reported (i.e., prior to clinical day 0), the cells must be reported as a product on the Pre-TED Form (Form 2400, question 51) and on a separate Cellular Therapy Infusion Product Form (Form 4006 4003). If the additional cells were infused post-HCT, for any reason other than a subsequent HCT, they should be reported as a DCI on the appropriate follow-up form. Reporting the additional cells (given pre-HCT and not intended to produce engraftment) on the Form 4006 4003 is the only mechanism the CIBMTR has in place to collect this data and ensure that the quality assurance data is reported to cord blood banks, if applicable.</td>
</tr>
<tr>
<td>2/27/19</td>
<td>2556: Myelofibrosis Pre-HCT Data and 2557: Myelofibrosis Post-HCT</td>
<td>Remove</td>
<td>Removed text referencing the CMS study for Myelofibrosis. The 2556 and 2557 are required for all patients with Myelofibrosis, not just patients enrolled in the CMS study. The titles of the forms have already been changed to remove CMS study from the title.</td>
</tr>
</tbody>
</table>
Added clarification (in red below):

What cellular therapies to report and when:

1. **Cellular therapy given in context of HCT (e.g. co-infusion, DLI/DCI):**
   When a cellular therapy is given in context of a transplant, such as a co-infusion with an HCT or a DLI/DCI post-HCT, these infusions need to be reported to the CIBMTR. This includes both autologous and allogeneic products, such as cell stored prior to an allogeneic HCT used for treatment of graft failure.

2. **Cellular therapy given with a prior HCT (e.g. CAR T-cell therapy for treatment of relapse):** When a cellular therapy (e.g. CAR T-cell therapy) is given and there is a prior HCT, reporting these infusions are voluntary at this time.

3. **Stand-alone cellular therapy (no prior HCT) (e.g. CAR T-cells):**
   reporting these infusions are voluntary at this time*.

   *Reporting of commercial products infusions (i.e. Kymriah, Yescarta) is strongly encouraged.

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### January 2019

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1/24/2019</td>
<td>4100: Cellular Therapy Essential Data Follow-</td>
<td>Modify</td>
<td>Added examples (in red below) in question 33 on when to use “previously reported” option: If a new malignancy is reported, please complete the Subsequent Neoplasms Form 3500 to answer questions specific to the new malignancy. The option of ‘Previously reported’ should only be used if the same new malignancy instance has already been reported on a F3500. See examples below. If there is a question</td>
</tr>
</tbody>
</table>
Example 1. Recipient develops a new malignancy at day +68. It is reported at the time the 100-day form 4100 is completed. Question 33 should be answered as 'yes' and the form 3500 should be completed to report all new malignancy information.

Example 2. Recipient develops a new malignancy at day +68 and had received a commercial CAR-T product. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The form 3500 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. No other new malignancy develops during the 100-day reporting period. When the 100-day form 4100 is completed, question 33 should be answered as 'previously reported'.

Example 3. Recipient develops a new malignancy at day +68 and had received a commercial CAR-T product. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The form 3500 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. Another new malignancy develops at day +100. It is decided to report the 2nd new malignancy on the 100-day form 4100 since it is due. Question 33 should be answered as 'yes' to create another form 3500.

1/17/2019

4100: Cellular Therapy Essential Data Follow-Up Modify

Added (in red below) clarification on how hypogammaglobulinemia is documented:
Report the date (YYYY-MM-DD) in question 126 when the hypogammaglobulinemia was documented by either a physician/health care provider or determined by lab results. If the hypogammaglobulinemia continues from a prior reporting period, report the original diagnosis date as the onset date and override the error.

Example 1. The recipient developed hypogammaglobulinemia at day +22 which was reported on the 4100 day 100 form. The lab results continue to show IgG levels < 600 mg/dl during the 6 month reporting period. Report the original diagnosis date on the 4100 6 month form and override the error.

1/17/2019

4000: Cellular Therapy Essential Data Pre-Infusion Remove

Removed the following blue note box instruction (struck out below) for questions 250 to 252 functional status. Functional status should be reported for every indication.
These questions are for malignant disease indications or relapsed, persistent, or progressive disease only.
# 2018 Manual Updates

**December 2018**

**November 2018**

**October 2018**

**September 2018**

**August 2018**

**July 2018**

**June 2018**

**May 2018**

**April 2018**

**March 2018**

**February 2018**

**January 2018**

Updates made during the current calendar year are included below. For updates prior to 2018, click on the subtopic corresponding to the year of interest. If you need to reference an archived manual section for a retired form, please refer to the [Retired Forms Manuals](#) webpage.

---

**Hyperlinks**

Please note, hyperlinks on this page will not work for any manual sections which have been retired and / or replaced by new versions.

---

## December 2018

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<tr>
<td>12/21/2018</td>
<td>2116: PCD Post-HCT</td>
<td>Remove</td>
<td>Removed the following blue note box instruction (struck out below) for questions 30 and 126 regarding Flow Cytometry reporting for Myeloma. These assessments can now be reported in the same way as all other disease assessments. <strong>An exception of the note above applies to multiple myeloma</strong> if the flow cytometry assessment has &lt; 5% malignant plasma cells, this result should not be reported because the result is not reliable; if no other cytogenetic or FISH assessments were performed, report “no.” However, if the flow cytometry assessment found ≥ 5% malignant plasma cells, this should be reported as evidence of disease.</td>
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<tr>
<td>12/21/2018</td>
<td>2450: Post-TED</td>
<td>Remove</td>
<td>Removed the following blue note box instruction (struck out below) above question 82 regarding Flow Cytometry reporting for Lymphoma and Myeloma. These assessments can now be reported in the same way as all other disease assessments. <strong>Myeloma and Lymphoma</strong> Flow cytometry assessments performed to detect myeloma or lymphoma should not be reported if negative (&lt; 5% malignant cells detected). If flow cytometry was performed to detect myeloma or lymphoma and showed less than 5% malignant cells, report “not applicable” for question 82 and go to question 85.</td>
</tr>
<tr>
<td>12/13/2018</td>
<td>Toxicities</td>
<td>Modify</td>
<td>Added clarification on how hypogammaglobulinemia is documented: <strong>Report the date (YYYY-MM-DD) in question 126 when the hypogammaglobulinemia was documented by either a physician/health care provider or determined by lab results.</strong></td>
</tr>
<tr>
<td>12/3/2018</td>
<td>Multiple Myeloma Response Criteria</td>
<td>Modify</td>
<td>Separated the blue note box regarding urine studies to better reflect requirements needed for sCR and CR versus requirements needed for nCR, VGPR, and PR.</td>
</tr>
<tr>
<td>12/3/2018</td>
<td>Amyloidosis Response Criteria</td>
<td>Add</td>
<td>Added further clarification for the Renal Response criteria (indicated in red below): • ≥ 50% decrease of at least 0.5 g/day (500mg/24hr) in 24-hour urine protein of &gt; 0.5 g/day (500mg/24hr) pre-treatment and • Creatinine clearance must not have worsened by ≥ 25% over baseline</td>
</tr>
<tr>
<td>12/3/2018</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Updated link in the 2400 Pre-TED to reflect current reporting instructions for autologous transplants.</td>
</tr>
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</table>

**November 2018**

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<tr>
<td>11/20/2018</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added the following text (in red below) for Question 5: Enter the ZIP code in which the recipient resides. Only five digits are required; however, if the ZIP+4 (nine digit) code is available, please report it in this field.</td>
</tr>
<tr>
<td>11/20/2018</td>
<td>Multiple Myeloma Response Criteria</td>
<td>Add</td>
<td>Added the following (in red) to the Near Complete Remission (nCR) response criteria: &lt; 5% plasma cells in bone marrow (confirmation with repeat bone marrow biopsy not needed).</td>
</tr>
<tr>
<td>11/20/2018</td>
<td>LYM Response Criteria</td>
<td>Modify</td>
<td>Modified the response criteria to show the metabolic response criteria first and then the radiographic response criteria for ease of use.</td>
</tr>
<tr>
<td>11/20/2018</td>
<td>4100:</td>
<td>Modify</td>
<td>Added further clarification for various portions of this manual to provide better</td>
</tr>
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</table>
October 2018

<table>
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</thead>
<tbody>
<tr>
<td>10/18/18</td>
<td>2018: LYM Pre-Infusion</td>
<td>Modify</td>
<td>For questions 231-232, a typographical error in the form was identified. These questions are intended to capture any extranodal involvement of a recipient’s Lymphoma. This section of the manual has been updated to reflect these changes.</td>
</tr>
<tr>
<td>10/18/18</td>
<td>2100: Post-HCT Follow-Up Data</td>
<td>Add</td>
<td>Added the following reporting instruction for Questions 486-487: Please indicate “no” if the patient received endotracheal intubation or mechanical ventilation during surgery.</td>
</tr>
<tr>
<td>10/17/18</td>
<td>2011: ALL Pre-Infusion Data</td>
<td>Modify</td>
<td>Modified (red text was added, struck out text was deleted) the instructional text for questions 37-38: Treatments vary based on protocol. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. If chemotherapy drugs were administered as part of the line of therapy, select the box for ‘chemotherapy’. You do not need to specify each drug. Select all chemotherapy drugs administered as part of the line of therapy being reported. If the recipient received a systemic therapy which is not listed, select “Other systemic therapy” and specify the treatment in question 38. Report the generic name of the agent, not the name brand.</td>
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<tr>
<td>9/20/2018</td>
<td>2018: LYM Pre-Infusion</td>
<td>Add</td>
<td>Added the following instruction for reporting pre-HCT lines of therapy: If this is a subsequent infusion and the 2018 was completed for the previous infusion, lines of therapy do not need to be reported in duplication on the subsequent 2018. Please report from post previous infusion to time of preparative regimen (or infusion) for the current HCT or cellular therapy. If no 2018 was completed previously, all lines of therapy from original diagnosis to current preparative regimen (or infusion) will have to be completed.</td>
</tr>
<tr>
<td>9/20/2018</td>
<td>2118: LYM Post-Infusion Data</td>
<td>Modify</td>
<td>Changed the instruction for for reporting questions 88 and 89 by removing (strike through) and adding (red) text as indicated below. The center does not need to repeat all disease-specific assessments (biopsies, i.e., CT (radiographic) or PET scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression. If a disease-specific assessment did not occur during this time period, please report the date of any disease related assessment (e.g. clinical assessments, labs, etc.) as the date assessed (Q88 or Q90) regardless of what the parent question states about the specific CT (radiographic) or PET criteria.</td>
</tr>
<tr>
<td>9/20/2018</td>
<td>2000: Recipient Baseline</td>
<td>Modify</td>
<td>Removed If the specific organism is not listed, use the “other, specify” code 209 – candida, 219 – aspergillus, or 259 – fungus and report the name of the organism in the space provided for question 59. Modified language to complete a Fungal Infection Form for all organisms. Removed the list of fungal organisms.</td>
</tr>
<tr>
<td>9/20/2018</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added in text that mid-level health care providers (NPs and PAs) can also assign performance scores.</td>
</tr>
<tr>
<td>09/20/2018</td>
<td>2004: Infectious Disease Markers</td>
<td>Add</td>
<td>Added the following text to Q10-46: Infectious Disease Markers section: If testing is only performed on the harvested product and not on the peripheral blood sample, report those samples accordingly.</td>
</tr>
</tbody>
</table>

**August 2018**

<table>
<thead>
<tr>
<th>Date</th>
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<tbody>
<tr>
<td>8/10/2018</td>
<td>2450: Post-TED</td>
<td>Modify</td>
<td>Modified (added text in red and deleted text is struck-out) the instructions for reporting the “date assessed” for questions 80, 83, 87, 90, 96, and 96: If the best response is “not in complete remission,” report the date of the most recent testing performed during the reporting period and prior to relapse or progression treatment for relapsed, progressive, or persistent disease, if applicable. If no treatment for relapsed, progressive, or persistent disease was given, report the date of the most recent disease-specific testing performed within approximately 30 days of the follow-up date.</td>
</tr>
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<tr>
<td>8/10/18</td>
<td>2014: MDS/MPN Pre-HCT</td>
<td>Added</td>
<td>Added an instructional blue box for question 123: <em>Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. The CIBMTR forms capture disease subtype using the WHO classification of myeloid neoplasms and acute leukemia. Secondary myelofibrosis is not included as a separate category per the WHO classification. Therefore, when reporting the disease subtype at the time of transplant for recipients with secondary myelofibrosis, report “Primary Myelofibrosis (PMF)” to accurately capture these cases on the CIBMTR Forms.</em></td>
</tr>
<tr>
<td>8/10/18</td>
<td>2402: Disease Classification</td>
<td>Modify</td>
<td>Modified (red text was added, struck out text was deleted) the instructional blue box for question 212: <em>Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. The CIBMTR forms capture disease subtype using the WHO classification of myeloid neoplasms and acute leukemia. Secondary myelofibrosis is not included as a separate category per the WHO classification. Therefore, when reporting the disease subtype at the time of transplant for recipients with secondary myelofibrosis, report “Primary Myelofibrosis (PMF)” to accurately capture these cases on the CIBMTR Forms.</em> Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. However, effective immediately, cases of post-essential thrombocythemia myelofibrosis (post-ET MF) or post-polycythemia vera myelofibrosis (post-PV MF) will now be reported as “Primary Myelofibrosis (PMF)” at the time of HCT. In order to capture accurate data, the secondary MF cases need to be lumped in with the PMF cases, since treatment for post-ET MF and post-PV MF is the same as PMF.*</td>
</tr>
<tr>
<td>8/10/18</td>
<td>2010: AML Pre-Infusion</td>
<td>Add</td>
<td>Added the following instruction for questions 72 – 74: <em>If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be reported on the form.</em></td>
</tr>
<tr>
<td>8/10/18</td>
<td>2450: Post-TED</td>
<td>Remove</td>
<td>Removed the following instruction from questions 157 and 231: <em>Reporting the administration of a cellular therapy / donor cellular infusion in question 231 will generate additional cellular therapy forms which are used to capture important details regarding the infusion(s).</em></td>
</tr>
<tr>
<td>8/10/18</td>
<td>2018: LYM Pre-Infusion</td>
<td>Add</td>
<td>Added instruction for question 217: <em>If the recipient had palpable disease on a physical exam, those results can be reported in the CT (radiographic) criteria.</em></td>
</tr>
<tr>
<td>8/9/18</td>
<td>2402: Disease Classification</td>
<td>Add</td>
<td>Added instruction for question 281-282: <em>If the PET scan result is only documented as an ‘X’, report this as “Unknown” for question 281.</em></td>
</tr>
</tbody>
</table>

July 2018
<table>
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<tr>
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<tbody>
<tr>
<td>7/25/18</td>
<td>2100: Post-HCT Follow-Up Data</td>
<td>Modify</td>
<td>Version 4 of the 2100: Post-HCT Follow-Up Data Form (Form 2100) (formerly 100 Day Post-HSCT Data Form) section of the Forms Instructions Manual released. Version 4 corresponds to revision 5 of the Form 2100.</td>
</tr>
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**June 2018**

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</table>
| 6/25/18    | 2150: Viral Infections                             | Modify              | Added (in red below) and removed (struck out below) text from the instructions for reporting infection status at the time of evaluation for this reporting period (question 77): If the status of the infection is not documented in the HCT / cellular therapy physician’s note summarizing their last evaluation performed during the reporting period, obtain documentation from the provider indicating which option to report. For reporting purposes, centers should indicate “Ongoing” if the infection is still present, but cannot be considered improved or resolved.  
  - Ongoing: Infection is still present, but cannot be considered improved or resolved  
  - Improved: Still on treatment, but responding to treatment and no longer showing signs / symptoms of infection  
  - Resolved: Treatment completed  
  - Unknown                                                                                                                                                                                                 |
| 6/25/18    | 2150: Viral Infections                             | Modify              | Added (in red below) further instruction on reporting therapy (question 51): Report “Yes” if the recipient received any antiviral medication between seven days prior to the date of diagnosis (refer to question two) and the date of contact for the reporting period (refer to the date of contact reported on the corresponding Post-HCT Follow-Up Data Form). Report all therapy received regardless of the infection being treated. |
| 6/22/18    | 4100 Cellular Therapy Essential Data Follow-Up     | Modify              | Added (in red below) further instruction on reporting symptoms in a reporting period: If “yes” is reported for a symptom, report the date of diagnosis (YYYY-MM-DD) of each symptom and indicate if the symptom was explained entirely by non-CRS causes (e.g. infection, therapy). If a symptom occurs multiple times within the same reporting period (e.g. fever), report the first occurrence.                      |
| 6/1/18     | 2400: Pre-TED                                       | Modify              | Re-formatted the reporting instructions for pre-HCT CMV-antibody results (question 94) and included the following additional consideration (in red below):                                                                                                                                                                               |
**Documented history of “reactive” CMV:** In cases where a recipient has a documented history of a “reactive” CMV test and does not have a history of IVIG or blood transfusions from a CMV positive donor, “reactive” should be reported for the CMV status even if the CMV test is repeated during the pre-HCT work-up phase and is “non-reactive”.

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<tbody>
<tr>
<td>6/1/18</td>
<td>AML Response</td>
<td>Add</td>
<td>Added (in red below) further instruction on reporting the CRi response criteria: <strong>Transfusion independent</strong> <em>(Please note, if the physician documents transfusion dependence related to treatment and not the patient’s underlying AML, CRi can be reported)</em></td>
</tr>
<tr>
<td>6/1/18</td>
<td>ALL Response</td>
<td>Add</td>
<td>Added (in red below) further instruction on reporting the CRi response criteria: <strong>Transfusion independent</strong> <em>(Please note, if the physician documents transfusion dependence related to treatment and not the patient’s underlying ALL, CRi can be reported)</em></td>
</tr>
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**May 2018**

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| 5/21/18  | 2400: Pre-TED  | Modify | Added (in red below) and removed (struck out below) text from the instructions for reporting comorbidities (questions 98-134).  
**Arrhythmia:** Any history of any type of arrhythmia that has necessitated the delivery of a specific antiarrhythmic agent. Examples include, but are not limited to, atrial fibrillation or flutter, sick sinus syndrome, or and ventricular arrhythmias requiring treatment.  
**Cardiac:** Any history of coronary artery disease (one or more vessel coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, and/or ejection fraction ≤ 50% (shortening fraction < 26 for pediatric recipients)% on the most recent test.  
**Cerebrovascular disease:** Any history of transient ischemic attack, subarachnoid hemorrhage, and/or cerebrovascular accident cerebral thrombosis embolism, or hemorrhage.  
**Diabetes:** Diabetes or steroid-induced hyperglycemia requiring continuous treatment with insulin or oral hypoglycemics in the last 4 weeks, but not diet alone  
**Heart valve disease:** Moderate or severe valve stenosis or insufficiency (mitral, aortic, tricuspid, or pulmonary) as determined by echocardiogram, prosthetic mitral or aortic valve, and/or symptomatic mitral valve prolapse. Except asymptomatic mitral prolapse.  
**Psychiatric disturbance:** The presence of any mood, anxiety, or other psychiatric disorder requiring continuous treatment during the last four weeks. Examples include, but are not limited to, depression, anxiety, bipolar disorder, or and schizophrenia requiring psychiatric treatment in the last 4 weeks.  
**Pulmonary (moderate):** Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 66-80% or dyspnea on slight activity at transplant. Use the Dinakara equation below to determine the DLCOc if only an uncorrected value is provided. For recipients assessed by a
postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity. Dinakara Equation: \( DLCOc = \frac{\text{uncorrected DLCO}}{0.06965 \times \text{hemoglobin/dL}} \)

**Pulmonary (severe):** Corrected diffusion capacity of carbon monoxide (e.g., \( DLCOc, DLCOcorr, DLCO \)) and/or FEV1 \( \leq 65\% \) or dyspnea at rest or requiring oxygen at transplant. Use the Dinakara equation above to determine the \( DLCOc \) if only an uncorrected value is provided. or recipients assessed by a postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity.

**Renal (moderate/severe):** Serum creatinine > 2 mg/dL or > 176.8 \( \mu \text{mol/L}, \) or on dialysis at transplant, or prior renal transplantation. See note in question 97.

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<tbody>
<tr>
<td>5/10/18</td>
<td>2100: Post-HCT</td>
<td>Add</td>
<td>Added <strong>Fecal Microbiota Transplant</strong> note box to acute (questions 185-233) and chronic (questions 328-399) GVHD treatment instructions.</td>
</tr>
<tr>
<td>5/10/18</td>
<td>LYM Response</td>
<td>Add</td>
<td>Added “Relapsed Disease” to “Progressive Disease” criteria and included clarification on when to report these disease status.</td>
</tr>
<tr>
<td>5/7/18</td>
<td>2553: VOD/SOS</td>
<td>Add</td>
<td>Added an example on how to report the <strong>planned total daily dose</strong> for Defibrotide</td>
</tr>
<tr>
<td>5/7/18</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Modified language on how to report Drugs After Transplant, replaced &quot;day 0&quot; with “transplant” to clarify how to report drugs planned for day 0</td>
</tr>
<tr>
<td>5/7/18</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added note box to capture all comorbidities including those that are considered complications of the primary disease for transplant and provided examples</td>
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**April 2018**
### April 2018

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<tr>
<td>4/30/18</td>
<td>2450: Post-TED</td>
<td>Add</td>
<td>Added the following instruction for question 34. <em>Please note, questions 35 and 36 must still be answered if question 34 is reported as “unknown.”</em></td>
</tr>
<tr>
<td>4/30/18</td>
<td>2450: Post-TED</td>
<td>Modify</td>
<td>Updated language on how to report the “Date of most recent disease assessment” for questions 237-238: current disease status.</td>
</tr>
<tr>
<td>4/20/18</td>
<td>Appendix M: Critical Data Fields</td>
<td>Modify</td>
<td>New version of Appendix M: Critical Data Fields of the Forms Instructions Manual released. Note, prior versions of this appendix were referred to as Appendix Y: Critical Data Fields.</td>
</tr>
<tr>
<td>4/20/18</td>
<td>4003: Cellular Therapy Product</td>
<td>Add</td>
<td>Added <em>Cryopreservation as a Manipulation</em> note box to the instructions for questions 31-32.</td>
</tr>
<tr>
<td>4/16/18</td>
<td>2000: Recipient Baseline</td>
<td>Add</td>
<td>Added Fungal Infection Diagnosis Reporting Scenario to the instructions for question 57.</td>
</tr>
<tr>
<td>4/10/18</td>
<td>2402: Disease Classification</td>
<td>Modify</td>
<td>Updated the Common Disease Transformation Table included in the instructions for questions 1 and 2. The CLL section of the form should not be completed for a Richter’s Transformation as of Revision 3 of the Form 2402.</td>
</tr>
<tr>
<td>4/10/18</td>
<td>4006: Cellular Therapy Infusion</td>
<td>Add</td>
<td>Added in additional clarification regarding total cell counts administered, what constitutes unselected lymphocytes, and T-helper cells (Q17-24).</td>
</tr>
<tr>
<td>4/9/18</td>
<td>2402: Disease Classification</td>
<td>Modify</td>
<td>Modified the following instruction for question 317: Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. A PET scan <em>Date of radiographic study (PET, MRI, CT) may be used if the same previous PET scan radiographic study had previously been obtained and only in limited circumstances (e.g., plasmacytomas, lytic lesions).</em></td>
</tr>
</tbody>
</table>

### March 2018

<table>
<thead>
<tr>
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<th>Description</th>
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<tbody>
<tr>
<td>4/23/18</td>
<td>2018: LYM Pre-Infusion Data</td>
<td>Modify</td>
<td>Corrected errors in the instruction manual by adding (in red below) and removing (struck out below) text to the instructions for questions 269-272, 273-276, and 277-280.</td>
</tr>
<tr>
<td>Date</td>
<td>Code</td>
<td>Action</td>
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</tr>
<tr>
<td>4/20/18</td>
<td>4003: Cellular Therapy Product</td>
<td>Add</td>
<td>Added Cryopreservation as a Manipulation note box to the instructions for questions 31-32.</td>
</tr>
<tr>
<td>3/27/18</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added HHV-6 to Definitions for Same Infection Table included in the instructions for questions 428-436.</td>
</tr>
<tr>
<td>3/22/18</td>
<td>2402: Disease Classification</td>
<td>Add</td>
<td>Added MDS/MPN note box below the instructions for question 256 regarding recipients who only received supportive care prior to transplant.</td>
</tr>
<tr>
<td>3/19/18</td>
<td>Multiple Myeloma Response Criteria</td>
<td>Add</td>
<td>Added in Progressive Disease (PD) response criteria (red) with regards to plasmacytomas: <em>Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas (≥ 50% increase from nadir in size of &gt;1 lesion, or a ≥ 50% increase in the longest diameter of a previous lesion &gt;1 cm in short axis).</em></td>
</tr>
<tr>
<td>3/19/18</td>
<td>2556: Myelofibrosis CMS Study Pre-HCT Data</td>
<td>Add</td>
<td>Added in instruction (red) on how to report previous JAK1 and JAK2 inhibitor therapy as indicated below: <em>Indicate “yes” if the recipient received JAK1 or JAK2 therapy prior to the current HCT (not including therapy given for past HCTs that have previously been reported) and continue with question 19. If “no,” continue with question 34.</em> This modification was also made to the blue note box above Q18.</td>
</tr>
<tr>
<td>3/19/18</td>
<td>4000: Cellular Therapy Essential Data Pre-Infusion</td>
<td>Add</td>
<td>Added in clarification regarding what constitutes a course of cellular therapy.</td>
</tr>
<tr>
<td>3/19/18</td>
<td>4000: Cellular Therapy Essential Data Pre-Infusion</td>
<td>Remove</td>
<td>Removed the following example regarding how to specify the total number of products for Q29: <em>Example 4. A recipient receives a post-HCT donor cellular infusion. Based on the disease status after the infusion, a second donor cellular infusion is planned to be given if the recipient does not respond. This is considered two different courses of cellular therapy and each product should be reported separately.</em></td>
</tr>
<tr>
<td>3/19/18</td>
<td>2116: PCD Post-HCT</td>
<td>Add</td>
<td>Added Current Disease Status note box above the instructions for Q137.</td>
</tr>
<tr>
<td>3/19/18</td>
<td>2118: LYM Post-Infusion</td>
<td>Modify</td>
<td>Change the instruction for question 89 by removing (strike through) and adding (red) text as indicated below.</td>
</tr>
</tbody>
</table>
The current disease status should reflect the most recent disease evaluations performed during the reporting period. Report “Not assessed” and submit the form if the recipient’s primary disease is a non-PET avid lymphoma or a PET scan was not performed during the reporting period since the infusion.

Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119). The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

Added the following instruction for question 235. The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

Added GVHD note box at the beginning of the GVHD section.

Added Product Identification note box above question 1.

Updated language on what to capture as a molecular assessment for questions 75-97.

Updated information regarding what cellular therapies to report and when.

Removed the following bullet from the CRi criteria.
   • No blasts with Auer rods

Added Infusion Without a Preparative Regimen note box at the beginning of Q6-14: Clinical Status of Recipient Prior to the Preparative Regimen (Conditioning), Q15-38: Organ Function Prior to the Preparative Regimen (Conditioning), and Q39-54: Hematologic Findings Prior to the Preparative Regimen (Conditioning).
<table>
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<tbody>
<tr>
<td>2/28/18</td>
<td>2402: Disease</td>
<td>Add</td>
<td>Added the following instruction for question 283.</td>
</tr>
<tr>
<td></td>
<td>Classification</td>
<td></td>
<td><em>When a transformation has occurred (e.g., follicular lymphoma (FL) transformed to DLBCL), count the response number (CR1, REL2, etc.) beginning with the transformed lymphoma (in this case the DLBCL). Do not include the responses to the lymphoma sub-type prior to the transformation.</em></td>
</tr>
<tr>
<td>2/27/18</td>
<td>2402: Disease</td>
<td>Add</td>
<td>Added instruction for questions 281-282.</td>
</tr>
<tr>
<td></td>
<td>Classification</td>
<td></td>
<td><em>If multiple scores are documented, report the highest.</em></td>
</tr>
<tr>
<td>2/22/18</td>
<td>2110: AML Post-Infusion Data</td>
<td>Modify</td>
<td>Added (in red) and removed (struck out) text from instructions for questions 51-52.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If any testing for molecular markers occurred detected the recipient's primary disease during the reporting period, report “Yes” for question 51 and report the date the sample was collected in question 52.</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If molecular marker testing did not detect disease at any time during the reporting period, report “No” for question 51 and go to question 63.</em></td>
</tr>
<tr>
<td></td>
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<td></td>
<td><em>If molecular marker testing was not performed during the reporting period, report “No Unknown” go to question 63.</em></td>
</tr>
<tr>
<td>2/22/18</td>
<td>2110: AML Post-Infusion Data</td>
<td>Modify</td>
<td>Added (in red) and removed (struck out) text from the beginning of section Q51-103: Disease Detection Since Date of Last Report.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If testing by a particular method for molecular or cytogenetic markers / abnormalities was not done during the reporting period or it is not known whether testing was performed, report “Unknown” for that method those methods (question 51 and 70). If testing by flow cytometry, clinical / hematologic assessment, or other assessment was not done during the reporting period or it is not known whether testing was performed, report “No” for those methods (questions 63, 80, and 87).</em></td>
</tr>
<tr>
<td>2/22/18</td>
<td>2110: AML Post-Infusion Data</td>
<td>Add</td>
<td>Added text (in red) to the Questions 51-103 warning box.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>For questions 51, 63, 70, 80, and 87, report “No” or “Unknown” (see instructions below) if the recipient did not relapse, have persistent or minimal residual disease even if testing was performed.</em></td>
</tr>
<tr>
<td>2/22/18</td>
<td>2111: ALL Post-Infusion Data</td>
<td>Modify</td>
<td>Added (in red) and removed (struck out) text from instructions for questions 48-49.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If any testing for molecular markers occurred detected the recipient’s primary disease during the reporting period, report “Yes” for question 48 and report the date the sample was collected in question 49.</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If molecular marker testing did not detect disease at any time during the reporting period, report “No” for question 48 and go to question 49.</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If molecular marker testing was not performed during the reporting period, report “No Unknown” go to question 53.</em></td>
</tr>
<tr>
<td>2/22/18</td>
<td>2111: ALL Post-Infusion Data</td>
<td>Modify</td>
<td>Added (in red) and removed (struck out) text from the beginning of section Q48-94: Disease Detection Since Date of Last Report.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If testing by a particular method for molecular or cytogenetic markers / abnormalities was not done during the reporting period or it is not known whether testing was performed, report “Unknown” for that method those methods (question 48 and 61). If testing by flow cytometry, clinical / hematologic assessment, or other assessment was not done during the reporting period or it is not known whether testing was performed, report “No Unknown” go to question 63.</em></td>
</tr>
</tbody>
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<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>2/15/18</td>
<td>4000: Cellular Therapy Essential Data Pre-Infusion</td>
<td>Modify</td>
<td>Removed text (struck out below) and added text (in red below) to the instructions for question 49. If the indication for cellular therapy is relapsed, persistent or progressive disease (post-HCT), the indication should be the primary disease for which the cellular therapy is being given. If the recipient is receiving post-HCT cellular therapy (e.g. DCI/DLI) for relapsed, persistent, or progressive disease, the indication should be recorded as “malignant hematologic disorders” and complete a new F2402 for the disease that has relapsed/persisted/progressed.</td>
</tr>
<tr>
<td>2/14/18</td>
<td>2402: Disease Classification</td>
<td>Remove</td>
<td>Removed incorrect instruction (struck out below) from question 271. If the histology reported at infusion (question 268) is a transformation from CLL, indicate “Yes,” and go to question 272. Also, complete the disease classification questions for CLL.</td>
</tr>
<tr>
<td>2/13/18</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added Liver Toxicity Prophylaxis note box above the instructions for question 490.</td>
</tr>
<tr>
<td>2/13/18</td>
<td>4000: Cellular Therapy Essential Data Pre-Infusion</td>
<td>Remove</td>
<td>Removed the instruction below from section Q68-93: Disease Assessment at Last Evaluation Prior to Cellular Therapy. Specify the method(s) of disease detection below. For each method used, if the result was positive report the first date the disease was detected; if the result was negative report the last date the method was used prior to cellular therapy.</td>
</tr>
<tr>
<td>2/22/18</td>
<td>2111: ALL Post-Infusion Data</td>
<td>Add</td>
<td>Added text (in red) to the Questions 48-94 warning box. For questions 48, 54, 61, and 78, report “No” or “Unknown” (see instructions below) if the recipient did not relapse, have persistent or minimal residual disease even if testing was performed.</td>
</tr>
<tr>
<td>2/20/18</td>
<td>Appendix C: Cytogenetic Assessments</td>
<td>Add</td>
<td>Added table below figure 3 to explain karyotype findings.</td>
</tr>
<tr>
<td>2/20/18</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added text (in red below) to the instructions for question 304. This instruction was / is available on the form. Report the date of maximum chronic GVHD involvement since the date of last report, based on clinical grade.</td>
</tr>
<tr>
<td>2/20/18</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added the following instruction for question 303. This instruction was / is available on the form. Report the extent of chronic GVHD since the date of last report.</td>
</tr>
<tr>
<td>2/15/18</td>
<td>4000: Cellular Therapy Essential Data Pre-Infusion</td>
<td>Modify</td>
<td>Removed text (struck out below) and added text (in red below) to the instructions for question 49. If the indication for cellular therapy is relapsed, persistent or progressive disease (post-HCT), the indication should be the primary disease for which the cellular therapy is being given. If the recipient is receiving post-HCT cellular therapy (e.g. DCI/DLI) for relapsed, persistent, or progressive disease, the indication should be recorded as “malignant hematologic disorders” and complete a new F2402 for the disease that has relapsed/persisted/progressed.</td>
</tr>
<tr>
<td>Date</td>
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<tr>
<td>2/13/18</td>
<td>2116: PCD Post-HCT</td>
<td>Add</td>
<td>Added <strong>Daratumumab</strong> note box to the instructions for questions 69-90.</td>
</tr>
<tr>
<td>2/13/18</td>
<td>2016: PCD Pre-HCT</td>
<td>Add</td>
<td>Added <strong>Daratumumab</strong> note box to the instructions for questions 196-222.</td>
</tr>
<tr>
<td>2/12/18</td>
<td>Appendix C: Cytogenetic Assessments</td>
<td>Add</td>
<td>Added the following description of constitutional abnormalities. <em>Karyotyping may also detect constitutional abnormalities. These are abnormalities present since birth. Examples include, but are not limited to, trisomy 21 and Klinefelter's syndrome. It is not necessary to report constitutional abnormalities when reporting karyotyping results.</em></td>
</tr>
<tr>
<td>2/7/18</td>
<td>2000: Recipient Baseline</td>
<td>Modify</td>
<td>Updated the list of fungal species that require Form 2046 to be completed. Items added are in red. Items removed are struck out. This list is provided in the instructions for questions 58-59. <em>Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Other Aspergillus specify, Aspergillus NOS, Aspergillus terreus, Aspergillus ustus, Blastomyces (dermatitidis), Candida albicans, Candida non-albicans, Cryptococcus gattii, Cryptococcus neoformans, Fusarium (all species), Histoplasma (capsulatum), Mucorales (all species), Mucormycosis, Rhizopus (all species), Scedosporium (all species), Zygomycetes NOS, Suspected fungal infection</em></td>
</tr>
<tr>
<td>2/2/18</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Modify</td>
<td>Removed text (struck out below) from the instructions for question 272.</td>
</tr>
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January 2018

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<tr>
<td>1/30/18</td>
<td>Add</td>
<td>3500: Subsequent Neoplasms</td>
<td>Version 1 of the 3500: Subsequent Neoplasms section of the Forms Instruction Manual released. Version 1 corresponds to revision 1 of the Form 3500.</td>
</tr>
<tr>
<td>1/30/18</td>
<td>Modify</td>
<td>4006: Cellular Therapy Infusion</td>
<td>Version 3 of the 4006: Cell Therapy Infusion section of the Forms Instruction Manual released. Version 3 corresponds to revision 3 of the Form 4006.</td>
</tr>
<tr>
<td>1/30/18</td>
<td>Modify</td>
<td>2402: Disease Classification</td>
<td>Version 3 of the 2402: Disease Classification section of the Forms Instruction Manual released. Version 3 corresponds to revision 3 of the Form 2402.</td>
</tr>
<tr>
<td>1/24/18</td>
<td>Add</td>
<td>2116: PCD Post-HCT</td>
<td>Added Not Applicable Amyloidosis note box to the instructions for question 135.</td>
</tr>
<tr>
<td>1/24/18</td>
<td>Remove</td>
<td>2116: PCD Post-HCT</td>
<td>Removed text (struck out below) from the instructions for question 96. <em>If the recipient had amyloidosis or POEMS syndrome, but no evidence of myeloma, select “Not Applicable (Amyloidosis with no evidence of myeloma).”</em></td>
</tr>
<tr>
<td>1/24/18</td>
<td>Add</td>
<td>2116: PCD Post-HCT</td>
<td>Added Amyloidosis note box to the instructions for question 96.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>Remove</td>
<td>2402: Disease Classification</td>
<td>Removed text (struck out below) from the instructions for question 307. <em>If the primary disease is Amyloidosis or POEMS, report “Not applicable” and go to the signature line.</em></td>
</tr>
<tr>
<td>1/23/18</td>
<td>Add</td>
<td>2402: Disease Classification</td>
<td>Added Amyloidosis note box to the instructions for question 307.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>Add</td>
<td>2450: Post-TED</td>
<td>Added Amyloidosis note box above the instructions for question 75.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>Remove</td>
<td>2016: PCD Pre-HCT</td>
<td>Removed text (struck out below) from the instructions for questions 229 and 363. <em>If the recipient had amyloidosis or POEMS syndrome, but no evidence of myeloma, select “Not Applicable (POEMS or Amyloidosis with no evidence of myeloma)” and continue with …</em></td>
</tr>
<tr>
<td>1/2016</td>
<td>Add</td>
<td>2016: PCD</td>
<td>Added Amyloidosis note box to the instructions for questions 229 and 363.</td>
</tr>
<tr>
<td>Date</td>
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<td>Action</td>
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<tr>
<td>23/18</td>
<td>Pre-HCT</td>
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</tr>
<tr>
<td>1/23/18</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added text (in red below) to the description of HLA-mismatched relative provided in the instructions for question 40. Includes: Siblings who are not HLA-identical and all other blood-related relatives who have at least one HLA mismatch (e.g., parents, aunts, uncles, children, cousins, half-siblings). <em>This includes haploidentical donors.</em></td>
</tr>
<tr>
<td>1/23/18</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added <strong>Haploidentical Donors</strong> note box to the instructions for question 40.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Modify</td>
<td>Added text (highlighted red below) to the instructions for question 272 to clarify hospitalization scenarios. Indicate “Yes” if the donor was hospitalized for complications during or after the collection for any reason. Indicate “No” if the donor was not hospitalized as an inpatient or if the donor was admitted to an observation unit and discharged in less than 24 hours.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>4100: Cellular Therapy Essential Data Follow-Up</td>
<td>Add</td>
<td>Added <strong>HCT and CT</strong> note box above question 44.</td>
</tr>
</tbody>
</table>
# 2017 Manual Updates

- **December 2017**
- **November 2017**
- **October 2017**
- **September 2017**
- **August 2017**
- **July 2017**
- **June 2017**
- **May 2017**
- **April 2017**
- **March 2017**
- **February 2017**
- **January 2017**

⚠️ **Hyperlinks**
Please note, hyperlinks on this page will not work for any manual sections which have been retired and / or replaced by new versions.

## December 2017

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<tr>
<td>12/6/17</td>
<td><strong>2028</strong>: Aplastic Anemia Pre-HCT</td>
<td>Add</td>
<td>Added the following instruction for question 31. <em>If this is a report of a second or subsequent transplant for aplastic anemia and this baseline disease insert has previously been completed for a prior transplant, indicate if the recipient received treatment for aplastic anemia between Day 0 of the previous HCT and the start of the preparative regimen for the subsequent HCT.</em></td>
</tr>
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## November 2017

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<tr>
<td>11/21/17</td>
<td>2010: AML Pre-Infusion Data</td>
<td>Modify</td>
<td>Corrected incorrect instruction provided for questions 6-9. The form asks for cytotoxic therapy; however, the manual incorrectly instructed centers to report any systemic therapies. <strong>Systemic Cytotoxic Therapy:</strong> chemotherapy, immunotherapy, or targeted therapies delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally.</td>
</tr>
<tr>
<td>11/20/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Modify</td>
<td>Added (in red) and removed (struck out) text from description of IPn / ARDS provided in the instructions for questions 441-485. <em>Interstitial pneumonitis / Acute respiratory distress syndrome (IPn/ARDS):</em> IPn refers to inflammation of the alveolar walls. Acute respiratory distress syndrome typically refers to fluid build-up within the alveoli. In either case, gas exchange is impaired resulting in oxygen deprivation. Both conditions can result from infectious or non-infectious causes. <em>Infectious causes may be bacterial, viral (CMV, adenovirus, RSV, influenza, etc.), or fungal. Only report IPn / ARDS resulting from non-infectious causes in questions 441-485.</em></td>
</tr>
<tr>
<td>11/20/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added instructions below for question 158. <em>If the date of diagnosis is unknown,</em> leave question 158 blank and override the validation error using the code “Unknown.” However, question 158 may <strong>not</strong> be left blank if treatment for acute GVHD (question 185) is reported “Yes.” If the exact clinical diagnosis date is unknown, but the treatment start date is known, report the date treatment started as the date of acute GVHD diagnosis.</td>
</tr>
<tr>
<td>11/15/17</td>
<td>4100: Cellular Therapy Essential Data Follow-Up</td>
<td>Modify</td>
<td>Replaced description of grade 4 organ toxicity provided in the instructions for Questions 82-138. <strong>Grade 4 organ toxicity:</strong> As defined by the CTCAE criteria, grade 4 toxicity represents life-threatening consequences and urgent intervention is indicated. Liver, lungs, heart, kidneys, gastrointestinal, musculoskeletal, neurologic, or other organ. Based on the CTC criteria.</td>
</tr>
<tr>
<td>11/15/17</td>
<td>4000: Cellular Therapy Essential Data Pre-Infusion</td>
<td>Modify</td>
<td>Replaced instructions for question 35 as indicated below. <em>Indicate whether the cellular therapy product reported in this instance contains viral-specific Cytotoxic T Lymphocytes (CTLs).</em> These products are generally from allogeneic donors that have been cultured / expanded and modified to treat specific viruses such as CMV, EBV, Adenovirus, etc. <strong>Cytotoxic T lymphocytes (CTLs):</strong> are a type of white blood cell that can kill foreign cells, cancer cells, and cells infected with a virus. Indicate “yes” or “no” for the donor being reported in this instance and continue with question 36.</td>
</tr>
<tr>
<td>11/15/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added the fungal infection codes below to the list of infections which will prompt the Fungal Infection Post-HCT Form to come due. The list is provided in the instructions for questions 428-436.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 270 Blastomyces (dermatitidis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 201 Candida albicans</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 208 Candida non-albicans</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 222 Cryptococcus gattii</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 221 Cryptococcus neoformans</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 261 Histoplamsa (capsulatum)</td>
</tr>
</tbody>
</table>
- 272 Scedosporium (all species)
- 503 Suspected fungal infection

October 2017

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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<tbody>
<tr>
<td>10/27/17</td>
<td>2402: Disease Classification</td>
<td>Modify</td>
<td>Corrected instruction for question 167. If the MDS/MPN subtype at diagnosis was “atypical chronic myeloid leukemia,” continue with question 265. continue to the signature line.</td>
</tr>
<tr>
<td>10/25/17</td>
<td>2556: Myelofibrosis CMS Study Pre-HCT Data</td>
<td>Add</td>
<td>Added instructions (highlighted red below) for questions 26-27. Indicate “yes” if the patient was treated with a different JAK1 or JAK2 inhibitor (other than ruxolitinib) and specify the drug in question 27. Also, indicate “yes” if the recipient started and stopped ruxolitinib multiple times prior to HCT. In this case, the center should use questions 26-31 to report each treatment interval not captured in questions 19-25.</td>
</tr>
<tr>
<td>10/25/17</td>
<td>2556: Myelofibrosis CMS Study Pre-HCT Data</td>
<td>Add</td>
<td>Added Ruxolitinib (Jakafi) note box above the instructions for question 18.</td>
</tr>
<tr>
<td>10/23/17</td>
<td>2402: Disease Classification</td>
<td>Remove</td>
<td>Removed criteria for Nodular Partial Remission included under the instructions for question 266. This disease status is no longer captured on the forms.</td>
</tr>
<tr>
<td>10/23/17</td>
<td>CLL Response Criteria</td>
<td>Remove</td>
<td>Removed criteria for Nodular Partial Remission as this disease status is no longer captured on the forms.</td>
</tr>
<tr>
<td>10/16/17</td>
<td>Appendix J: Reporting Comorbidities</td>
<td>Modify</td>
<td>Updated the Hepatic and Renal Comorbidities note box to match the note box included in the Form 2400 section of the manual. For review of renal and hepatic comorbidities, criteria are met when the patient has two or more laboratory values meeting the threshold for reporting between days -24 and -10 (or the date of the last test prior to start of the preparative regimen). If the laboratory values are only assessed once in that period, extend review to between days -40 and -10. In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities Hepatic Comorbidity: The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 &amp; -25 as the second...</td>
</tr>
</tbody>
</table>
### Renal (Moderate/Severe) Comorbidity:

Serum creatinine > 2 mg/dL or > 177 μmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

### Hepatic Comorbidity:

The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between days – 24 & -10 (or between days -40 & -10 if only a single value was reported between days -24 & day -10) before HCT, and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

<table>
<thead>
<tr>
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<th>Description</th>
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</thead>
<tbody>
<tr>
<td>10/14/17</td>
<td>Modify</td>
<td>Updated text in Hepatic and Renal Comorbidities note box. Added text is highlighted red and deleted text is struck out.</td>
</tr>
<tr>
<td>10/14/17</td>
<td>Add</td>
<td>Added the following instruction for questions 75-76: The reported value must be in units of cells / µL.</td>
</tr>
<tr>
<td>10/14/17</td>
<td>Add</td>
<td>Added the bullet points below to General Reporting Guidelines. Note, the second bullet point above was previously available in this section as a footnote.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use the multiple myeloma response criteria when determining the disease status for multiple myeloma and solitary plasmacytoma.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR. Electrophoresis (SPEP and UPEP) are, however, different assessments.</td>
</tr>
<tr>
<td>10/14/17</td>
<td>Add</td>
<td>Version 1 of the Plasma Cell Leukemia Response Criteria section of the Forms Instructions Manual released.</td>
</tr>
</tbody>
</table>

September 2017
<table>
<thead>
<tr>
<th>Date</th>
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<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/28/17</td>
<td>2402: Disease Classification</td>
<td>Remove</td>
<td>Removed an incorrect instruction (struck out below) for question 59. <em>Indicate whether cytogenetic studies were performed at the last evaluation prior to HCT / cellular therapy. Do not report any testing performed after treatment for AML has started. If cytogenetic studies were obtained at this time point, check “Yes” and go to question 60.</em></td>
</tr>
<tr>
<td>9/26/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added Pneumocystis jiroveci warning box above the instructions for questions 428-436.</td>
</tr>
<tr>
<td>9/26/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Remove</td>
<td>Removed Pneumocystis jiroveci from the list of scenarios not to report included in the instructions for questions 428-436.</td>
</tr>
<tr>
<td>9/15/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added Pregnancy Questions warning box above the instructions for question 654.</td>
</tr>
<tr>
<td>9/7/17</td>
<td>2014: MDS/MPN Pre-HCT</td>
<td>Modify</td>
<td>Replaced note box regarding transformation of essential thrombocytopenia and polycythemia vera to myelofibrosis located below instructions for question 123 with Transformation to Myelofibrosis notebox. New text is highlighted red below while old text is struck out. <em>Recipients transplanted for post-essential thrombocytopenia myelofibrosis (post-ET MF) or post-polycythemia vera myelofibrosis (post-PV MF) will be reported as ET or PV at diagnosis (Q2). Question 123: ‘Did the recipient progress or transform to a different MDS/MPN subtype between diagnosis and the start of the preparative regimen?’ must be answered “Yes”. Myelofibrosis that develops in patients with essential thrombocytopenia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. Do not report this as a transformation; when a patient with ET or PV develops fibrosis, do not report primary myelofibrosis as the primary indication for transplant.</em></td>
</tr>
</tbody>
</table>

**August 2017**

<table>
<thead>
<tr>
<th>Date</th>
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<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/31/17</td>
<td>2011: ALL Pre-Infusion Data</td>
<td>Add</td>
<td>Added CNS Prophylaxis Reporting Scenarios A and B located below the instructions for questions 20-26.</td>
</tr>
<tr>
<td>8/31/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added text (in red below) to the description of stage 4 gut GVHD provided in the Acute GVHD Grading and Staging Table located below the instructions for question 169.</td>
</tr>
<tr>
<td>Date</td>
<td>Code</td>
<td>Action</td>
<td>Changes</td>
</tr>
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<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>8/31/17</td>
<td>2450: Post-TED</td>
<td>Add</td>
<td>Added text (in red below) to the description of stage 4 gut GVHD provided in the Acute GVHD Grading and Staging Table located below the instructions for question 22. Severe abdominal pain, with or without ileus, and/or grossly bloody stool</td>
</tr>
</tbody>
</table>
| 8/1/17     | 2014: MDS/MPN Pre-HCT    | Modify | Added text (in red below) and removed text (struck out below) from instructions for question 121. Refer to the MDS / MPN Response Criteria section when determining the recipient’s disease status. Indicate if the disease relapsed from CR or progressed from hematologic improvement. If the disease relapsed or progressed, answer “Yes” and go to question 122. If “No,” go to question 123. Progression or relapse should be reported even if it was reported in the previous set of questions regarding response to therapy (questions 118-120). Relapse is the recurrence of disease after CR. MDS/MPN relapse requires one of the following:
- Return to pre-treatment bone marrow blast percentage.
- Decrease of ≥ 50% from maximum response levels in granulocytes or platelets.
- Transfusion dependence, or hemoglobin level ≥ 1.5 g/dL lower than prior to therapy.
Progression is the worsening of the disease following hematologic improvement or stable disease. Progression requires at least one of the following in the absence of another explanation (e.g., infection, bleeding, ongoing chemotherapy, etc.):
- ≥ 50% reduction from maximum response levels in granulocytes or platelets.
- Reduction in hemoglobin by ≥ 1.5 g/dL.
- Transfusion dependence.
- Progression to AML: ≥ 20% blasts in the blood or bone marrow. |
| 8/1/17     | 2100: Post-HCT Follow-Up | Add    | Added the text below to the instructions for question 169. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic). |
| 8/1/17     | 2100: Post-HCT Follow-Up | Add    | Added the text below to the instructions for questions 170-175. Report the stage of each organ at diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic). |
| 8/1/17     | 2450: Post-TED           | Add    | Added the text below to the instructions for question 22. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic). |
Report the stage of each organ at diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic).

### July 2017

<table>
<thead>
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<th>Date</th>
<th>Manual Section</th>
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</thead>
<tbody>
<tr>
<td>7/26/17</td>
<td>2450: Post-TED</td>
<td>Add</td>
<td>Added text (in red) to instructions for question 36 to clarify intent of question. Report the date of maximum chronic GVHD involvement, based on clinical grade, during the current reporting period.</td>
</tr>
<tr>
<td>7/26/17</td>
<td>2450: Post-TED</td>
<td>Modify</td>
<td>Modified instructions for question 34 to clarify intent of question. Added text in red and removed text which is struck out. Report the maximum chronic GVHD involvement, based on clinical grade, since the date of the last report, as documented by the recipient’s primary care provider.</td>
</tr>
<tr>
<td>Date</td>
<td>Section</td>
<td>Action</td>
<td>Description</td>
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</tr>
<tr>
<td>7/25/17</td>
<td>Infusion</td>
<td>Modify</td>
<td>Version 3 of the 2111: ALL Post-Infusion Data section of the Forms Instructions Manual released. Version 3 corresponds to revision 4 of the Form 2111.</td>
</tr>
<tr>
<td>7/11/17</td>
<td>Appendix D: Distinguish Infusion</td>
<td>Modify</td>
<td>Version 3 of Appendix D: How to Distinguish Infusion Types of the Forms Instructions Manual released. Note, versions 1 &amp; 2 of this appendix were referred to as Appendix O: How to Distinguish Infusion Types.</td>
</tr>
<tr>
<td>7/11/17</td>
<td>Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added the following text to the description of lower GI GVHD provided in the instructions for questions 170-175: Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.</td>
</tr>
<tr>
<td>7/11/17</td>
<td>Post-TED</td>
<td>Add</td>
<td>Added the following text to the description of lower GI GVHD provided in the instructions for questions 23-28: Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.</td>
</tr>
<tr>
<td>7/10/17</td>
<td>Post-TED</td>
<td>Add</td>
<td>Added Intervention Reporting Scenarios A, B, C, and D below the instructions for question 172.</td>
</tr>
<tr>
<td>7/10/17</td>
<td>Post-TED</td>
<td>Modify</td>
<td>Added (in red) and removed (crossed out) text to / from the instructions for question 172 as indicated below. Report the date of earliest administration of therapy for relapsed, persistent, or progressive disease or decreasing / loss of donor chimerism within the report period therapy was started for the reason specified in question 165; if multiple instances, cycles, or lines of therapy are administered, report the date of the first treatment. If treatment was started in a prior reporting period and continues into the current reporting period, report the original therapy start</td>
</tr>
</tbody>
</table>
date (prior to the start of the current reporting period) and override the validation error in FormsNet3SM using the code “verified correct.” If therapy was stopped in a prior reporting period and restarted (or a new therapy was started) during the current reporting period, report the earliest date treatment was administered during the current reporting period. See the intervention reporting scenarios provided below for further clarification.

If therapy was stopped in a prior reporting period and restarted (or a new therapy was started) during the current reporting period, report the earliest date treatment was administered during the current reporting period. See the intervention reporting scenarios provided below for further clarification.

Indicate the methods detecting the reason for which therapy for persistent disease, relapsed / progressive disease, or for decreased / loss of donor chimerism was given (as reported in question 165). For each option, select “yes” if the last assessment by that method was performed prior to the start of the intervention(s) and was consistent with the rationale reported in question 165.

If multiple therapies were given during the reporting period for different reasons (e.g., the recipient initially receives treatment for decreased chimerism and subsequently receives different treatment for relapse during the same reporting period), report “yes” for any methods of detection confirming the reason in question 165. See the intervention reporting scenarios provided below for further clarification.

Indicate whether therapy was given for persistent disease, relapsed / progressive disease, or for decreased / loss of donor chimerism. In some instances, therapy may be given to treat disease and decrease / loss of chimerism. In these cases, report the indication pertaining to the recipient’s disease status (i.e., “persistent disease” or “relapsed / progressive disease”). If therapy continued from a prior reporting period and a new therapy was started for a different reason during the current reporting period, report the reason the new therapy was started. See the intervention reporting scenarios provided below for further clarification.

Added (in red) text to the instructions for questions 166-171 as indicated below.

Added (in red) text to the instructions for question 165 as indicated below.

Added Liver Toxicity Prophylaxis warning box above question 39.

Added all information pertaining to Determining a Baseline. This information was taken from the retired Appendix V: Multiple Myeloma – Defining What Baseline to Use When Determining Disease Status.
<table>
<thead>
<tr>
<th>Date</th>
<th>Appendix/Section</th>
<th>Action</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>6/30/17</td>
<td><strong>Appendix F: Response Evaluation Criteria in Solid Tumors</strong></td>
<td>Add</td>
<td>Added all retired content from Appendix N: Response Evaluation Criteria in Solid Tumors (RECIST) to Appendix F.</td>
</tr>
<tr>
<td>6/30/17</td>
<td><strong>Appendix A: Abbreviations and Definitions</strong></td>
<td>Add</td>
<td>Added all information pertaining to US Abbreviations. This information was taken from the retired Appendix Q: United States Abbreviations.</td>
</tr>
<tr>
<td>6/30/17</td>
<td>Multiple Sections</td>
<td>Modify</td>
<td>The names of the appendices list below have been changed. References and links to these appendices have also been updated throughout the Forms Instructions Manual.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Appendix M: Reporting Comorbidities is now Appendix J: Reporting Comorbidities</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>• Appendix N: Response Evaluation Criteria in Solid Tumors (RECIST) is now Appendix F: Response Evaluation Criteria in Solid Tumors (RECIST)</td>
</tr>
<tr>
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<td>• Appendix O: How to Distinguish Infusion Types is now Appendix D: How to Distinguish Infusion Types</td>
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<td>• Appendix P: Definition of a Product is now Appendix E: Definition of a Product</td>
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<td>• Appendix R: Cytogenetic Abbreviations and Terminology is now Appendix C: Cytogenetic Assessments</td>
</tr>
<tr>
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<td></td>
<td>• Appendix W: Tracking Disease Status for Multiple Myeloma is now Appendix G: Tracking Disease Status for Multiple Myeloma</td>
</tr>
<tr>
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<td></td>
<td>• Appendix X: MDS/MPN Subtypes is now Appendix H: MDS/MPN Subtypes</td>
</tr>
<tr>
<td>6/30/17</td>
<td>Multiple Sections</td>
<td>Remove</td>
<td>The following appendices have been removed from the Forms Instructions Manual:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Appendix C: CIBMTR Data collection Forms – This information is now available in the Data Management Guide.</td>
</tr>
<tr>
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<td></td>
<td>• Appendix D: Unique ID Assignment Form (CRID), Form 2804 – This information can be found in the 2804: CIBMTR Research ID Assignment Form section of the Forms Instructions Manual.</td>
</tr>
<tr>
<td></td>
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<td>• Appendix E: Public Health Authority (PHA) Status – This information is now available in the Data Management Guide.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>• Appendix F: Validation Ranges – This appendix has been retired. An archived copy can be found on the Retired Forms Manuals webpage.</td>
</tr>
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</table>

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<table>
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<tr>
<th>Date</th>
<th>Code</th>
<th>Action</th>
<th>Notes</th>
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<tbody>
<tr>
<td>6/8/17</td>
<td>2100:</td>
<td>Remove</td>
<td>Removed incorrect instruction from instructions for questions 185-233. When reporting the date started, report the first day the drug as given on or after the GVHD diagnosis date (reported in question 158). If acute GVHD persisted since the date of the last report, report the first day the drug was given during the current reporting period. For prophylaxis medications continued after the date of diagnosis of acute GVHD, report the date of diagnosis as the date started. If an acute GVHD treatment has continued from a previous reporting period, report the original start date and override the error in FormsNetSM using the code “verified correct.”</td>
</tr>
<tr>
<td>6/8/17</td>
<td>2450:</td>
<td>Remove</td>
<td>Removed unnecessary text from the following instruction for question 31 to clarify instructions. Report “no” if chronic GVHD was not clinically diagnosed – initially or as a flare – in the reporting period; this includes instances where chronic GVHD persists from a prior reporting period, without flare in the current reporting period.</td>
</tr>
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</table>
## May 2017

<table>
<thead>
<tr>
<th>Date</th>
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<th>Add/ Remove/ Modify</th>
<th>Description</th>
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| 5/31/17  | 2100: Post-HCT Follow-Up  | Add                 | Added two additional bullets to the instructions for Questions 428-436 under “Do not report the following scenarios:”:
  - Yeast infection in the groin, vagina, or under the breasts
  - Pneumocystis jiroveci                                                                                                                                                                                                                                                              |
| 5/25/17  | 2450: Post-TED Data       | Add                 | Added **Steroids and Non-Steroid Immunosuppression for GVHD** warning box to the instructions for question 37 and 38.                                                                                                                                                                                                                          |
| 5/24/17  | 2012: CML Pre-Infusion Data Form | Modify             | Corrected an error in Table 3 by adding the text in red below to the definition of complex variation.

Translocation of three or more chromosomes, one of which must be chromosome 22 [e.g., t(3; 9; 22)]                                                                                                                                                                                                                                          |
| 5/24/17  | 2553: VOD/SOS             | Add                 | Updated the description of the VOD / SOS Form on the title page by adding the text in red below:

*The Veno-occlusive Disease (VOD) / Sinusoidal Obstruction Syndrome (SOS) Form, Form 2553, must be completed when VOD / SOS has been reported to have developed on the 100 Day Post-HCT Data Form (F2100) or the 100 Day Post-TED Form (Form 2450). Additionally, a Six Month VOD/SOS Form will come due if the center has reported VOD/SOS did not resolve during the 100 day reporting period (question 124). This form captures laboratory and pathologic studies at the time of diagnosis, treatment administered during the reporting period.*
<table>
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<th>Date</th>
<th>Section</th>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/24/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Modify</td>
<td>Corrected an error on multiple pages of the 2100 manual. The manual incorrectly instructed centers to skip the engraftment section of the form (Q108-130). This instruction has been removed. Centers should complete the engraftment section of the form for autologous and allogeneic HCTs.</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added text (in red below) to description of graft failure included in the instructions for questions 664 and 665.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Graft failure / insufficient hematopoietic recovery:</strong> Additional hematopoietic stem cells are required because the hematopoietic recovery indefinitely declined after the initial hematopoietic recovery (ANC was greater than or equal to $0.5 \times 10^9/L$ for three consecutive days, and then declined to below $0.5 \times 10^9/L$ for at least three consecutive days). This option also includes primary graft failure (no ANC recovery following HCT).</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2450: Post-TED Data</td>
<td>Add</td>
<td>Added the following information regarding Non-Malignant Diseases to the Post-TED Title Page:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Non-Malignant Diseases</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If the HCT being reported was given to treat a non-malignant disease (as reported on the Pre-TED Disease Classification Form (Form 2402)), do not complete the following sections of the Post-TED Form:</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Q75-97: Disease Assessment at the Time of Best Response to HCT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Q98-160: Post-HCT Therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Q235-238: Current Disease Status</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Questions 161-163 will also be left blank if the HCT being reported was given to treat a non-malignant disease.</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2100: Post-HCT Follow-Up</td>
<td>Add</td>
<td>Added <strong>Therapy Over Multiple Reporting Periods</strong> note box to the instructions for question 4.</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2450: Post-TED Data</td>
<td>Add</td>
<td>Added <strong>Therapy Over Multiple Reporting Periods</strong> note box to the instructions for question 12.</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2450: Post-TED Data</td>
<td>Add</td>
<td>Added <strong>Malignant Diseases Only</strong> warning box to the following pages of the Post-TED Manual:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Q75-97: Disease Assessment at the Time of Best Response to HCT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Q98-160: Post-HCT Therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Q161-234: Relapse or Progression Post-HCT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Q235-238: Current Disease Status</td>
</tr>
<tr>
<td>5/24/17</td>
<td>4006: Cellular Therapy Infusion</td>
<td>Modify</td>
<td>Updated instructions for questions 23-26. New text is highlighted red and removed text has been struck out.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>If the product was manufactured by a cell processing laboratory at the same center as the product is being infused, continue with question 27. If the product is from an NMDP donor used for a prior HCT, please select this option.</em></td>
</tr>
</tbody>
</table>
If the product was manufactured by another site that does not fit a category listed above, specify the other site in question 24 and report the name and location in question 26.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/23/17</td>
<td>2100: Post-HCT</td>
<td>Add</td>
<td>Added scenarios of when to use “Not Applicable” to the instructions for questions 401.</td>
</tr>
<tr>
<td>5/23/17</td>
<td>2100: Post-HCT</td>
<td>Remove</td>
<td>Removed references to “Previously Reported” from the instructions for questions 402-403 and 405-406.</td>
</tr>
<tr>
<td>5/23/17</td>
<td>2100: Post-HCT</td>
<td>Add</td>
<td>Added Previously Reported warning box to instructions for questions 402-403 and 405-406.</td>
</tr>
<tr>
<td>5/23/17</td>
<td>2100: Post-HCT</td>
<td>Add</td>
<td>Added Previously Reported warning box to instructions for questions 402-403 and 405-406.</td>
</tr>
<tr>
<td>5/23/17</td>
<td>2100: Post-HCT</td>
<td>Add</td>
<td>Added Corticosteroids note box to instructions for question 401.</td>
</tr>
<tr>
<td>5/1/17</td>
<td>Multiple Myeloma</td>
<td>Modify</td>
<td>Corrected an error in the criteria for Near Complete Remission. A treatment where all of the following criteria met:</td>
</tr>
</tbody>
</table>
|          | Response Criteria   |                   | • Serum and Urine M-protein detectable by immunoelectrophoresis\(^1\) (immunofixation, IFE) but not on electrophoresis (SPEP and UPEP)  
  • \(\leq 5\)\% plasma cells in bone marrow.                                                                                                                                                                                                                                                                                                                                                                                                       |

**April 2017**

<table>
<thead>
<tr>
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<th>Manual Section</th>
<th>Add/Remove/Modify</th>
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<tr>
<td>4/19/17</td>
<td>2450: Post-TED Data</td>
<td>Remove</td>
<td>Removed incorrect instruction from question 231. Cellular therapy refers to the infusion of human or animal derived cells, which may or may not be modified or processed to achieve a specific composition. Examples include T-cell, NK cell, and mesenchymal cell infusions as well as donor cellular infusions. Indicate “yes” if the recipient received any form of cellular therapy for reasons other than relapse, persistent, or progressive disease or decreasing / loss of donor chimerism; hematopoietic cell transplantation should not be reported as cellular therapy, as this is captured in questions 7-13 of the Post-TED form.</td>
</tr>
<tr>
<td>4/19/17</td>
<td>4100: Cellular Therapy</td>
<td>Add</td>
<td>Added instructions, in red below, to question 39. Report the date (YYYY-MM-DD) the sample was collected for chimerism.</td>
</tr>
<tr>
<td>Date</td>
<td>Form</td>
<td>Description</td>
<td></td>
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<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>4/17/17</td>
<td>Essential Data Follow-Up</td>
<td>Added instructions, in red below, to question 29. Report the date (YYYY-MM-DD) the sample was collected for molecular assay. If multiple studies were performed in the reporting period, report the most recent testing that documents persistence of cells by molecular assay. If all the molecular assays are negative for persistence of cells, then report the most recent test performed in the reporting period.</td>
<td></td>
</tr>
<tr>
<td>4/19/17</td>
<td>Essential Data Follow-Up</td>
<td>Added instructions, in red below, to question 34. Report the date (YYYY-MM-DD) the sample was collected for flow cytometry testing (immunophenotyping). If multiple studies were performed in the reporting period, report the most recent testing that documents persistence of cells by flow cytometry. If all the flow cytometry tests are negative for persistence of cells, then report the most recent test performed in the reporting period.</td>
<td></td>
</tr>
</tbody>
</table>
| 4/19/17    | Essential Data Follow-Up | Added instructions, in red below, regarding how to report the start date for multiple infusions (question 31). Report the intended start date of the infusion for the instance being reported. If multiple infusions are planned within the first 100 days, each infusion must be reported as a separate instance / copy of questions 31-35 and the planned infusion date, question 31, will correspond to the specific infusion being reported. The planned infusion date of the earliest infusion must match the planned infusion date reported on one of the following forms:  
• Indication for CRID Assignment Form (Form 2814) – This form will be used to generate a Cellular Therapy Essential Data Form (Form 4000) when the recipient has not received a HCT.  
• Post-Transplant Essential Data Form (Form 2450) – This form will generate a Cellular Therapy Essential Data Form (Form 4000) when the recipient has received an HCT followed by a donor cellular infusion (excluding subsequent HCTs) or other cellular therapy.  
• Post-HCT Follow-Up Data Form (Form 2100) – This form will generate a Cellular Therapy Essential Data Form (Form 4000) when the recipient has received an HCT followed by a donor cellular infusion (excluding subsequent HCTs) or other cellular therapy. |
| 4/7/17     | Post-HCT Follow-Up     | Added the following clarification, in red below, regarding the enabling / disabling of questions 645-647: Questions 645-647 will only be enabled / answered for pediatric patients (≤ 16 years old) when the form visit ID is 6 months or greater. These questions will be disabled / not answered for all recipients on the day 100 follow-up. |
Added further clarification, in red below, to the instructions for question 34: The intent of question 34 is to determine whether an HLA Form (Form 2005) has already been completed for this donor so that duplicate reporting may be avoided. For infusions using an NMDP donor or cord blood unit, the donor’s HLA typing is reported on NMDP Form 22 (Confirmation of Donor HLA Typing) and the recipient’s HLA typing is reported on NMDP Form 117 (Final Recipient HLA Typing). Please contact your CRC if you think the Form 2005(s) should be removed.

Added the following note box to the instructions for question 164 regarding Interventions for Decreased / Loss of Chimerism:
The Post-TED Form (Form 2450) captures interventions given for decreased or loss of chimerism in the relapse / progression section of the form. If the recipient receives an intervention for decreased or loss of chimerism during the reporting period, report the therapy in questions 164-234. This instruction may differ from prior guidelines regarding how to report interventions for decreased / loss of chimerism on past revisions (1-3) of the Post-TED Form.

Added instructions to questions 170-175 to clarify how to report transaminitis under “other site” for acute GVHD. Other site(s) involved with acute GVHD: Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 28. If reporting transaminitis under “other site,” write in “transaminitis” rather than “liver” when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under “other site.”

Added instructions to questions 23-28 to clarify how to report transaminitis under “other site” for acute GVHD. Other site(s) involved with acute GVHD: Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 28. If reporting transaminitis under “other site,” write in “transaminitis” rather than “liver” when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under “other site.”

Added instruction to report site of bone marrow infections as Blood in the instructions for questions 428-436. Blood: includes blood or serum obtained from a central IV line, catheter tip, or from a direct needle stick (Peripheral draw). Blood should be the reported site for infections identified in the bone marrow.
<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Action</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/6/17</td>
<td>Post-HCT Follow-Up</td>
<td>Remove</td>
<td>Removed incorrect instruction form Organism description in the instructions for questions 428-436. Suspected bacterial or viral infections should not be reported. Select the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. If the specific organism is not listed, use the code “777 – Other organism” and report the name of the organism in the space provided. If a fungal infection is suspected, but not identified, report using code “503 – Suspected fungal infection.” If a bacterial or viral infection is suspected, but not identified, report using code “777 – Other organism” and specify “suspected bacterial infection” or “suspected viral infection” as applicable. As noted above, only report infections which are clinically significant.</td>
</tr>
<tr>
<td>4/6/17</td>
<td>Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Modify</td>
<td>Updated the following text on the 2006 Title Page: All recipients on the Comprehensive Report Form track must complete the Form 2006. Recipients on the Transplant Essential Data track must complete the Form 2006 for each product when the following product types are infused as part of the transplant: - NMDP donor products - NMDP and non-NMDP cord blood units</td>
</tr>
<tr>
<td>4/6/17</td>
<td>Post-HCT Follow-Up</td>
<td>Modify</td>
<td>Updated instructions for question 159 to clarify reporting questions. The wording has changed, but the intent of the instructions is the same. <strong>Question 159 will only be enabled in FormsNet3SM if the center has reported “no” for question 157 and, therefore, has not reported a date of diagnosis in question 158. If prompted to answer question 159, report “yes” if acute GVHD was diagnosed in a prior reporting period and any of the following conditions are met:</strong>  - The recipient’s acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).  - The recipient’s acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred within 30 days of symptom resolution / quiescence.  - The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 157). Report “no” for questions 157 and 159 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 157). Indicate whether acute GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive acute GVHD, or a prior history of GVHD. If “yes,” continue with...</td>
</tr>
</tbody>
</table>
Questions concerning acute GVHD at the time of diagnosis will be skipped. See question 157 for instructions on reporting an acute GVHD flare or acute GVHD occurring after the onset of chronic GVHD.

If the recipient has no active symptoms during the reporting period, report “no” and continue with question 234.

Updated instructions for question 157 to clarify reporting questions. The wording has changed, but the intent of the instructions is the same. Questions 157 and 159 on the Post-HCT Follow-Up Data Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 157 or question 158 must be answered “yes” unless there has been a prior / concurrent diagnosis of chronic GVHD (refer to the note above question 157). There will not be a situation where “yes” is reported for both question 157 and question 159. If question 157 is answered yes and a diagnosis date has been reported in question 158, question 159 will be disabled in FormsNet3SM. Centers should report “yes” for question 157 to indicate the recipient developed acute GVHD in the following scenarios:

- Acute GVHD is diagnosed for the first time during the reporting period.
- An acute GVHD flare is diagnosed during the current reporting period and all of the following conditions are met:
  - The recipient’s prior acute GVHD symptoms did not persist from the prior reporting period into the beginning of the current reporting period.
  - The flare is diagnosed after at least 30 days without any active acute GVHD symptoms.
  - The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 157).

If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report “no” for question 157 and “yes” for question 159. Question 159 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis.
Scenarios below to see examples of how to answer questions 157 and 159. Report “no” for questions 157 and 159 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 157).

Indicate whether a new clinical diagnosis of acute GVHD was documented during the reporting period. If acute GVHD was diagnosed during the reporting period, report “yes” and continue with question 158. If the recipient had a flare of acute GVHD occurring after at least a 30 day period of symptom quiescence, report “yes” and continue with question 158. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent acute GVHD which is captured in question 159. Indicate “no” if acute GVHD was not clinically diagnosed—initially or as a flare—in the reporting period; this includes instances where acute GVHD persists from a prior reporting period without flare in the current reporting period.

Updated instructions for question 21 to clarify reporting questions. The wording has changed, but the intent of the instructions is the same. Question 21 will only be enabled in FormsNet3SM if the center has reported “no” for question 19 and, therefore, has not reported a date of diagnosis in question 20. If prompted to answer question 21, report “yes” if acute GVHD was diagnosed in a prior reporting period and any of the following conditions are met:

- The recipient’s acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).
- The recipient’s acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred within 30 days of symptom resolution / quiescence.
- The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 19). Report “no” for questions 19 and 21 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after

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<table>
<thead>
<tr>
<th>Date</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/6/17</td>
<td>2450: Post-TED Data</td>
</tr>
<tr>
<td></td>
<td>Modify</td>
</tr>
</tbody>
</table>
a diagnosis of chronic GVHD (see note above question 19).
Indicate whether acute GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive acute GVHD, or a prior history of GVHD. If "yes," continue with question 29; questions concerning acute GVHD at the time of diagnosis will be skipped. See question 19 for instructions on reporting an acute GVHD flare or acute GVHD occurring after the onset of chronic GVHD.
If the recipient has no active symptoms during the reporting period, report “no” and continue with question 31.

Updated instructions for question 19 to clarify reporting questions. The wording has changed, but the intent of the instructions is the same. Questions 19 and 21 on the Post-TED Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 19 or question 21 must be answered "yes" unless there has been a prior / concurrent diagnosis of chronic GVHD (see note above question 19). There will not be a situation where “yes” is reported for both question 19 and question 21. If question 19 is answered yes and a diagnosis date has been reported in question 20, question 21 will be disabled in FormsNet3SM. Centers should report “yes” for question 19 to indicate the recipient developed acute GVHD in the following scenarios:

• Acute GVHD is diagnosed for the first time during the reporting period.

• An acute GVHD flare is diagnosed during the current reporting period and all of the following conditions are met:
  ◦ The recipient’s prior acute GVHD symptoms did not persist from the prior reporting period into the beginning of the current reporting period.
  ◦ The flare is diagnosed after at least 30 days without any active acute GVHD symptoms.
  ◦ The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 19). If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report “no” for question 19 and “yes” for question 21. Question 21 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet
the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer questions 19 and 21.

Report “no” for questions 19 and 21 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 19).

Indicate whether a new clinical diagnosis of acute GVHD was documented during the reporting period. If acute GVHD was diagnosed during the reporting period, report “yes” and continue with question 20.

If the recipient had a flare of acute GVHD occurring after at least a 30 day period of symptom quiescence, report “yes” and continue with question 20. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent acute GVHD which is captured in question 21.

Indicate “no” if acute GVHD was not clinically diagnosed—initially or as a flare—in the reporting period; this includes instances where acute GVHD persists from a prior reporting period without flare in the current reporting period.

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### Instruction change for any questions asking for performance status (Karnofsky / Lansky Score):

**April 4, 2017**

<table>
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</thead>
<tbody>
<tr>
<td>4/4/17</td>
<td>Manual Wide</td>
<td>Modify</td>
<td>Instruction change for any questions asking for performance status (Karnofsky / Lansky Score): Age range for Lansky Scale has been updated from recipients less than 16 years old to recipients one year old to less than 16 years old. If the recipient is less than one year old, performance status questions should be left blank.</td>
</tr>
</tbody>
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March 2017

<table>
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<th>Manual Section</th>
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<th>Description</th>
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</thead>
<tbody>
<tr>
<td>3/29/17</td>
<td>2100: Post-HCT Follow-Up Data</td>
<td>Add</td>
<td>Added the following text (in red) to the instructions for question 325: Indicate whether systemic therapy was given to treat chronic GVHD during the reporting period. If systemic therapy was given as treatment for chronic GVHD, report “yes” and continue with question 326. If systemic therapy was not given for</td>
</tr>
</tbody>
</table>
treatment of chronic GVHD, report “no” and continue with question 399. See questions 328-399 for Chronic GVHD Treatment Reporting Scenarios.

Added the following instruction to question 326:
If treatment is started for a flare of chronic GVHD (see question 234 for definition of flare), report “no” for question 326 and report the date treatment was started for the flare in question 327.

Added the following text (in red) to the instructions for question 327:
Report the first date when therapy was started for chronic GVHD if the date has not been previously reported. If the recipient continued GVHD prophylaxis drugs after the onset of chronic GVHD, report the date of diagnosis of chronic GVHD as the treatment start date. If the recipient starts treatment multiple times during the same reporting period, report the earliest treatment start date.

Modified the instructions for questions 328-399 to correct an error (deleted text) and provide further clarification (in red):
For each agent listed, indicate whether or not it was used to treat chronic GVHD during the reporting period. If a therapy was started or escalated for chronic GVHD during the reporting period, report “yes” and answer any additional questions (if applicable). If a dose is required, report the total ordered dose planned to be given at the time treatment was initiated. This may include doses which are planned to be given after the date of contact. % Report %@(marker-red)”yes” for prophylactic drugs if they were continued after the onset of chronic GVHD. Report the date of diagnosis of chronic GVHD as the treatment start date for any prophylactic medications which were continued. See Chronic GVHD Treatment Reporting Scenarios below.

Added the following text (in red) to the instructions for question 327:
If treatment is started and subsequently escalated during the same reporting period, report the earliest date treatment was actually given during the reporting period. If a dose is required, contact your center’s liaison to determine how to complete the data field. Additionally, report the earliest start date if a drug is started multiple times during the same reporting period.

Added Chronic GVHD Treatment Scenarios A, B, and C.

Added another example to questions 169 and 176 regarding when to report “Not Applicable” for the grade of acute GVHD. This instruction was previously available in the description of staging acute lower intestinal tract GVHD.
* Lower intestinal tract involvement where the stage cannot be determined in select scenarios lower intestinal tract involvement description above

Added another example to questions 22 and 29 regarding when to report “Not Applicable” for the grade of acute GVHD. This instruction was previously available in the description of staging acute lower intestinal tract GVHD.
* Lower intestinal tract involvement where the stage cannot be determined in select scenarios lower intestinal tract involvement description below

Added instruction to question 177:
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<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>27/17</td>
<td>Post-HCT Follow-Up Data</td>
<td>Add</td>
<td>If “not applicable” was reported for question 176, question 177 must be left blank.</td>
</tr>
<tr>
<td>3/27/17</td>
<td>2450: Post-TED Data</td>
<td>Add</td>
<td>Added instruction to question 30: If “not applicable” was reported for question 29, question 30 must be left blank.</td>
</tr>
<tr>
<td>3/17/17</td>
<td>4000: Cellular Therapy Essential Data Pre-Infusion</td>
<td>Add</td>
<td>Added the following note box to the instructions for question 1: Reporting Consent Status for DCI If this form is being completed for a DCI reported on a Post-TED Form (Form 2450) or Post-HCT Follow-Up Data Form (Form 2100), report “Not applicable” for question 1. The consent status will be reported on the Pre-TED Form (Form 2400) and should not be re-reported here. If the recipient’s consent status has changed since the Pre-TED Form was completed, update the consent status on the Pre-TED Form.</td>
</tr>
<tr>
<td>3/15/17</td>
<td>2100: Post-HCT Follow-Up Data</td>
<td>Add</td>
<td>Clarification was added regarding the intent of questions 658-660. The intent of this question is to determine the recipient’s history of smoking cigarettes only. Do not report the use of cigars, pipe tobacco, chewing tobacco, or other drugs. Indicate whether the recipient has smoked tobacco cigarettes since the date of the last report. If “yes,” complete questions 659-660. If the recipient has not smoked tobacco cigarettes since the date of the last report, or their smoking history is not known, report “no” or “unknown” respectively and continue with question 661.</td>
</tr>
<tr>
<td>3/15/17</td>
<td>2100: Post-HCT Follow-Up Data</td>
<td>Add</td>
<td>The following instruction has been added to questions 645-647. Questions 645-647 will only be enabled / answered for pediatric patients (≤ 16 years old).</td>
</tr>
</tbody>
</table>
| 3/15/17    | 2450: Post-TED Data | Add    | Added instruction to question 37 regarding when to use Not Applicable. Instructions for this option choice were not previously available. Indicate “not applicable” in any of the following scenarios:  
  • The recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD.  
  • This form is being completed for a subsequent HCT and the recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen is given).  
  • The recipient stopped taking systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD in a previous reporting period and did not restart systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) during the current reporting period. |
<p>| 3/15/17    | 2450: Post-TED Data | Add    | Added instruction to question 38 regarding when to use Not Applicable. Instructions for this option choice were not previously available.                                                            |</p>
<table>
<thead>
<tr>
<th>Date</th>
<th>Change</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/15/17</td>
<td></td>
<td>Data</td>
<td>Indicate &quot;not applicable&quot; in any of the following scenarios: • The recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD. • This form is being completed for a subsequent HCT and the recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen was given). • The recipient stopped taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD in a previous reporting period and did not restart non-steroidal immunosuppressive agents (including PUVA) during the current reporting period.</td>
</tr>
<tr>
<td>3/14/17</td>
<td>Modify</td>
<td>AML Response Criteria</td>
<td>Modified AML relapse criteria to clarify that only one of the criteria need to be met to report relapse. Relapse is defined as the recurrence of disease after CR, meeting one or more of the following criteria: • ≥ 5% blasts in the marrow or peripheral blood • Extramedullary disease • Disease presence determined by a physician upon clinical assessment</td>
</tr>
<tr>
<td>3/14/17</td>
<td>Add</td>
<td>2450: Post-TED</td>
<td>Added Scenario D to Acute GVHD Grading Scenarios under question 29.</td>
</tr>
<tr>
<td>3/14/17</td>
<td>Add</td>
<td>2450: Post-TED</td>
<td>Added the following instruction below to question 29. This instruction was previously provided under question 19, but has been added to question 29 for further clarification. If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. See question 19 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.</td>
</tr>
<tr>
<td>3/14/17</td>
<td>Add</td>
<td>2450: Post-TED</td>
<td>Added scenario B to Acute GVHD Diagnosis Scenarios under question 19.</td>
</tr>
<tr>
<td>3/14/17</td>
<td>Modify</td>
<td>2450: Post-TED</td>
<td>Modified the note above question 19 to address questions received. The instructions have not changed, but the wording has been updated to be clearer. If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 19-30). Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section. Report any new or persistent acute GVHD symptoms (persistent or newly diagnosed) occurring on or after the date of diagnosis onset of chronic GVHD only in the chronic GVHD section of the form (questions 234-323). See the examples included in the instructions for questions 252-301. If chronic GVHD was diagnosed while completing the acute GVHD section, report these questions as not applicable.</td>
</tr>
</tbody>
</table>
Once diagnosed in a prior reporting period, the center should report “no” for questions 19 and 21 in each subsequent reporting period. Any GVHD symptoms occurring in each subsequent reporting period must be reported in the chronic GVHD section of the form and should not be re-reported in the acute GVHD data fields. See reporting scenarios included in question 19.

### 3/14/17 2100: Post-HCT Follow-Up Data

**Modify**

Modified instructions for Q252-301 to address questions received. The instructions have not changed, but the question now refers to instructions for question 157 which provide greater detail. Examples C and D, which were previously available, are also reference. *If a recipient has signs / symptoms of both acute and chronic GVHD on or after the date chronic GVHD is diagnosed, report all signs / symptoms in the chronic GVHD section of the form. If acute GVHD signs / symptoms are identified prior to the diagnosis of chronic GVHD, they should also be reported in the acute GVHD section of the form (questions 157-183) during the reporting period. Refer to question 157 for additional instructions. Scenarios C and D below have also been provided for further clarification.*

### 3/14/17 2100: Post-HCT Follow-Up Data

**Modify**

Modified instructions for Q238 to address questions received. The instructions have not changed, but the question now refers to instructions for question 157 which provide greater detail. *Chronic GVHD can be separated into two different categories; classical chronic GVHD and overlap syndrome. Overlap syndrome is a condition where there are features of both acute and chronic GVHD at the time of diagnosis. Indicate whether signs of acute GVHD were present at the time of diagnosis of chronic GVHD (overlap syndrome). Ensure any features of acute GVHD are reported in questions 169-183. Report all GVHD signs / symptoms (acute and chronic) occurring on or after the diagnosis of chronic GVHD in the chronic GVHD section of the form. See questions 252-301 below for further instructions on reporting acute and chronic GVHD signs / symptoms. Refer to question 157 for instructions on how to complete acute and chronic GVHD sections for recipients with overlap syndrome.*

### 3/14/17 2100: Post-HCT Follow-Up Data

**Add**

Added Scenario D to Acute GVHD Grading Scenarios under question 176.

### 3/14/17 2100: Post-HCT Follow-Up Data

**Add**

Added the following instruction below to question 176. This instruction was previously provided under question 157, but has been added to question 176 for further clarification. *If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. See question 157 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.*

### 3/14/17 2100: Post-HCT Follow-Up Data

**Add**

Added scenario B to Acute GVHD Diagnosis Scenarios under question 157.

### 3/ 2100

**Modify**

Modified the note above question 157 to address questions received. The
<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
</table>
| 14/17      | Post-HCT Follow-Up Data            | Instructions have not changed, but the wording has been updated to be clearer. *If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 157-233). Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section. Report any **new or persistent acute** GVHD symptoms (persistent or newly diagnosed) occurring on or after the date of diagnosis onset of chronic GVHD only in the chronic GVHD section of the form (questions 234-323). See the examples included in the instructions for questions 252-301. If chronic GVHD was diagnosed in a prior reporting period, the center should report “no” for questions 157 and 159 in each subsequent reporting period. Any GVHD symptoms occurring in each subsequent reporting period must be reported in the chronic GVHD section of the form and should not be re-reported in the acute GVHD data fields. See reporting scenarios included in question 157.*  
| 3/13/17    | 2450: Post-TED                     | Added the following instruction to **Lower Intestinal Tract** description beneath questions 23-28: *If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, report “stage 0” for lower intestinal tract involvement. In this case, report "Not Applicable" for the overall grade unless stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status was also documented at the time point being reported (at diagnosis or maximum grade during the reporting period). Report an overall grade of IV if stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status is documented at the time point being reported (see GVHD Staging and Grading Table).*  
| 3/13/17    | 2100: Post-HCT Follow-Up Data     | Added the following instruction to **Lower Intestinal Tract** description beneath questions 170-175: *If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, report “stage 0” for lower intestinal tract involvement. In this case, report "Not Applicable" for the overall grade unless stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status was also documented at the time point being reported (at diagnosis or maximum grade during the reporting period). Report an overall grade of IV if stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status is documented at the time point being reported (see GVHD Staging and Grading Table).*  
| 3/10/17    | 2400: Pre-TED                      | Clarification has been added to the instructions for questions 136-155 (in bold below): *Use questions 153-155 to report any prior **hematologic** malignancies that were not listed in questions 136-152. **Solid tumors should be reported in questions 144-131, not in questions 153-155.***  
| 3/10/17    | 2100: Post-HCT Follow-Up Data     | Added “stool” to the definition of GI, lower infection site. This instruction is included for questions 428-326.  
| 3/8        | 2100:                              | Added instruction to Questions 185-233: |
If an acute GVHD treatment has continued from a previous reporting period, report the original start date and override the error in FormsNet3<sup>SM</sup> using the code “verified correct.”

### Added instruction to Question 173:
If therapy has continued from a previous reporting period, report the original start date and override the validation error in FormsNet3<sup>SM</sup> using the code “verified correct.”

The note box above question 19 referred to the incorrect question numbers. The question numbers have been updated to the correct values.

If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 19-30). Report any GVHD symptoms (persistent or newly diagnosed) occurring on or after the date of diagnosis of chronic GVHD in the chronic GVHD section of the form (questions 31-36). See the examples included in the instructions for question 19.

If chronic GVHD was diagnosed in a prior reporting period, the center should report “no” for questions 31-19 and 33-21 in each subsequent reporting period.

Any GVHD symptoms occurring in each subsequent reporting period must be reported in the chronic GVHD section of the form and should not be re-reported in the acute GVHD data fields.

Updated liver scoring criteria on Chronic GVHD Organ Scoring table included under questions 252-301. The criteria were documented incorrectly and have been updated to match the 2014 NIH Consensus Criteria.

Updated liver scoring criteria on Chronic GVHD Organ Scoring table included under question 34. The criteria were documented incorrectly and have been updated to match the 2014 NIH Consensus Criteria.

The note box above question 14 has been updated to indicate question 16 must be completed on all follow-up forms:

**Questions 14-16 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.**

**Questions 14-15 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods. Question 16 must be answered on all follow-up forms.**

### February 2017

<table>
<thead>
<tr>
<th>Date</th>
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<tr>
<td>2/27/17</td>
<td>2016: PCD Pre-HCT</td>
<td>Remove</td>
<td>Removed the following warning box from the instructions for questions 237-239: Currently there is an issue on Form 2400 regarding the ISS Staging: Stage I</td>
</tr>
</tbody>
</table>
requires albumin greater or equal to 3.5 g/dL. This question was removed from the Form 2400 and included in the Form 2402 during the Winter Forms Revision 2017 (January 31, 2017). The ISS staging criteria are correct on the Form 2402.

2/24/17 Comprehensive Disease-Specific Manuals Modify Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)

2/22/17 4000: Cellular Therapy Essential Data Pre-Infusion Add Added instructions to question 34 (bold text): Indicate if the allogeneic unrelated or related donor reported in question 32 was used for prior cellular therapies or HCT for this recipient. Do not answer this question for autologous donors. The intent of question 34 is to determine whether an HLA Form (Form 2005) has already been completed for this donor so that duplicate reporting may be avoided.

2/20/17 2016: PCD Pre-HCT Modify Updated the multiple myeloma diagnostic criteria provided in the instructions for question 1 to match the IMWG criteria released October 2015.

2/20/17 2402: Pre-TED Disease Classification Modify Updated the multiple myeloma diagnostic criteria provided in the instructions for questions 232-233 to match the IMWG criteria released October 2015.

2/15/17 4000: Cellular Therapy Essential Data Pre-Infusion Add Added note box above question 19: Questions 19-27 HCT History

2/15/17 4100: Cellular Therapy Essential Data Follow-Up Add Added note box above question 1: Question 1 Date of Contact

2/15/17 4100: Cellular Therapy Essential Data Follow-Up Add Added note box above questions 15: Questions 15-16 Subsequent HCT

2/15/17 4100: Cellular Therapy Essential Data Follow-Up Add Added note box above question 22: Questions 22-26 New Malignancy

January 2017

<table>
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<tr>
<td>1/31</td>
<td>2112: CML Post-</td>
<td>Add</td>
<td>Version 1 of the 2012: CML Post-Infusion Data Form section of the Forms</td>
</tr>
<tr>
<td></td>
<td>Details</td>
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<tr>
<td>------------------</td>
<td>-------------------------------------------------------------------------</td>
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</tr>
<tr>
<td><strong>Infusion Data Form</strong></td>
<td>Instructions Manual released. Version 1 corresponds to revision 2 of the Form 2112.</td>
<td></td>
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</tr>
<tr>
<td><strong>1/31/17</strong></td>
<td><strong>2012: CML Pre-Infusion Data Form</strong> Add Version 1 of the 2012: CML Pre-Infusion Data Form section of the Forms Instructions Manual released. Version 1 corresponds to revision 2 of the Form 2012.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1/31/17</strong></td>
<td><strong>2556: Myelofibrosis CMS Study Pre-HCT Data</strong> Add Version 1 of the 2556: Myelofibrosis CMS Study Pre-HCT Data section of the Forms Instructions Manual released. Version 1 corresponds to revision 1 of the Form 2556.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1/31/17</strong></td>
<td><strong>2557: Myelofibrosis CMS Study Post-HCT Data</strong> Add Version 1 of the 2557: Myelofibrosis CMS Study Post-HCT Data section of the Forms Instructions Manual released. Version 1 corresponds to revision 1 of the Form 2557.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1/31/2017</strong></td>
<td><strong>2450: Post-TED</strong> Modify Version 3 of the 2450: Post-TED section of the Forms Instruction Manual released. Version 3 corresponds to revision 4 of the Form 2450.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1/31/2017</strong></td>
<td><strong>2402: Pre-TED Disease Classification</strong> Modify Version 1 of the 2402: Pre-TED: Disease Classification section of the Forms Instructions Manual released. Version 1 corresponds to revision 1 of the Form 2402.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1/31/2017</strong></td>
<td><strong>2400: Pre-TED</strong> Modify Version 4 of the 2400: Pre-TED section of the Forms Instruction Manual released. Version 4 corresponds to revision 5 of the Form 2400.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1/23/17</strong></td>
<td><strong>Multiple Myeloma Response Criteria</strong> Add Added General Reporting Guidelines. This information was previously available in Pre-TED and Multiple Myeloma Response Criteria sections of the Forms Instructions Manual.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1/23/17</strong></td>
<td><strong>Appendix V</strong> Add Added examples 1 and 2 which were previously available in the Pre-TED section of the Forms Instructions Manual.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **1/19/17**      | **General Instructions** Remove The following subsections were removed Forms Instructions Manual and are being transferred into other data management resources:  
  • Stem Cells Therapeutic Outcomes Database  
  • Center Type and Data Collection Forms  
  • Autologous Hematopoietic Stem Cell Transplant  
  • EBMT Centers  
  • Protocols and Consent Forms  
  • Unique ID Assignment (CRID) & Protected Health Information, Form 2804  
  • FormsNet |
| • Forms Due Report          |
| • CIBMTR Campus & CRC Assignment |
| • Declaring Recipients Lost to Follow-Up |
| • Recipient Transfers       |
| • How to Avoid Errors       |
| • Reimbursement for Forms Completion |
| • Continuous Process Improvement |
| • On-site Data Audits       |
| • Helpful Websites and CIBMTR Contact Information |

Please contact your center’s CRC for assistance with any of these topics while this information is being updated and transferred. Retired versions of these sections may be found here.
# 2016 Manual Updates

**December 2016**

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>12/12/2016</td>
<td><strong>2013: CLL Pre-Infusion</strong></td>
<td>Modify</td>
<td>Instructions for Revision 2 of the CLL Pre- and Post-HCT Forms were retired and instructions for Revision 3 of the CLL Pre- and Post-Infusion Forms were released.</td>
</tr>
<tr>
<td>12/12/2016</td>
<td><strong>2113: CLL Post-Infusion</strong></td>
<td>Modify</td>
<td>Instructions for Revision 2 of the CLL Pre- and Post-HCT Forms were retired and instructions for Revision 3 of the CLL Pre- and Post-Infusion Forms were released.</td>
</tr>
</tbody>
</table>

**August 2016**

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/29/16</td>
<td><strong>2804: CIBMTR Research ID Assignment form</strong></td>
<td>Add</td>
<td>Added information banner to <a href="#">2804 introduction page</a>: Reporting of all HCTs is important to ensure the continued epidemiological integrity of the CIBMTR outcomes registry. The exception to this is if your center performs but does not report autologous HCTs.</td>
</tr>
<tr>
<td>Date</td>
<td>Question/Description</td>
<td>Action</td>
<td>Description</td>
</tr>
<tr>
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<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>8/29/16</td>
<td>2131: ID Post-HCT</td>
<td>Add</td>
<td>Added information box under question 25: If CD56+ cells were not tested, centers may report CD16+ results in these data fields.</td>
</tr>
<tr>
<td>8/29/16</td>
<td>2031: ID Pre-HCT</td>
<td>Add</td>
<td>Added information box under question 33: If CD56+ cells were not tested, centers may report CD16+ results in these data fields.</td>
</tr>
<tr>
<td>8/29/16</td>
<td>2200: Six Months to Two Years Post-HCT</td>
<td>Add</td>
<td>Added text to information banner beneath question 43: The CD20+ data field can capture CD19+ or CD20+ cells. The CD56+ data field can capture CD56+ or CD16+ cells.</td>
</tr>
<tr>
<td>8/29/16</td>
<td>2100: 100 Days Post-HCT</td>
<td>Add</td>
<td>Added text to the information banner beneath question 72: The CD20+ data field can capture CD19+ or CD20+ cells. The CD56+ data field can capture CD56+ or CD16+ cells.</td>
</tr>
<tr>
<td>8/26/16</td>
<td>2131: ID Post-HCT</td>
<td>Add</td>
<td>Added information box under question 24: If CD20+ cells were not tested, centers may report CD19+ results in these data fields.</td>
</tr>
<tr>
<td>8/26/16</td>
<td>2031/2131: Immune Deficiencies</td>
<td>Add</td>
<td>Added information box under question 32: If CD20+ cells were not tested, centers may report CD19+ results in these data fields.</td>
</tr>
<tr>
<td>8/26/16</td>
<td>2200: Six Months to Two Years Post-HCT</td>
<td>Add</td>
<td>Added text to Table 3 to clarify how centers should report chimerism testing performed on sorted marrow samples.</td>
</tr>
<tr>
<td>8/26/16</td>
<td>2100: 100 Days Post-HCT</td>
<td>Add</td>
<td>Added text to Table 3 to clarify how centers should report chimerism testing performed on sorted marrow samples.</td>
</tr>
<tr>
<td>8/26/16</td>
<td>ALL Response Criteria</td>
<td>Add</td>
<td>Added alternative post-HCT CR criteria for pediatric recipients.</td>
</tr>
<tr>
<td>8/26/16</td>
<td>ALL Response Criteria</td>
<td>Modify</td>
<td>Updated relapse criteria: Relapse is defined as the recurrence of disease after CR, meeting at least one of the following criteria</td>
</tr>
<tr>
<td>8/26/16</td>
<td>Multiple Myeloma Response Criteria</td>
<td>Modify</td>
<td>Updated PR criteria: If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):</td>
</tr>
<tr>
<td>8/26/16</td>
<td>2100: 100 Days Post-HCT</td>
<td>Add</td>
<td>Added the following information text to question 452: If the recipient receives a subsequent HCT prior to day 100, do not include the start date of the preparative regimen for the subsequent HCT (or the date of the subsequent infusion if no preparative regimen was given).</td>
</tr>
</tbody>
</table>

July 2016
<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>7/29/16</td>
<td>4000: Cellular Therapy Essential Data Pre-Infusion</td>
<td>Add</td>
<td>Version 1 Released</td>
</tr>
<tr>
<td>7/29/16</td>
<td>4006: Cellular Therapy Infusion</td>
<td>Add</td>
<td>Version 1 Released</td>
</tr>
<tr>
<td>7/29/16</td>
<td>4100: Cellular Therapy Essential Data Follow-Up</td>
<td>Add</td>
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</tr>
<tr>
<td>7/26/16</td>
<td>2553: VOD/SOS</td>
<td>Add</td>
<td>Version 1 Released</td>
</tr>
<tr>
<td>7/26/16</td>
<td>2814: Indication for CRID Assignment</td>
<td>Modify</td>
<td>Version 2 Released</td>
</tr>
<tr>
<td>7/18/16</td>
<td>2013: CLL Pre-HCT</td>
<td>Modify</td>
<td>Updated all question numbers to match the current version of the CLL Pre-HCT Disease Insert</td>
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</tbody>
</table>

**June 2016**

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/27/16</td>
<td>Multiple Myeloma Response Criteria</td>
<td>Modify</td>
<td>Changed text in information box regarding <strong>Urine Studies</strong>: In order to report a Stringent Complete Remission (sCR) or Complete Remission (CR), urine studies MUST be performed and agree with the international myeloma working group (IMWG) criteria provided above. As long as the negative serum electrophoresis and immunofixation studies have been confirmed, only one set of negative urine studies needs to be documented to report sCR or CR. Urine electrophoresis and immunofixation studies may not be performed in all cases. The disease response options below (Near Complete Remission, Very Good Partial Response, and Partial Response) may still be reported even if urine studies were never obtained or were only obtained at diagnosis. If urine studies were performed following the most recent line of therapy, the results must agree with the international working group IMWG criteria for the disease status being reported. In any case, serum studies MUST be performed and agree with the international working group criteria for the disease status being reported (excluding non-secretory myeloma).</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Date</th>
<th>Manual</th>
<th>Add/ Modify</th>
<th>Description</th>
</tr>
</thead>
</table>
| 6/24/16 | Multiple Myeloma Response Criteria | Add         | Added information box: **Urine Studies**
In order to report a Stringent Complete Remission or Complete Remission, urine studies MUST be performed and agree with the international working group criteria provided above. Urine electrophoresis and immunofixation studies may not be performed in all cases. The disease response options below (Near Complete Remission, Very Good Partial Response, and Partial Response) may still be reported even if urine studies were never obtained or were only obtained at diagnosis. If urine studies were performed following the most recent line of therapy, the results must agree with the international working group criteria for the disease status being reported. In any case, serum studies MUST be performed and agree with the international working group criteria for the disease status being reported. |
| 6/24/16 | Multiple Myeloma Response Criteria | Add         | Added link to Appendix W below disease status criteria.                                                                                                                                                                      |
| 6/24/16 | MDS/MPN Response Criteria    | Add         | Added information box to MDS Disease Status Criteria, [Hematologic Improvement](#) Section:
Hypomethylating agents (e.g. Vidaza) should not be considered cytotoxic therapy; therefore, Hematologic Improvement may still be reported if the recipient meets the criteria below while continuing to receive hypomethylating agents. |
| 6/24/16 | MDS/MPN Response Criteria    | Modify      | Added language to note beneath [Hematologic Improvement](#) for MDS and MPN Response Criteria:
If the above criteria for progression have been met, but a hematologic improvement was not previously achieved, report “No Response (NR) / Stable Disease (SD)”. |
| 6/24/16 | MDS/MPN Response Criteria    | Add         | Added language to MPN Disease Status Criteria, [Hematologic Improvement](#): Requires one measurement of the following maintained for at least eight weeks without ongoing cytotoxic therapy: |
| 6/24/16 | 2014: MDS/MPN Pre-HCT        | Add         | Added information box to [Q157](#): “Never Treated” is not an option choice on revision three of the Myelodysplasia / Myeloproliferative Disorders Pre-HSCT Data (MDS) Form. When completing revision three of this form, centers should report “No Response (NR) / Stable Disease (SD)” for recipients who have only received supportive care prior to transplant. |
| 6/24/16 | 2400: Pre-TED                | Add         | Added information box to [Q568](#): “Never Treated” is not an option choice on revision four of the Pre-TED Form. When completing revision four of this form, centers should report “No Response (NR) / Stable Disease (SD)” for recipients who have only received supportive care prior to transplant. |

April 2016
### 4/6/16

**2814: Indication for CRID Assignment**

**Add**

Added the following warning box to the 2814 topic: Reporting a subsequent transplant using the indication form is not allowed. Report the subsequent transplant on the latest follow up form for the most recent transplant.

---

**2800: Log of Appended Documents**

**Add**

Added the following information box: **New FormsNet3 feature**:

---

**2400: Pre-TED**

**Modify**

Updated donor section reflect reporting of different products from same donor in questions 46-50:

Previous CIBMTR forms required you to enter two instances of the donor section when a single donor donated multiple products. This is no longer required. Report all products collected from a single donor in the same instance of the donor section.

If the recipient receives a cord blood unit and another product from the same related donor, complete two instances of the Donor Information section (questions 31-62) on the Pre-TED Form 2400.

For example, if a related donor gave a cord blood unit and bone marrow, you would report the cord blood unit information in one instance with the donor type listed as ‘Related cord blood unit’. Create another instance with the donor type reported as ‘Related donor’ to report the bone marrow information. This allows CIBMTR to capture all the necessary donor information needed.

For these cases, complete a Form 2004 for each product. When the donor type is an HLA matched or mismatched relative, only one Form 2005 is required.

---

**2450: Post-TED**

**Modify**

Changed the wording in questions 66-73 to reflect the possibility of multiple causes of death (i.e., select all that apply), rather than a single primary cause of death.

---

### March 2016

<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
</table>
| 3/31/16    | **Appendix R: Cytogenetic Abbreviations and Terminology** | **Add**           | Added the following text to Appendix R:

The website Human Gene Nomenclature Committee or Genenames.org may be helpful in deciphering common cytogenetic abnormalities.                                                                                                                                                                                                                                                                                      |

| 3/31/16    | **2014: MDS/MPN Pre-HCT** | **Add**           | Added an information box about transformation of polycythemia vera and essential thrombocytemia to question 123:

Myelofibrosis that develops in patients with essential thrombocytemia (ET) or... |
polycythemia vera (PV) is considered secondary myelofibrosis. Do not report this as a transformation; when a patient with ET or PV develops fibrosis, do not report primary myelofibrosis as the primary indication for transplant.

<table>
<thead>
<tr>
<th>Date</th>
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<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/31/16</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added an information box about transformation of polycythemia vera and essential thrombocythemia to question 525: Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. Do not report this as a transformation; when a patient with ET or PV develops fibrosis, do not report primary myelofibrosis as the primary indication for transplant.</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2100: 100 Days Post-HCT</td>
<td>Add</td>
<td>Added the following informational text to question 74: The CD20+ data field can capture CD19+ or CD20+ cells</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2200: Six Months to Two Years Post-HCT</td>
<td>Add</td>
<td>Added the following informational text to question 46: The CD20+ data field can capture CD19+ or CD20+ cells</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2118: LYM Post-HCT</td>
<td>Add</td>
<td>Added informational box for questions 35-36: Questions 35 and 36 are meant to refer to the PET or PET/CT scan at relapse.</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2016: PCD Pre-HCT</td>
<td>Add</td>
<td>Added information box to question 188: If this form is being completed for a second or subsequent transplant for relapse or progression of the same disease, report all therapy given for relapse or progression of disease. Do not report maintenance therapy given after the prior transplant, as this will be captured on the post-transplant disease inserts associated with the prior transplant.</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2016: PCD Pre-HCT</td>
<td>Modify</td>
<td>Changed disease characteristics for plasma cell leukemia in question 1 to: more than ≥ 20% plasma cells in the peripheral differential white blood cell count</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Changed disease characteristics for plasma cell leukemia in question 589 to: more than ≥ 20% plasma cells in the peripheral differential white blood cell count</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Added table explaining how to report IgG versus IgM CMV results to question 93. [see table in text]</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2000: Recipient Baseline</td>
<td>Modify</td>
<td>Added table explaining how to report IgG versus IgM CMV results to question 65. [see table in text]</td>
</tr>
</tbody>
</table>

February 2016
2/16/16 2100: 100 Days Post-HCT  Add  Added Codes for Indication of Therapy Table for questions 9-33. [see table in text]

2/9/16 2400: Pre-TED  Modify  Modified text in obesity comorbidity to include pediatric patients: **Obesity:** Patients with a body mass index > 35 kg/m² or BMI-for-age ≥ 95% (pediatric recipients only) during pre-transplant work-up period.

2/9/16 2131: ID Post-HCT  2133: WAS Post-HCT  Add  Added CD15+ cells to the text in question 171 [2131] and question 173 [2133]: Myeloid subsets may be reported as CD15+ or CD33+ on the laboratory report.

2/9/16 2450: Post-TED  2100: 100 Days Post-HCT  2200: Six Months to Two Years Post-HCT  2300: Greater Than Two Years Post-HCT  Modify  Modified pediatric acute GVHD Gut guidelines to questions 15 [2450], 151 [2100], 92 [2200], and 22 [2300]. See table for details.

2/9/16 2400: Pre-TED  Modify  Changed the text of question 53 to: Report the total number of mobilization events performed for this HCT. Include all mobilization events, even if a product from the mobilization event for this HCT was not used during the transplant. For example, if 2 mobilization events were performed to collect enough stem cells for this transplant, but the first collection wasn’t necessary for the transplant, report two mobilization events.

2/9/16 Appendix V: Multiple Myeloma – Defining What Baseline to Use When Determining Disease Status  Modify  Changed title of Appendix V: Multiple Myeloma – Defining What Baseline to Use When Determining The Best Response to HCT to Appendix V: Multiple Myeloma – Defining What Baseline to Use When Determining Disease Status

**January 2016**

<table>
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<tr>
<th>Date</th>
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<tbody>
<tr>
<td>1/22/16</td>
<td>2450: Post-TED 2100: 100 Days Post-HCT 2200: Six</td>
<td>Modify</td>
<td>Updated footnote 4 below acute GVHD staging and grading table: Persistent nausea with or without histologic evidence of GVHD in the stomach or duodenum.</td>
</tr>
<tr>
<td>Months to Two Years Post-HCT 2300: Greater Than Two Years Post-HCT</td>
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<td>----------------</td>
<td>----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/19/16</td>
<td>Added Multiple Myeloma Response Criteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Add the following text to CR:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>The method of the two consecutive assessments may be any of the biochemical tests (urine/serum testing) listed in the disease status criteria available in the manual. Though it is preferable the biochemical confirmatory testing include both the urine &amp; serum, this disease status does not require two consecutive assessments by each method. As an example: [see in text]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2015 Manual Updates

December 2015
September 2015
August 2015
July 2015
June 2015
May 2015

Hyperlinks
Please note, hyperlinks on this page will not work for any manual sections which have been retired and / or replaced by new versions.

December 2015

<table>
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<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
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</thead>
<tbody>
<tr>
<td>12/9/15</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Edited the following text in question 62: Stem cells do not typically circulate in the bloodstream. Therefore, in order to increase the quantity of cells for collection, an agent is frequently given to the allogeneic donor or autologous recipient. The purpose of the agent is to move the stem cells from the bone marrow into the peripheral blood. This practice is often referred to as mobilization or priming. Indicate if the donor received plerixafor at any time prior to the preparative regimen. start of stem cell collection.</td>
</tr>
<tr>
<td>12/7/15</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Modify/ Add</td>
<td>Edited the text regarding manipulation of products in questions 73-95: Steps in Manipulation If the manipulation consists of several steps, individual steps do not need to be reported as separate manipulations. For example, washing that is part of CD34+ expansion selection does not need to be reported as a separate manipulation. Similarly, T-cell depletion that is part of expansion does not need to be reported. If dilution is performed as part of washing, dilution does not need to be reported. In the cases above, if T-cell depletion and/or washing are done as stand-alone manipulations, they should be reported.</td>
</tr>
<tr>
<td>12/7/15</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Added MPN to the following text in the MDS/MPN Disease specific section: If the recipient is being transplanted for AML that has transformed from MDS/MPN, the primary disease for HCT must be reported as AML. Disease Classification questions must be completed for both AML and MDS/MPN.</td>
</tr>
<tr>
<td>Date</td>
<td>Section</td>
<td>Type</td>
<td>Action</td>
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<tr>
<td>12/3/15</td>
<td>Appendix Z: Primary Disease and Disease Inserts Due</td>
<td>Modify</td>
<td>Updated Appendix Z</td>
</tr>
<tr>
<td>12/3/15</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Updated</td>
</tr>
<tr>
<td>12/3/15</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added the following text to question 158: Based on the CIBMTR operational guidelines below, report if the regimen was myeloablative, reduced intensity, or non-myeloablative. The determination of whether the intent of the regimen was reduced intensity or non-myeloablative should be based either on the protocol at your center or the opinion of the physician overseeing the care of the recipient at your center. However, if there’s a protocol utilized at your center that doesn’t fall within CIBMTR operational guidelines for regimen intensity, you may report the regimen intensity based on the protocol intent.</td>
</tr>
<tr>
<td>12/3/15</td>
<td>2450: Post-TED</td>
<td>Modify</td>
<td>Updated description of DLI indication reporting in Questions 118-119: From the list provided, indicate the reason the cells were infused. If there was more than one reason for the DLI, check all applicable indications. If the recipient received multiple DCIs for more than one indication, report the DLI and the new indication in the second DLI section. If multiple DCIs were given within the 10-week period, check all applicable indications.</td>
</tr>
<tr>
<td>12/3/15</td>
<td>2010: AML Pre-HCT</td>
<td>Modify</td>
<td>Updated text in question 12: If the patient is suspected to have had a preceding hematologic disorder, but it was not definitively documented or diagnosed, indicate “suspected” and continue with question 14.</td>
</tr>
<tr>
<td>12/3/15</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added the following italic text to questions 366-401: If question 365 indicates that abnormalities were identified, each of questions 366-400 must be answered as &quot;yes&quot; or &quot;no.&quot; Do not leave any response blank. Indicate &quot;yes&quot; for each cytogenetic abnormality identified at any time prior to the start of the preparative regimen. Indicate &quot;no&quot; for all options not identified by cytogenetic assessment at any time prior to the start of the preparative regimen. For cases where AML has transformed from MDS, only report &quot;yes&quot; for cytogenetic abnormalities identified on or after the date of diagnosis for AML. If one or more abnormalities are best classified as “other abnormality,” specify in question 401.</td>
</tr>
<tr>
<td>12/3/15</td>
<td>2800: Log of Appended Documents</td>
<td>Modify</td>
<td>Changed email link on subject topic to <a href="mailto:cibmtrrecipientforms@ndmp.org">cibmtrrecipientforms@ndmp.org</a>.</td>
</tr>
<tr>
<td>12/2005</td>
<td></td>
<td>Add</td>
<td>Added the following text to question 4:</td>
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**September 2015**

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</thead>
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<tr>
<td>3/15</td>
<td>Confirmation of HLA Typing</td>
<td></td>
<td>Indicate if the maternal HLA typing is available and continue with question 7; if yes, also complete Form 2005 reporting maternal HLA typing. <em>The form will not come due on its own, so must be added by the data manager.</em></td>
</tr>
</tbody>
</table>

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>9/27/15</td>
<td><strong>2100: 100 Days Post-HCT</strong></td>
<td>Remove</td>
<td>Removed information box in Engraftment Syndrome [2100] [2200] Section: If this was an autologous or syngeneic HCT, continue with the Infection section at question 201.</td>
</tr>
<tr>
<td></td>
<td><strong>2200: Six Months to Two Years Post-HCT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/27/15</td>
<td>Multiple Myeloma Response Criteria</td>
<td>Add</td>
<td>Added a footnote: Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR. Electrophoresis (SPEP and UPEP) are, however, different assessments.</td>
</tr>
<tr>
<td>9/27/15</td>
<td>MDS/MPN Response Criteria</td>
<td>Modify</td>
<td>Added language to NR/SD criteria: Does not meet the criteria for at least HI, but no evidence of disease progression to AML.</td>
</tr>
<tr>
<td>9/27/15</td>
<td>MDS/MPN Response Criteria</td>
<td>Add</td>
<td>Added MPN criteria</td>
</tr>
<tr>
<td>9/27/15</td>
<td><strong>2400: Pre-TED</strong></td>
<td>Modify</td>
<td>Modified MDS transformation table [2400] [2014] to include RA, 5q-syndrome, MDS-U, and chronic eosinophilia transformations</td>
</tr>
<tr>
<td>9/27/15</td>
<td><strong>2400: Pre-TED</strong></td>
<td>Modify</td>
<td>Modified myeloablative, reduced intensity, and non-myeloablative regimens table for thiopeta. Thiopeta ≥ (greater than or equal to) 10 mg/kg is myeloablative, and thiopeta &lt; (less than) 10 mg/kg is non-myeloablative.</td>
</tr>
<tr>
<td>9/27/15</td>
<td><strong>2450: Pre-TED</strong></td>
<td>Modify</td>
<td>Added language to question 65: Cause of death is considered the main disease, complication, or injury that leads to death. Do not report the mode of death (e.g., cardiopulmonary arrest). Only one primary cause of death may be specified; however, under “HSCT-related causes,” multiple contributing causes may be listed if relevant.</td>
</tr>
<tr>
<td>9/27/15</td>
<td><strong>2450: Pre-TED</strong></td>
<td>Remove</td>
<td>Removed the following phrase from “Subsequent Transplant” for clarification purposes. This does not change the intention of the question; if a recipient receives an autologous rescue, new forms should not come due:</td>
</tr>
</tbody>
</table>
However, if the recipient receives an autologous HCT as a result of a poor graft or graft failure, the TED form sequence **will not** start over again. Generally this type of infusion (autologous rescue) is used to treat the recipient’s poor graft response, rather than to treat the recipient’s disease, and is therefore not considered a subsequent HCT.

### 9/14/15

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<tr>
<td>9/14/15</td>
<td>2028/2128: Aplastic Anemia</td>
<td>Modify</td>
<td>Updated questions number is <strong>2028</strong> and <strong>2128</strong> Aplastic Anemia Pre- and Post-HCT</td>
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### 9/11/15

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<tr>
<td>9/11/15</td>
<td>2033/2133: Wiskott Aldrich Syndrome</td>
<td>Add</td>
<td>Published new manual for <strong>2033</strong> &amp; <strong>2131</strong> WAS Pre- and Post-HCT.</td>
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### August 2015

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<tr>
<td>8/28/15</td>
<td>2031/2131: Immune Deficiencies</td>
<td>Modify</td>
<td>Published new manual for <strong>2031</strong> &amp; <strong>2131</strong> Pre- and Post-HCT Immune Deficiencies Data</td>
</tr>
<tr>
<td>8/28/15</td>
<td>2047/2147: Hepatitis Serology</td>
<td>Add</td>
<td>Published new manual for <strong>2047</strong> &amp; <strong>2147</strong> Hepatitis Serology Pre- and Post-HCT Data.</td>
</tr>
<tr>
<td>8/3/15</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Add</td>
<td>Added additional product analysis reporting instructions to question <strong>158</strong>: To assist centers in reporting product analysis timepoints, the CIBMTR has developed guidelines specific to the product type being reported. … This may be different than the date testing for cell counts or cell viability was performed. [see text for full detail]</td>
</tr>
<tr>
<td>8/3/15</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Remove</td>
<td>Removed the following information bubble in question <strong>158</strong>: This instruction is under review. If the product is thawed, but not retested prior to infusion, you can report the values prior to cryopreservation as “at infusion.” If a viability assessment is completed, ensure that it is reported accurately for the at infusion time point.</td>
</tr>
</tbody>
</table>

### July 2015

<table>
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<tr>
<th>Date</th>
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</tr>
<tr>
<td><strong>6/26/15</strong></td>
<td>• 2450: Post-TED</td>
<td>Modify</td>
<td>Updated/Added language to warnings in Chimerism Studies [2100 &amp; 2200 ], Engraftment Syndrome [2100 &amp; 2200 ], and GVHD [2450 ] [Acute: 2100 , 2200 , &amp; 2300 and Chronic: 2100 , 2200 , &amp; 2300 ] sections that state autologous and sygeneic HCTs should skip the applicable sections.</td>
</tr>
<tr>
<td></td>
<td>• 2100: 100 Days Post-HCT</td>
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<tr>
<td></td>
<td>• 2200: Six Months to Two Years Post-HCT</td>
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<tr>
<td></td>
<td>• 2300: Greater Than Two Years Post-HCT</td>
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<tr>
<td><strong>6/26/15</strong></td>
<td>• 2400: Pre-TED</td>
<td>Modify</td>
<td>Edited Progression to AML text in Questions 525 [2400], MDS/MPN Response Criteria, 121 &amp; 123 [2014], 30 [2114], and 63 [2015] to include the following concept: ≥ 20% blasts in the blood or bone marrow</td>
</tr>
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<td></td>
<td>• MDS/MPN Response Criteria</td>
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<tr>
<td></td>
<td>• 2014: MDS/MPN Pre-HCT</td>
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<tr>
<td></td>
<td>• 2114:</td>
<td></td>
<td></td>
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<tr>
<td>Date</td>
<td>Section</td>
<td>Action</td>
<td>Notes</td>
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</tr>
<tr>
<td>6/26/15</td>
<td>MDS/MPN Post-HCT</td>
<td>Add</td>
<td>Added the following explanatory text to questions 256-263: Report the recipient’s source of health insurance as of the date of HCT. If the recipient carries more than one source, select “yes” for all that apply. For each option, select “yes” or “no” and do not leave any options blank. U.S.-based, government-sponsored health insurance should be reported in question(s) 256 and/or 257. Non-U.S.-based, government-sponsored health insurance (such as the National Health Service in the United Kingdom) should be reported in question 258. <em>Insurance purchased through an U.S. Affordable Care Act Government Exchange should report this in questions 262-263.</em> If the recipient has a health insurance that is not listed, select “yes” for “other” and specify the health insurance in question 263.</td>
</tr>
</tbody>
</table>
| 6/26/15    | AML Response Criteria             | Add    | Added the following text to AML CR: Alternative post-transplant CR criteria are accepted in the setting of pediatric AML when the center does *not* routinely perform bone marrow biopsies post-transplant and the patient was in CR pre-transplant. These criteria are not used for pre-transplant AML disease status. The criteria are as follows:  
  - Complete donor chimerism (≥ 95% donor chimerism without recipient cells detected)  
  - No extramedullary disease (e.g., CNS, soft tissue disease)  
  - Neutrophils ≥ 1,000/µL  
  - Platelets ≥ 100,000/µL  
  - Transfusion independent |
<p>| 6/12/15    | 2118: LYM Post-HCT                | Add    | Added instruction for METHOD and DATE reporting in the Q55-65: <em>Disease Status at the Time of Evaluation for this Reporting Period</em> section. <em>See text for full detail.</em> |
| 6/12/15    | 2116: PCD Post-HCT                | Add    | Added instruction for METHOD and DATE reporting in the Q102-136: <em>Disease Status at the Time of Evaluation for this Reporting Period</em> section just prior to question 126. <em>See text for full detail.</em> |
| 6/12/15    | 2111: ALL Post-HCT                | Add    | Added instruction for METHOD and DATE reporting in the Q73-96: <em>Disease Status at the Time of Evaluation for This Reporting Period</em> section. <em>See text for full detail.</em> |
| 6/12/15    | 2110: AML Post-HCT                | Add    | Added instruction for METHOD and DATE reporting in the Q186-107: <em>Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen</em> section. <em>See text for full detail.</em> |</p>
<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>6/12/15</td>
<td>Manual-wide</td>
<td>Modify</td>
<td>Language relating to the Lost-to-Follow-Up (2802) has been removed.</td>
</tr>
<tr>
<td>6/12/15</td>
<td>2450: Pre-TED</td>
<td>Add</td>
<td>Added explanatory text to question 106:</td>
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<td>The date reported should be that of the most disease-specific assessment</td>
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<td>within a reasonable timeframe of the date of contact (approximately 30</td>
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<td>days). Indicate the date the sample was collected for examination for</td>
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<td>pathological and laboratory evaluations; enter the date the imaging took</td>
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<td>place for radiographic assessments, or the date of physical examination.</td>
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<td>6/12/15</td>
<td>2100: 100 Days</td>
<td>Modify</td>
<td>Modified the informational text prior to question 110:</td>
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<tr>
<td></td>
<td>Post-HCT</td>
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<td>ATG given before Day 0 as GVHD prophylaxis should be reported in the</td>
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<td>preparative regimen section on the Baseline Form (questions 107-111) and</td>
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<td>on the Pre-TED form (questions 168-172). Report ATG given after Day 0 as</td>
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<td>GVHD prophylaxis in the acute GVHD prophylaxis section on the 100 Day</td>
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<td>Post-HCT Data Form (questions 111-113) and on the Pre-TED form (questions</td>
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<td>317-319). Please note, ATG given pre and post transplant for GVHD</td>
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<td>prophylaxis would be reported in both the preparative regimen and GVHD</td>
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<td>prophylaxis sections of the Pre-TED form. For ATG, Campath, and</td>
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<td>Cyclophosphamide: If these agents are given for GVHD prophylaxis both</td>
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<td>prior to and after Day 0, they must be reported in separate sections of</td>
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<td>the Pre-TED form, and Recipient Baseline Forms. Report doses given prior</td>
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<td>to Day 0 in the preparative regimen section of the Pre-TED (questions</td>
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<td>168-315) and Recipient Baseline (107-242). If given after Day 0 as</td>
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<td>planned GVHD prophylaxis, report in the GVHD prophylaxis section of the</td>
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<td>Pre-TED (questions 316-341) and below.</td>
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<tr>
<td>6/12/15</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Modified the informational text in question 168 and before question</td>
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<td>316: ATG or alemtuzumab (Campath) given for GVHD prophylaxis planned</td>
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<td>prior to Day 0 should be reported in the preparative regimen section of</td>
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<td>the Pre-TED. If ATG, alemtuzumab, or cyclophosphamide is planned after</td>
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<td>Day 0, it should be reported in the GVHD prophylaxis section (questions</td>
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<td>316-341). For ATG, Campath, and Cyclophosphamide: If these agents are</td>
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<td>given for GVHD prophylaxis both prior to and after Day 0, they must be</td>
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<td>reported in separate sections of the Pre-TED form. Report doses given</td>
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<td>prior to Day 0 in the preparative regimen section of the Pre-TED</td>
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<td>(questions 168-315). If given after Day 0 as GVHD prophylaxis, report in</td>
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<td>the GVHD prophylaxis section of the Pre-TED (questions 316-341).</td>
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<tr>
<td>6/12/15</td>
<td>2000: Recipient</td>
<td>Modify</td>
<td>Modified the informational text in question 105: ATG or alemtuzumab</td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
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<td>(Campath) given for GVHD prophylaxis prior to Day 0 should be reported</td>
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<td>in the preparative regimen section of the Baseline Form. If ATG,</td>
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<td>alemtuzumab, or cyclophosphamide is given after Day 0 for GVHD</td>
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<td>prophylaxis, it should be reported in the acute GVHD prophylaxis section</td>
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<td>on the 100 Day Post-HCT Data Form. For ATG, Campath, and Cyclophosphamide</td>
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<td>: If these agents are given for GVHD prophylaxis both prior to and after</td>
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<td>Day 0, they must be reported in separate sections of the Comprehensive</td>
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<td></td>
<td>Report Forms. Report doses given prior to Day 0 in the preparative</td>
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<td>regimen section of the Baseline Form (questions 107-242). If given after</td>
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<td>Day 0 as GVHD prophylaxis, report in the GVHD prophylaxis section of the</td>
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<td>Pre-TED (questions 316-341).</td>
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<tr>
<td>Date</td>
<td>Event</td>
<td>Action</td>
<td>Details</td>
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<tr>
<td>6/12/15</td>
<td>Indicate the maximum grade of acute GVHD present during this</td>
<td>Add</td>
<td>Added text to questions 151 [2100], 92 [2200], and 22 [2300]: Indicate the maximum grade of acute GVHD present during this reporting period [including acute GVHD that persists from a previous HCT or donor cellular infusion (DCI)]. If acute GVHD was present, but the maximum grade was not documented nor is it able to be determined from the grading and staging table, leave the maximum overall grade blank and override the error as “Unknown.” <strong>Example 1:</strong> A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging/grading can be determined using Table 4 [2100, 2200] or 1 [2300]. <strong>Example 2:</strong> A recipient developed acute liver GVHD with elevated LFTs with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in Table 1; “present, grade unknown” would be the best option to report.</td>
</tr>
<tr>
<td>6/12/15</td>
<td>Added the following text to question 96: If antibodies were used</td>
<td>Add</td>
<td>Added the following text to question 96: If antibodies were used during product manipulation, select “yes” and continue with question 97. <strong>However, it is not necessary to report antibody use as part of CD34+ enrichment using the CliniMacs, Isolex, or Miltenyi devices.</strong> If antibodies were not used, select “no” and continue with question 109.</td>
</tr>
<tr>
<td>6/5/15</td>
<td>Updated daylight savings time reference webpage to</td>
<td>Modify</td>
<td>Updated daylight savings time reference webpage to <a href="http://www.timeanddate.com/time/dst/">http://www.timeanddate.com/time/dst/</a></td>
</tr>
<tr>
<td>6/5/15</td>
<td>Removed the following words from the comorbidities section in</td>
<td>Remove</td>
<td>Removed the following words from the comorbidities section in question 97: Hepatic (mild): Chronic hepatitis, bilirubin &gt; upper limit of normal to 1.5x upper limit of normal, or AST/ALT &gt; upper limit of normal to 2.5x upper limit of normal at the time of transplant, or any history of hepatitis B or hepatitis C infection. <strong>See note in question 96.</strong></td>
</tr>
<tr>
<td>6/5/15</td>
<td>Added the following box to question 6: There is an exception to this</td>
<td>Add</td>
<td>Added the following box to question 6: There is an exception to this guidance. <strong>Do not report a 10-CBA recipient’s participation using this question;</strong> select “no” for question 6 if the patient is enrolled in 10-CBA.</td>
</tr>
<tr>
<td>6/5/15</td>
<td>Modified the explanation for question 451: If more than one “other</td>
<td>Modify</td>
<td>Modified the explanation for question 451: If more than one “other molecular marker” is identified, add an additional instance in the FormsNet application for questions 453-454. … Assessments for other molecular markers known or believed to be associated with ALM may be performed. If these studies are performed, indicate “yes” “positive” or “negative” and specify the marker in</td>
</tr>
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</table>
**question 454. If another molecular marker was not performed, select “not done.”**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/5/15</td>
<td>2400: Pre-TED Modify</td>
<td>Modified the explanation for question 403: Add an additional instance in the FormsNet application for questions 410-411 if more than one “other molecular marker” is identified. … Assessments for other molecular markers known or believed to be associated with AML may be performed. If these studies are performed, indicate “yes” “positive” or “negative” and specify the marker in question 411. If another molecular marker was not performed, select “not done.”</td>
</tr>
<tr>
<td>6/5/15</td>
<td>MDS/MPN Response Criteria Modify</td>
<td>Changed the following text in HI-P: • For pre- transplant treatment platelet count of &gt; 20 ×10^9, platelet absolute increase of ≥ 30 ×10^9 • For pre- transplant treatment platelet count of &lt; 20 ×10^9, platelet absolute increase of ≥ 20 ×10^9 and ≥ 100% increase from pre-treatment level</td>
</tr>
<tr>
<td>6/5/15</td>
<td>Add</td>
<td>Added pediatric acute GVHD Gut guidelines to questions 15 [2450], 151 [2100], 92 [2200], and 22 [2300]. See table for details.</td>
</tr>
<tr>
<td>6/5/15</td>
<td>2100: 100 Days Post-HCT 2200: Six Months to Two Years Post-HCT</td>
<td>Modified text of questions 291-295 [2100] and 231-235 [2200]: Organism: From the table “Codes for Commonly Reported Organisms,” drop down menu, select the code corresponding to the identified or suspected organism … Site: From the table “Codes for Common Sites of Infection,” drop down menu, select the code corresponding to the site of the infection…</td>
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<td>Date</td>
<td>Manual Section</td>
<td>Add/Remove/Modify</td>
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<td>6/5/15</td>
<td><strong>2400: Pre-TED</strong></td>
<td>Modify</td>
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<tr>
<td>6/5/15</td>
<td><strong>2400: Pre-TED</strong></td>
<td>Modify</td>
</tr>
<tr>
<td>6/5/15</td>
<td>• <strong>2200: Six Months to Two Years Post-HCT</strong> • <strong>2300: Greater Than Two Years Post-HCT</strong></td>
<td>Add</td>
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</tbody>
</table>

May 2015

<table>
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<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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<tbody>
<tr>
<td>5/29/15</td>
<td>• <strong>2100: 100 Days Post-HCT</strong></td>
<td>Modify</td>
<td>Modified text in questions 500-506 [2100], 441-447 [2200], and 262-268 [2300] to clarify FormsNet reporting: Report the total number of cells infused and specify the exponent for each cell type. If the cells were cryopreserved, report the totals after processing,</td>
</tr>
</tbody>
</table>
| 5/29/15 | **2016:** PCD Pre-HCT | **2116:** PCD Post-HCT | **Modify** | Added text for clarification in questions 42 [2016], 249 [2016], 18 [2116], and 114 [2116]:

\[
\text{total in g/dL of monoclonal protein} \times \text{total urine volume} = \text{urinary M-protein/24 hours}
\]

\[
(0.145 \text{ g/dL of monoclonal protein}) \times (1500 \text{ mL total urine}) \times (1 \text{ dL/100 mL})
\]

= 2.175 g/24 hours

| 5/29/15 | **2116:** PCD Post-HCT | **Add** | Added an informational bubble in questions 30 and 126:

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in question 31 [or 127].

An exception to the note above applies to multiple myeloma. If the flow cytometry assessment has < 5% malignant plasma cells, this result should not be reported because the result is not reliable; if no other cytogenetic or FISH assessments were performed, report “no.” However, if the flow cytometry assessment found ≥ 5% malignant plasma cells, this should be reported as evidence of disease.

| 5/29/15 | **2119:** WM Post-HCT | **Modify** | Clarified explanatory text for questions 22-23:

Indicate if the number of cycles is “known” or “unknown.” If the number of cycles is known, continue with question 23 and specify the number of cycles of chemotherapy administered. If the patient received a single administration or one line of chemotherapy, indicate a single cycle. If the patient received long-term maintenance therapy consisting of a single agent, indicate “known” for question 82; leave question 83 blank and override the error as “not applicable.” Indicate if the number of cycles is “known” or “unknown.” If known, report the number of cycles the recipient received during the reporting period for the line of therapy reported in question 23. If the therapy is not given in cycles or the...
<table>
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<th>Date</th>
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<th>Action</th>
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<tr>
<td>5/29/15</td>
<td>number of cycles is not known, select “unknown” and continue with question 24. If the number of cycles is unknown, continue with question 24.</td>
<td>Add</td>
</tr>
<tr>
<td>5/29/15</td>
<td>Added text to questions 67-68: Indicate if the number of cycles is “known” or “unknown.” If known, report the number of cycles the recipient received during the reporting period for the line of therapy being reported in question 68. If the therapy is not given in cycles or the number of cycles is not known, select “unknown” and continue with question 69.</td>
<td>Modify</td>
</tr>
<tr>
<td>5/29/15</td>
<td>Modified the text in question 363 for clarity: Example 1: A 62-year-old man is diagnosed with IgG Kappa multiple myeloma. He receives initial therapy with 6 cycles of bortezomib and lenalidomide/dexamethasone; and achieves a near complete remission (nCR). The values used to determine disease status at transplant are the values obtained at diagnosis. The comparison values used to determine disease status at transplant are the values obtained at diagnosis.</td>
<td>Add</td>
</tr>
<tr>
<td>5/29/15</td>
<td>Added the following text to VGPR: … then a ≥ 90% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria.</td>
<td>Modify</td>
</tr>
<tr>
<td>5/29/15</td>
<td>Modified explanatory text for questions 619 [2400], 229 [2016], 363 [2016], 96 [2116], and 135 [2116]: If the recipient had amyloidosis or POEMS syndrome, but no evidence of myeloma, select “Not Applicable (POEMS or Amyloidosis with no evidence of myeloma)”</td>
<td>Add</td>
</tr>
<tr>
<td>5/29/15</td>
<td>Added the following text to the subsequent transplant text: If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than Plasma Cell Disorder/Multiple Myeloma), select “no” and begin at question 1.</td>
<td>Modify</td>
</tr>
<tr>
<td>5/29/15</td>
<td>Added the following instruction to question 4: If the recipient is White, Southeast Asian, or Pacific Islander, but a more specific Race Detail is not available, report the patient is “Other [White, Southeast Asian, or Pacific Islander respectively].”</td>
<td>Modify</td>
</tr>
<tr>
<td>5/29/15</td>
<td>Added text to question 14: • The National MDS Study: The National MDS Study refers to an NHLBI-sponsored study looking at the natural history of MDS; this is not the same as 10-CMSMDS-1, the HCT for MDS</td>
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</table>
Medicare Study. If the individual’s data are being reported to the National MDS Study, continue with question 17.

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<th>Date</th>
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<tr>
<td>5/22/15</td>
<td>• 2100: 100 Days Post-HCT  • 2200: Six Months to Two Years Post-HCT  • 2300: Greater Than Two Years Post-HCT</td>
<td>Modify</td>
<td>Added “Oral Beclomethasone” to the following text in question 161-187 [2100], 102-128 [2200], and 32-58 [2300]: “Systemic” refers to drugs given by mouth, intramuscularly (IM), or intravenously (IV). “Topical” refers to drugs applied to the skin, eye drops, or inhalation therapy. An exception to this guidance would be the drugs budesonide and oral beclomethasone. They are drugs given by mouth for treatment of gut GVHD, but considered a “topical” since they’re not absorbed.</td>
</tr>
<tr>
<td>5/22/15</td>
<td>MDS/MPN Response Criteria</td>
<td>Add</td>
<td>Added the following text to CR: In some cases, there may not be a four-week interval between completion of therapy and the pre-transplant disease assessment. In this case, CR should still be reported as the status at transplant since it represents the “best assessment” prior to HCT. This is an exception to the criteria that CR be durable beyond four weeks; the pre-transplant disease status should not be changed based on early relapse or disease assessment post-transplant.</td>
</tr>
</tbody>
</table>
| 5/16/15    | 2400: Pre-TED | Modify | Removed the following text from the main page: Although data regarding recipients receiving autologous HCT are not required to be submitted as part of the C.W. Bill Young Transplant Program, the CIBMTR is highly committed to collecting data on these recipients for research studies. Centers choosing to report autologous data to the CIBMTR must report on all autologous transplants performed at their center. For more information regarding data reporting for autologous HCT, see General Instructions, Autologous Hematopoietic Stem Cell Transplant, and added information about autologous reporting: “Centers are required to complete a Pre-TED Form (F2400) for all autologous transplant recipients, whether or not they agree to have their data used in research.  

  ...  

  • Pre-TED data will make federally required annual Center Volumes report more complete and better able to inform the public about the types of HCTs occurring in the United States." |
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<tr>
<td>5/16/15</td>
<td>Removed the following text from Q159: Use the earliest date from questions 161-167 (radiation) or questions 168-315 (chemotherapy). All dates reported in the preparative regimen section must be equal to or after the date reported for this question, and added information about autologous reporting: “Use the earliest date from questions 163, (radiation), or 170-236, 253-311 (systemic therapy) and 314. Additional radiation and/or intrathecal chemotherapy start dates may be prior to the date the preparative regimen began.”</td>
</tr>
<tr>
<td>5/16/15</td>
<td>Removed the following text from Q78: Enter the date the preparative regimen began. Use the earliest date from questions 82, (radiation), or 109-176 and 193-241 (systemic therapy). All dates reported in the preparative regimen section must be equal to or after the date reported for this question, and added information about autologous reporting: “Use the earliest date from questions 82 (radiation), or 109-176 and 193-241 (systemic therapy). Additional radiation and/or intrathecal chemotherapy start dates may be prior to the date the preparative regimen began.”</td>
</tr>
<tr>
<td>5/16/15</td>
<td>Added to “Cultured (ex-vivo expansion)” under questions 73-95: If the product is expanded, also report the expansion protocol under “other” in addition to checking “cultured.”</td>
</tr>
<tr>
<td>5/16/15</td>
<td>Added the following text to question 20: “Non-U.S. centers should answer this question, regardless of FDA licensure.”</td>
</tr>
<tr>
<td>5/12/15</td>
<td>Updated manual for new 2814</td>
</tr>
<tr>
<td>5/12/15</td>
<td>Updated manual for new 2804</td>
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</table>
General Instructions

The General Instructions section of the Forms Instruction Manual contains several sections meant to aid in forms completion.

Introduction
Key Fields & Signature Lines
General Guidelines for Completing Forms

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
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<th>Description</th>
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</table>
| 1/19/17  | General Instructions | Remove            | The following subsections were removed Forms Instructions Manual and are being transferred into other data management resources:  
  - Stem Cells Therapeutic Outcomes Database
  - Center Type and Data Collection Forms
  - Autologous Hematopoietic Stem Cell Transplant
  - EBMT Centers
  - Protocols and Consent Forms
  - Unique ID Assignment (CRID) & Protected Health Information, Form 2804
  - FormsNet
  - Forms Due Report
  - CIBMTR Campus & CRC Assignment
  - Declaring Recipients Lost to Follow-Up
  - Recipient Transfers
  - How to Avoid Errors
  - Reimbursement for Forms Completion
  - Continuous Process Improvement
  - On-site Data Audits
  - Helpful Websites and CIBMTR Contact Information

Please contact your center’s CRC for assistance with any of these topics while this information is being updated and transferred. Retired versions of these sections may be found here.
Introduction

The Center for International Blood and Marrow Transplant Research (CIBMTR) brings together the expertise and unique resources of two leaders in the field of blood and marrow transplant research: the National Marrow Donor Program® (NMDP) and the Medical College of Wisconsin’s International Bone Marrow Transplant Registry and Autologous Blood and Marrow Transplant Registry.

This partnership makes it easier to design, conduct and support clinical studies that involve large numbers of recipients from multiple transplant centers. The CIBMTR is committed to increasing application and access to cellular transplant therapy, as well as improving outcomes. The ultimate goal is to help more transplant recipients live longer, healthier lives.

The CIBMTR will expand research activities to increase scientific knowledge of blood and marrow transplantation through:

- Retrospective studies of the world’s largest blood and marrow transplant databases and tissue sample repositories to identify the most promising transplant approaches and the recipients most likely to benefit from this therapy.
- Research in immunobiology to better understand how transplantation works including how to harness the power of the immune system to control cancer.
  - Prospective, multi-center trials to increase the safety and success of transplantation.
- Transplant-focused biostatistics expertise to assist researchers in accessing, analyzing and presenting scientific studies.
- Research to improve access to health care services.

Specifically, the CIBMTR will:

- Define key areas for future research in collaboration with leading scientists, physicians and others in the blood and marrow transplant community.
- Secure critical research funding through partnerships with government, industry and other private parties.
- Design and implement clinical studies.
- Offer expertise for the application of biostatistics, database development and study design in blood and marrow transplant.
- Make available research resources including the world’s largest clinical database of related blood and marrow transplants, along with repositories of thousands of matched tissue samples from transplant recipients and their donors – including significant numbers of samples for many rare diseases.
Key Fields & Signature Lines

Key Fields

Accuracy of the Key Fields is essential for ensuring that:

- Data are being reported for the correct recipient.
- Outcomes data accurately reflects appropriate transplant type and product for each transplant center.
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other agency.

The Key Fields precede the form body and are automatically populated in the FormsNet3 application based on information provided on the CRID Assignment Form 2804. If errors are noted in the key fields, correct Form 2804 and then review it for accuracy. After Form 2804 has been corrected, verify data has been updated on all completed forms. If the data has not been updated automatically, centers will need to reprocess the completed forms to correct the key field data. If errors are noted in key fields for second or subsequent transplants, contact your CRC to make any necessary corrections to the transplant or product type. Transplant and product type will not be automatically populated on product or donor specific forms (Forms 2004, 2005, and 2006) and will need to be manually reported.

Signature Lines

The FormsNet3 application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.
General Guidelines for Completing Forms

Fields Requiring a Date

For fields that require a date, if an exact date is not known use the process listed below. This process should be used only if the dates fit within the logical timeframe of the form (i.e. contact date, diagnosis date, relapse date, etc). To assist with the audit process, transplant centers should briefly note their logic in assigning dates that are unknown in the medical record.

**Day is Unknown:** Report the day of the month as the 15th. If the 15th does not make logical sense in relation to the other date fields reported on the form, then use either the 1st or 30th. Report month and year as documented in the medical record.

*Example 1:* The month and year of diagnosis is May 2006; the first treatment was given on May 17, 2006. The date of diagnosis should be reported as May 15, 2006, as this fits logically within the timeframe of the form.

*Example 2.* The month and year of diagnosis is May 2006; the first treatment was given on May 4, 2006. The date of diagnosis should be reported as May 1, 2006, since May 15, 2006 is not logical within the timeframe of the form.

**Month and Day Are Unknown:** Report the month as June and the day as the 15th. If the 15th does not make logical sense in relation to the other date fields reported on the form, then report the day as either the 1st or the 30th. Report the year as documented in the medical record.

*Example 1:* The year of diagnosis is 2006, but an exact diagnosis date is not known; the first treatment was given August 1, 2006. The date of diagnosis should be reported June 15, 2006, as this fits logically within the timeframe of the form.

*Example 2.* The year of diagnosis is 2006, but an exact diagnosis date is not known; the first treatment was given on June 14, 2006. The date of diagnosis should be reported as June 1, 2006, since June 15, 2006 is not logical within the timeframe of the form.

*Example 3:* The recipient is described as being diagnosed in the winter of 1998 with CLL, however no specific date can be verified. The transplant center may report a date in the middle of the season range, in this case February 15, 1998, as the designated date of diagnosis.

**Month, day, and year are unknown:** In the FormsNet3 application, leave the date field blank and override the error. For paper form submission, draw a single line through the date field, write “unknown” in the margin and date and initial.
The remainder of this section is undergoing revision. For an archived copy of this information, please see Retired Form Manuals.
2804/2814: CRID Assignment and Indication

Find information for the 2804: CIBMTR Research ID Assignment Form and Indication for CRID Assignment Form in the navigation of the table of contents. These forms are required to receive a CRID for a new individual and to report their indication for assignment.

- [2804: CIBMTR Research ID Assignment Form](#)
- [2814: Indication for CRID Assignment](#)
2804: CIBMTR Research ID Assignment Form

The CIBMTR Research ID (CRID) is a unique identifier assigned when an individual is registered with the CIBMTR as receiving a cellular therapy, including hematopoietic stem cell transplant (HCT), treatment for marrow toxic injuries, and certain non-cellular therapies. The CRID Assignment Form 2804 collects the information required to create a lifelong identification number specific to an individual, and certain data fields are used to ensure that the same individual does not inadvertently receive multiple CRID assignments.

By creating a unique identifier and ensuring participants receive only a single CRID, the CIBMTR is better able to carry out its charge as a co-contractor of the C.W. Bill Young Transplantation Program with the responsibility for maintaining the Stem Cell Therapeutic Outcomes Database (SCTOD). The CRID is used to ensure the accuracy of center-specific outcomes by adjusting survival expectation for patients receiving multiple HCTs and allowing for verification of survival status within the National Death Index. Additionally, the CRID can be used to help re-establish contact with individuals who are lost to follow-up and to ensure that all allogeneic HCT recipients in the United States, or who receive a product from the United States, are reported to the CIBMTR.

Completeness of the Form 2804 is important for ensuring that individuals are not assigned multiple CRIDs over their lifetime. The system is able to assign an identification number when some identifying fields are missing, but this increases the risk of duplicate reporting. Therefore, the following guidelines have been established:

- **For all individuals**, complete the form as thoroughly as possible.
- In the event of a state law or IRB policy that supersedes federal statute, centers may opt out of providing some of these data.

The CIBMTR carefully ensures that identifying information is collected and stored in a secure manner. The electronic systems that generate CRIDs have undergone rigorous certification and authorization from HRSA’s Office of Information Technology and they comply with all United States regulations relevant to security of data in federal databases.

Once the identifying data are entered into FormsNet and a CRID is assigned, the identifying data are no
longer visible to the transplant center or CIBMTR staff. For that reason, it is important that the information is accurate when submitted. The identifying information used to create the CRID will not appear on any subsequent forms or correspondence.

Transplant centers need to take appropriate measures at their site to secure the identifying information used to generate the CRID.

This form only needs to be completed for patients who have not previously been assigned a CIBMTR Research ID (CRID). If a duplicate CRID is inadvertently created or identified, please contact your CRC to resolve.

**Q1-9: Demographics**
**Q10-13: Recipient Identifiers**
**Q14-17: Outcomes Registry Reporting**

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below.

If you need to reference the historical version for this form, please find the retired manual section on the [Retired Forms Manuals](#) webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
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<tr>
<td>8/29/16</td>
<td>2804: CIBMTR Research ID Assignment form</td>
<td>Add</td>
<td>Added information banner to <a href="#">2804 introduction page</a>: Reporting of all HCTs is important to ensure the continued epidemiological integrity of the CIBMTR outcomes registry. The exception to this is if your center performs but does not report autologous HCTs.</td>
</tr>
</tbody>
</table>
| 5/29/15| 2804: CIBMTR Research ID Assignment form | Add               | Added text to [question 14](#): 
- The National MDS Study: The National MDS Study refers to an NHLBI-sponsored study looking at the natural history of MDS; this is not the same as 10-CMSMDS-1, the HCT for MDS Medicare Study. If the individual’s data are being reported to the National MDS Study, continue with question 17. |
| 05/12  | 2804: CIBMTR                     | Add               | Updated manual for new 2804                                                               |
| 2015 | Research ID Assignment form |
Q1-9: Demographics

This form must be completed for all individuals on whom data is submitted to CIBMTR. CIBMTR is a Public Health Authority (PHA) under the Health Insurance Portability and Accountability Act (HIPAA). In this capacity, CIBMTR is authorized to collect individually identifiable health information without consent or authorization of the individual. The PHA designation also allows transplant centers, which fit the definition of covered entities, to disclose these data to CIBMTR under 45 CFR 164.512 (Privacy Rule) without direct consent or authorization of the recipient.

Complete all data fields as thoroughly as possible.

Questions 1-2: First Name, Last Name

Report the individual’s complete legal first name in question 1 and complete legal last name in question 2. If you are unable to report the full legal name, reporting initials or partial name can reduce duplicate CRIDs.

Question 3: Date of birth

Reporting the individual’s date of birth is required for all Form 2804 submissions. Report the individual’s date of birth and continue with question 4.

Questions 4-6: Location of birth

Report the individual’s country of birth in question 4. If applicable, specify city and state of birth in questions 5-6, respectively.

Question 7: Sex

Report the individual’s biological sex.

Question 8: Social security number

Report the individual’s social security number. If the individual’s social security number is unknown or the individual is not a United States citizen, leave this data field blank.

Question 9: Patient’s mother’s maiden name (optional for non-U.S. centers)

Report the individual’s mother’s maiden name. This field may be left blank if the individual’s mother’s maiden name is unknown, the autologous HCT recipient declined to release mother’s maiden name, or your
transplant center is located outside the United States.
Q10-13: Recipient Identifiers

Complete all additional individual identifiers, as applicable.

**Question 10: Recipient NMDP ID**

Report the seven-digit recipient ID (RID) assigned by the National Marrow Donor Program (NMDP). If the individual has never been assigned an NMDP RID, leave this data field blank.

**Question 11: Recipient IUBMID**

Report the six-digit IUBMID previously assigned to the individual. The IUBMID is the individual identifier previously assigned by the International Bone Marrow Transplant Registry (IBMTR), which was the precursor to the current CRID system. If an IUBMID was previously assigned, complete and continue with question 12; if no IUBMID was previously assigned, continue with question 13.

**Question 12: Team ID**

Report the four-digit team ID; this data field is required if question 11 is answered. The Team ID is a precursor to the current CIBMTR center number (CCN) system, used by the IBMTR. If the individual has a previously assigned IUBMID, there should be an associated Team ID.

**Question 13: Institution-specific subject ID**

Report the subject identifier used for any center-specific outcomes registration, transplant study protocol(s), or other unique subject identifier used for internal institutional tracking. Do not report the recipient medical record number (MRN). If the individual does not have an institution-specific subject ID, leave this data field blank.
Q14-17: Outcomes Registry Reporting

Indicate and provide identifiers for all other outcomes registries the individual’s data are being reported to. If the individual's data are not being reported to any other outcomes registries, continue with the signature section of the form. If the individual’s data are being reported to multiple additional outcomes registries, create a new instance for each additional outcomes registry.

Question 14: Specify outcomes registry

Indicate all outcomes registries the individual’s data are being reported to; if the individual is participating in more than one registry, add a new instance for each. As a reference, the registry acronyms and instructions for proceeding with the remainder of the form are detailed below:

- EBMT: European Society for Blood and Marrow Transplantation, continue with question 15.
- USIDNET: United States Immunodeficiency Network, continue with question 17.
- APBMT: Asia-Pacific Blood and Marrow Transplantation Group, continue with question 17.
- CBMTG: Canadian Blood and Marrow Transplant Group, continue with the signature section of the form or create an additional instance of questions 14-17 to report additional outcomes registries.
- EMBMT: Eastern Mediterranean Blood and Marrow Transplantation Group, continue with question 17.
- The National MDS Study: The National MDS Study refers to an NHLBI-sponsored study looking at the natural history of MDS; this is not the same as 10-CMSMDS-1, the HCT for MDS Medicare Study. If the individual’s data are being reported to the National MDS Study, continue with question 17.
- Other outcomes registry, continue with question 16

Question 15: EBMT CIC

For individual with data reported to EBMT, report the four- to five-digit Centre Identification Code (CIC) identifying the transplant center. Continue with question 17 and specify the EBMT subject identifier.

Question 16: Specify other outcomes registry

Report the other outcomes registry individual data are being reported to. Use the complete registry name, rather than acronyms or abbreviations. Continue with question 17.

Question 17: Outcomes registry subject ID

Report the registry subject ID for the applicable registry; if multiple instances of questions 14-17 are being reported, ensure the registry subject ID corresponds with the registry indicated in the same instance of question 14. Continue with the signature section of the form or create an additional instance of questions...
14-17 to report additional outcomes registries.
2814: Indication for CRID Assignment

The Indication for CRID Assignment (Form 2814) collects information to initiate CIBMTR reporting on appropriate research or data collection forms. This form must be completed for the first indication requiring the individual to register for a CIBMTR Research ID (CRID). Subsequent interventions of the same indication – hematopoietic cellular transplant, non-transplant cellular therapy, marrow toxic injury, and non-cellular therapy – do not require an additional Form 2814; however, a subsequent, new indication may require completion of another Form 2814. Examples of an indication change that would require completion of another Form 2814 include:

- Transplant recipient becomes a marrow toxic injury RITN patient
- Cellular therapy recipient becomes a marrow toxic injury RITN patient
- Marrow toxic injury RITN patient receives cellular therapy or transplant
- Non-cellular therapy patient with any indication change

Reporting a subsequent transplant using the indication form is not allowed. Report the subsequent transplant on the latest follow up form for the most recent transplant.

Another Form 2814 would not be required for interventions such as subsequent transplant or subsequent round of cellular therapy.

Q1: Indication
Q2-5: Hematopoietic Cellular Transplant
Q6: Cellular Therapy
Q7: Marrow Toxic Injury
Q8-10: Non-Cellular Therapy

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
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</thead>
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<tr>
<td>7/26/16</td>
<td>2814: Indication for CRID Assignment</td>
<td>Modify</td>
<td>Version 2 Released</td>
</tr>
</tbody>
</table>
Q1: Indication

Question 1: What is the indication for CIBMTR Research ID (CRID) assignment?

Indicate whether the individual will be receiving hematopoietic cellular transplant (HCT), non-transplant cellular therapy, marrow toxic injury therapy, or non-cellular therapy.

Hematopoietic cellular transplant (HCT) is a transplant of bone marrow, peripheral blood stem cells, umbilical cord blood, or other cellular product containing CD34+ cells, also known as hematopoietic progenitor cells.

Non-transplant cellular therapies may be derived from a hematopoietic or non-hematopoietic tissue source and can be utilized for a broad range of indications, including autoimmune, cardiovascular, peripheral vascular, and neurologic diseases; these are often referred to as cellular therapies for regenerative medicine (CTRM).

Marrow toxic injury should only be reported by Radiation Injury Treatment Network (RITN) centers in the event of mass casualty incident resulting in marrow toxic injury. Do not report marrow toxic injury for individuals receiving pre-transplant radiation therapy or for accidental, isolated exposures to radiation.

If you are completing this form for a patient at a RITN center and are uncertain if the patient’s data should be reported using the marrow toxic injury indication, contact your CIBMTR CRC or email RITN@nmdp.org.

Non-cellular therapy may include vaccine or immunomodulatory trials; report non-cellular therapy when the patient is enrolled on a trial or protocol requiring data submission to CIBMTR.

If the reported indication is:

- Hematopoietic cellular transplant, complete questions 2-5.
- Non-transplant cellular therapy, complete question 6
- Marrow toxic injury, complete question 7
- Non-cellular therapy, complete questions 8-10.
**Q2-5: Hematopoietic Cellular Transplant (HCT)**

**Questions 2-4: Specify the planned cell source(s) for this HCT**

Indicate if the recipient will be receiving cells from an autologous, related allogeneic, or unrelated allogeneic source. Indicate all that apply; if the recipient is receiving multiple products, ensure all product sources are specified. Report only the sources for the current hematopoietic cellular transplant; do not report cellular sources for previous hematopoietic cellular transplant(s), co-infusions, or planned subsequent hematopoietic cellular transplant(s).

**Question 5: Planned HCT date**

Report the planned date of transplant; this should be the first date of transplant reported to CIBMTR for this recipient. If the planned date of infusion changes, the electronic form should be updated in FormsNet3SM, as this data field is used to populate the date of infusion on the patient’s other case report forms. If the recipient has a previous transplant already reported to CIBMTR, review previous transplant follow-up forms and ensure the subsequent transplant is correctly reported on the follow-up forms, which will prompt appropriate follow-up forms to come due; a new or additional Form 2814 is not required. Continue with the signature section of the form.
Q6: Cellular Therapy

Question 6: Planned infusion date

Report the planned date of cellular infusion. If the planned date of infusion changes, the electronic form should be updated in FormsNet3<sup>SM</sup>, as this data field is used to populate the date of infusion on the patient’s other case report forms. Continue with the signature section of the form.
Q7: Marrow Toxic Injury

Question 7: Event date

Report the date the patient was exposed to radiation. This should be the same as the date of the mass casualty event resulting in marrow toxic injury. A Radiation Injury Treatment Network (RITN) center should only report marrow toxic injury in the event of mass casualty incident resulting in marrow toxic injury. Do not report marrow toxic injury for individuals receiving pre-transplant radiation therapy or for accidental, isolated exposures to radiation. Continue with the signature section of the form.
Q8-10: Non-Cellular Therapy

Questions 8-9: Specify the disease for which non-cellular therapy was given

Indicate if the individual is receiving non-cellular therapy as treatment for MDS, multiple myeloma, myelofibrosis, sickle cell disease, or another disease. If the research participant is receiving therapy for a disease that is not captured in any of the above categories, specify in question 9.

Question 10: Enrollment date (date of consent)

Report the date of consent for enrollment on non-cellular therapy protocol. Continue with the signature section of the form.

Signature Lines:
The FormsNet3SM application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.
Transplant Essential Data (TED) Manuals

The Transplant Essential Data (TED) Manual section contains information on the successful completion of TED forms. The Pre-TED Manual has several links to disease specific response criteria which can be found in the Comprehensive Disease Specific Manual subsections.

Contents of this section:

2400: Pre-TED
2402: Disease Classification
2450: Post-TED

* If a Form 2004, Form 2005, or Form 2006 is required, please find these manuals in the Comprehensive Baseline & Follow-up Forms Manuals.
All transplant centers participating in the CIBMTR must submit a Pre-TED Form for each allogeneic (related or unrelated) hematopoietic cell transplant (HCT). The Pre-TED is a requirement of the SCTOD for all United States transplant centers when either the stem cell donation or the transplant occurs within the United States. For more information regarding the SCTOD, see General Instructions, Stem Cell Therapeutics Outcomes Database.

Although data regarding recipients receiving autologous HCT are not required to be submitted as part of the C.W. Bill Young Transplant Program, the CIBMTR is highly committed to collecting data on these recipients for research studies. Centers choosing to report autologous data to the CIBMTR must report on all autologous transplants performed at their center. For more information regarding data reporting for autologous HCT, see HCT.

The Pre-TED may be submitted to the CIBMTR up to two weeks prior to the start of the recipient’s preparative regimen (see Helpful Hint below). The Pre-TED is due the day of the HCT (day 0), and is past due if not received by that date.

**Helpful Hint:**
In order to avoid having to make changes to the HCT date, complete the data for the Pre-TED (in FormsNet3 or on paper), but do not submit the form until the first dose of the preparative regimen is given.

**For recipients receiving a subsequent HCT:**
Transplant centers must submit a Pre-TED for all subsequent HCTs; this includes recipients assigned to the TED Forms and the Comprehensive Report Forms by the form selection algorithm.

For the majority of subsequent HCTs, the recipient will remain on the original follow-up form track assigned by the form selection algorithm. For more information regarding center type and the form selection algorithm, see Section 1 in the Center Reference Guide. A recipient may need to change tracks if enrolled on a study that requires comprehensive forms.

For recipients of multiple transplants, transplant centers are not granted access to the new Pre-TED Form in
FormsNet3 until the Post-TED (Form 2450) or Post-Infusion Data Form (Form 2100) from the previous transplant has been completed.

Transplant centers can use the FormsNet3 application to determine if a Pre-TED is due by either: 1) accessing the Forms Due Report, or 2) entering the recipient’s unique ID (CRID) in the Patient Forms Due field.

**Links to Sections of the Form:**
- Q1-10: Recipient Data
- Q11-28: Hematopoietic Cellular Transplant
- Q29-63: Donor Information
- Q64-71: Consent
- Q72-90: Product Processing/Manipulation
- Q91-94: Clinical Status of Recipient Prior to the Preparative Regimen
- Q95-155: Comorbid Conditions
- Q156-316: Pre-HCT Preparative Regimen
- Q317-343: GVHD Prophylaxis
- Q344: Other Toxicity Modifying Regimen
- Q345-357: Post-HCT Disease Therapy Planned as of Day 0

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
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</table>
| 2/27/19 | 2400: Pre-TED  | Modify            | Modified (removed text is struck out below, updated text is in red) the instructions for question 52 on where to report cellular therapy product data for products that are not intended to achieve hematopoietic engraftment. If infusions of additional cells (not intended to produce engraftment) were given prior to the HCT being reported (i.e., prior to clinical day 0), the cells must be reported as a product on the Pre-TED Form (Form 2400, question 51) and on a separate Cellular Therapy Infusion Product Form (Form 4006 4003). If the additional cells were infused post-HCT, for any reason other than a subsequent HCT, they should be reported as a DCI on the appropriate follow-up form. Reporting the additional cells (given pre-HCT and not intended to produce engraftment) on the Form 4006 4003 is the only mechanism the CIBMTR has in place to collect this data and ensure that the quality assurance data is reported to CIBMTR.org.
<table>
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<tr>
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<th>Action</th>
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<tbody>
<tr>
<td>12/3/18</td>
<td>Modify</td>
<td>Updated link in the 2400 Pre-TED to reflect current reporting instructions for autologous transplants.</td>
</tr>
<tr>
<td>11/20/18</td>
<td>Add</td>
<td>Added the following text (in red below) for Question 5: Enter the ZIP code in which the recipient resides. Only five digits are required; however, if the ZIP+4 (nine digit) code is available, please report it in this field.</td>
</tr>
<tr>
<td>9/20/18</td>
<td>Add</td>
<td>Added in text that mid-level health care providers (NPs and PAs) can also assign performance scores.</td>
</tr>
<tr>
<td>6/1/18</td>
<td>Modify</td>
<td>Re-formatted the reporting instructions for pre-HCT CMV-antibody results (question 94) and included the following additional consideration (in red below): Documented history of “reactive” CMV: In cases where a recipient has a documented history of a “reactive” CMV test and does not have a history of IVIG or blood transfusions from a CMV positive donor, “reactive” should be reported for the CMV status even if the CMV test is repeated during the pre-HCT work-up phase and is “non-reactive”.</td>
</tr>
</tbody>
</table>
| 5/21/18    | Modify    | Added (in red below) and removed (struck out below) text from the instructions for reporting comorbidities (questions 98-134).  

**Arrhythmia:** Any history of any type of arrhythmia that has necessitated the delivery of a specific antiarrhythmic agent. Examples include, but are not limited to, atrial fibrillation or flutter, sick sinus syndrome, or and ventricular arrhythmias requiring treatment.  

**Cardiac:** Any history of coronary artery disease (one or more vessel coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, and / or ejection fraction ≤ 50% (shortening fraction < 26 for pediatric recipients)% on the most recent test.  

**Cerebrovascular disease:** Any history of transient ischemic attack, subarachnoid hemorrhage, and / or cerebrovascular accident cerebral thrombosis embolism, or hemorrhage.  

**Diabetes:** Diabetes or steroid-induced hyperglycemia requiring continuous treatment with insulin or oral hypoglycemics in the last 4 weeks, but not diet alone.  

**Heart valve disease:** Moderate or severe valve stenosis or insufficiency (mitral, aortic, tricuspid, or pulmonary) as determined by echocardiogram, prosthetic mitral or aortic valve, and / or symptomatic mitral valve prolapse. Except asymptomatic mitral prolapse.  

**Psychiatric disturbance:** The presence of any mood, anxiety, or other psychiatric disorder requiring continuous treatment during the last four weeks. Examples include, but are not limited to, depression, anxiety, bipolar disorder, or and schizophrenia requiring psychiatric treatment in the last 4 weeks.  

**Pulmonary (moderate):** Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 66-80% or dyspnea on slight activity at transplant. Use the Dinakara equation below to determine the DLCOc if only an uncorrected value is provided. For recipients assessed by a postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity.  

Dinakara Equation: DLCOc = {uncorrected DLCO} / [0.06965 x {hemoglobin g/dL}]  

**Pulmonary (severe):** Corrected diffusion capacity of carbon monoxide (e.g.,
<table>
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<th>Description</th>
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<td>5/7/18</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Modified language on how to report Drugs After Transplant, replaced “day 0” with “transplant” to clarify how to report drugs planned for day 0.</td>
</tr>
<tr>
<td>5/7/18</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added note box to capture all comorbidities including those that are considered complications of the primary disease for transplant and provided examples.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added text (in red below) to the description of HLA-mismatched relative provided in the instructions for question 40. Includes: Siblings who are not HLA-identical and all other blood-related relatives who have at least one HLA mismatch (e.g., parents, aunts, uncles, children, cousins, half-siblings). This includes haploidentical donors.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Added Haploidentical Donors note box to the instructions for question 40.</td>
</tr>
<tr>
<td>10/14/17</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Updated text in Hepatic and Renal Comorbidities note box. Added text is highlighted red and deleted text is struck out. Hepatic Comorbidity: The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between days – 24 &amp; -10 (or between days – 40 &amp; -10 if only a single value was reported between days – 24 &amp; day -10) before HCT, and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days – 40 &amp; -25 as the second value. Renal (Moderate/Severe) Comorbidity: Serum creatinine &gt; 2 mg/dL or &gt; 177 μmol/L, as detected in at least two lab values on two different days within a period extending between days – 24 &amp; -10 (or between days – 40 &amp; -10 if only a single value was reported between days – 24 &amp; day -10) before HCT, and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days – 40 &amp; -25 as the second value.</td>
</tr>
<tr>
<td>4/4/17</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Instruction change for questions 91-93: Age range for Lansky Scale has been updated from recipients less than 16 years old to recipients one year old to less than 16 years old. If the recipient is less than one year old, questions 91-93 should be left blank.</td>
</tr>
<tr>
<td>3/10/17</td>
<td>2400: Pre-TED</td>
<td>Add</td>
<td>Clarification has been added to the instructions for questions 136-155 (in bold below): Use questions 153-155 to report any prior hematologic malignancies that were not listed in questions 136-152. Solid tumors should be reported in questions 144-131, not in questions 153-155.</td>
</tr>
<tr>
<td>1/31/17</td>
<td>2400: Pre-TED</td>
<td>Modify</td>
<td>Version 4 of the 2400: Pre-TED section of the Forms Instruction Manual released. Version 4 corresponds to revision 5 of the Form 2400.</td>
</tr>
</tbody>
</table>
Q1-10: Recipient Data

Question 1: Date of Birth

The date of birth is automatically populated based on the value reported on the CRID Assignment Form (2804). Verify that the date of birth is correct. If an error is noted, correct Form 2804 and verify that the date of birth has been updated on the Pre-TED Form.

Question 2: Sex

The recipient’s sex is automatically populated based on the value reported on the CRID Assignment Form (2804). Verify that the recipient’s sex is correct. If an error is noted, correct Form 2804 and verify that the recipient’s sex has been updated on the Pre-TED Form.

Question 3: Ethnicity

Indicate the recipient’s ethnicity. The United States Office of Management and Budget (OMB) has defined ethnicity as culturally or geographically determined. The distinction between Hispanic and non-Hispanic is for the purpose of the United States census and reporting of SCTOD data. According to the OMB, “Hispanic” is an ethnic designation based upon where someone (his or her ancestors) was raised (e.g., “Latin America”). Hispanic people may be of any race. The CIBMTR recognizes regional differences with regard to the interpretation of ethnicity throughout the world.

If the recipient is not a resident of the USA, select “not applicable.”

If the recipient declines to provide this information or the recipient’s ethnicity is not documented, select “unknown.”

For more information regarding ethnicity, see Appendix I.

⭐ Reporting More Than One Race

**FormsNet3 application:** Complete question 4 for each race the recipient identifies with by adding an additional instance in the FormsNet application.

**Paper form submission:** Copy question 4 and complete for each race the recipient identifies with.

Question 4: Race

Indicate the recipient’s race. If this recipient has reported that they are more than one race, you may
indicate each race by adding an additional instance in the FormsNet application. The race groups provided are specific to the United States.

For non-U.S. centers, select “not reported” if the rules/regulations of your country prohibit the collection or reporting of race data (or due to lack of documentation). If race is reported, it may be necessary to consult with the recipient to select the race group(s) with which they most closely identify.

If the recipient declines to provide this information, select “not reported.”

If the recipient’s race is not documented, select “unknown.”

For more information regarding race, see Appendix I.

Question 5: ZIP or postal code for place of recipient’s residence (USA recipients only)

Enter the ZIP code in which the recipient resides. Only five digits are required; however, if the ZIP+4 (nine digit) code is available, please report it in this field.

Question 6: Is the recipient participating in a clinical trial?

Indicate if the recipient is a registered participant with BMT-CTN, RCI-BMT, USIDNET, COG, and/or another clinical trial sponsor that uses CIBMTR forms to capture outcomes data. If “yes,” continue with question 7. If “no,” continue with question 11.

• BMT-CTN: Blood and Marrow Transplant Clinical Trials Network
• RCI-BMT: Resource for Clinical Investigation in Blood and Marrow Transplant
• USIDNET: United States Immunodeficiency Network
• COG: Children’s Oncology Group

* Reporting Participation in More Than One Study

FormsNet3 application: Complete questions 7-10 for each study the recipient is participating in by adding an additional instance in the FormsNet application.

Paper form submission: Copy questions 7-10 and complete for each study in which the recipient is participating.

If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.

Questions 7-8: Study Sponsor

Select the study sponsor of the clinical trial the recipient is participating in. If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.
If the study sponsor is reported as “BMT-CTN” or “RCI-BMT,” continue with question 9.

If the study sponsor is reported as “USIDNET” or “COG,” continue with question 10.

If “other sponsor” is reported, specify the study sponsor in question 8 and continue with question 10.

**Question 9: Study ID Number**

Select the recipient’s Study ID number.

**Question 10: Subject ID**

Enter the recipient’s USIDNET, COG, or other sponsor Subject ID.

If the recipient is participating in a BMT-CTN study and the EMMES ID is known, enter it here.

If the recipient is participating in an RCI-BMT study, enter the Subject ID given at the time of successful enrollment.
Q11-28: Hematopoietic Cellular Transplant (HCT)

Question 11: Date of this HCT

Report the intended start date of the HCT. If the infusion is planned to last several days, enter the first day the infusion is scheduled to start.

If the Pre-TED was submitted prior to day 0, and the planned infusion date has changed, the original planned date of the HCT will automatically be reported in FormsNet3 on either the Post-TED (Form 2450) or the Post-HCT Data Form (Form 2100). For the recipient’s first transplant, the HCT date may be changed on the Form 2804. For a subsequent transplant, the date may be changed on the form (Form 2100 or 2450) where the subsequent transplant was originally reported.

If the recipient is scheduled to receive a combination of cellular therapy and stem cell infusions, contact your center’s CIBMTR CRC for reporting requirements.

Question 12: Was this the first HCT for this recipient?

Indicate if this is the recipient’s first transplant. First transplant is defined as the first transplant the recipient ever receives, not the first transplant the recipient receives at your facility.

If “yes,” and this is an autologous transplant, continue with question 13.

If “yes,” and this is an allogeneic transplant, continue with question 29.

If “no,” continue with question 15.

Question 13: For autologous HCTs only: Is a subsequent HCT planned as part of the overall treatment protocol (not as a reaction to post-HCT disease assessment)?

If, at the time of the current HCT, a second (tandem transplant) or subsequent HCT is planned according to the protocol, check “yes” even if the recipient does not receive the planned subsequent HCT. The word “planned” should not be interpreted as: if the recipient relapses, then the “plan” is to perform a subsequent HCT. If “yes,” continue with question 14. If “no,” continue with question 29.

Question 14: Specify subsequent HCT planned:

Indicate whether the planned subsequent HCT is autologous or allogeneic and continue with question 29.
Question 15: Specify the number of prior HCTs:

Enter the number of prior HCTs for the recipient. An HCT event is defined as an infusion of mobilized peripheral blood stem cells (PBSC), bone marrow, or cord blood. For more information on how to distinguish infusion types [example: HCT versus donor cellular infusion (DCI)], see Appendix D.

For recipients who have received a previous HCT (prior to the HCT for which this form is being completed), the following are examples of how to calculate the number of prior HCTs.

**Example 1:** A recipient was previously transplanted under a protocol that included an infusion of cells over multiple days: day 0, day +1 and day +2. This series of infusions is considered one HCT event (as opposed to three HCT events) and should be counted as HCT Event #1.

After receiving the infusion, the recipient had relapse of disease. The recipient is scheduled to receive a subsequent HCT including a preparative regimen. This HCT is HCT Event #2. One prior HCT should be reported.

**Example 2:** A recipient previously received an allogeneic HCT (HCT Event #1). Then, due to delayed neutrophil recovery, the recipient received additional cryopreserved allogeneic mobilized PBSC from the original donor, without a preparative regimen (i.e., “boost” – HCT Event #2).

After receiving the boost, the recipient had relapse of disease. The recipient is scheduled to receive a subsequent allogeneic HCT with preparative regimen (HCT Event #3). Two prior HCTs should be reported.

**Example 3:** A recipient previously received an autologous HCT (HCT Event #1). Then due to delayed neutrophil recovery, the recipient received additional cryopreserved autologous cells without a preparative regimen (i.e., “boost” which is not counted as an HCT event because the intent of the autologous infusion is to treat the graft failure).

The boost is successful, but a few years later the recipient develops a new malignancy. The recipient is scheduled to receive a subsequent autologous HCT with preparative regimen (HCT Event #2). One prior HCT should be reported.

If the recipient receives an infusion due to poor graft response, count the infusion as a subsequent HCT. The exception to this is “autologous rescue.” Autologous rescue should not be counted as a separate HCT, and the data collection forms will not start over (i.e., the forms will continue from the previous HCT).
Questions 16-19: What was (were) the prior HCT source(s)?

Select the cellular source for each of the recipient’s previous HCTs as either autologous, allogeneic unrelated, allogeneic related, or syngeneic (identical twin).

Question 20: Date of the last HCT (just before current HCT):

Report the date of the recipient’s last autologous or allogeneic (related or unrelated) HCT. Although the CIBMTR requests a Pre-TED for each HCT, there may be circumstances where a prior HCT was not reported (e.g., prior autologous HCT or HCT performed at another center). Reporting the recipient’s last HCT enables the CIBMTR to appropriately account for recipient survival status in the database.

Question 21: Was the last HCT performed at a different institution?

Indicate if the last HCT was performed at another institution. If “yes” continue with question 22. If “no” continue with question 23.

Question 22: Specify the institution that performed the last HCT:

Report the name, city, state, and country of the institution where the recipient’s last HCT was performed. These data are used to identify and link the recipient’s existence in the database and, if necessary, obtain data from the previous transplant center.

Question 23: What was the HSC source for the last HCT?

Report the stem cell source of the recipient’s last HCT as either autologous, allogeneic unrelated or allogeneic related (including syngeneic).

Question 24-28: Reason for current HCT:

Indicate the reason for the current HCT (check only one). If this was a subsequent transplant, verify that this answer is consistent with the reason for the subsequent transplant reported on the previous series of report forms.

No hematopoietic recovery: Additional stem cells are required because the recipient did not recover their granulocytes following previous high-dose therapy and HCT.

Partial hematopoietic recovery: Additional stem cells are required because the recipient’s hematopoietic recovery was deemed insufficient or too slow for the recipient to survive following previous high-dose therapy and HCT (ANC was never greater than or equal to $0.5 \times 10^9/L$ for three consecutive days).
**Graft failure/rejection after achieving initial hematopoietic recovery:** Additional stem cells are required because the recipient's hematopoietic recovery declined indefinitely after the initial hematopoietic recovery (ANC was greater than or equal to $0.5 \times 10^9$/L for three consecutive days, and then declined to below $0.5 \times 10^9$/L for three consecutive days). If the reason is graft failure or rejection after initial recovery, also complete question 25.

**Persistent primary disease:** Additional stem cells are required because the recipient was transplanted with disease present, and never entered a remission following the previous transplant.

**Recurrent primary disease:** Additional stem cells are required because the disease for which the recipient was transplanted relapsed following the previous transplant. If the reason is recurrent primary disease, also complete question 26. Ensure that the date of recurrent primary disease matches the relapse/progression date reported on the previous transplant’s appropriate follow-up form.

**Planned second HCT, per protocol:** Additional stem cells are given because the protocol planned for a subsequent transplant/infusion. This includes all planned subsequent transplants (including triple or quadruple transplants). This transplant is not based upon recovery, disease status, or any other assessment.

**New malignancy (including PTLD and EBV lymphoma):** Additional stem cells are required because the recipient has developed a new malignancy. This does not include a transformation or progression of the original malignancy for which the recipient was transplanted. If the reason is a new malignancy, also complete question 27, and attach a copy of the pathology report using the “Add Attachment” feature in FormsNet3. Ensure that the date of diagnosis for the new malignancy matches the date of diagnosis for the new malignancy reported on the previous transplant’s appropriate follow-up form.

**Stable, mixed chimerism:** Verify with the transplant physician that the cells given should be reported as a subsequent transplant and that stable, mixed chimerism is the reason for the transplant.

**Declining chimerism:** Additional stem cells are required because the percentage of donor cells present versus recipient cells present is decreasing. This is usually due to an underlying cause such as graft failure, graft rejection, or recurrent disease.

**Other:** Additional stem cells are required and/or given for a reason other than the options listed. If the HCT is for another reason, select “other” and complete question 28.
Q29-63: Donor Information

Question 29: Multiple donors

Indicate if cells from multiple different donors (multiple CBUs, combinations of other products from different donors) are to be used for this HCT. If “yes,” continue with question 30. If “no,” continue with question 31.

A supplemental infusion is defined as an infusion of cells given prior to clinical day 0 (of an HCT) for any reason other than to produce engraftment. An infusion of supplemental cells is often given in conjunction with a preparative regimen for HCT. Supplemental infusions should be included when determining if multiple donors were used for this HCT event.

For more information on supplemental infusions, see Appendix D.

Question 30: Specify number of donors

Report the number of donors used for this HCT. Note that this value should never be “1,” since multiple donors were reported in question 29.

Related CBU and Related Product from Same Donor

If the recipient receives a cord blood unit and another product from the same related donor, complete two instances of the Donor Information section (questions 31-62) on the Pre-TED Form 2400. For example, if a related donor gave a cord blood unit and bone marrow, you would report the cord blood unit information in one instance with the donor type listed as ‘Related cord blood unit’. Create another instance with the donor type reported as ‘Related donor’ to report the bone marrow information. This allows CIBMTR to capture all the necessary donor information needed. For these cases, complete a Form 2004 for each product. When the donor type is an HLA matched or mismatched relative, only one Form 2005 is required.

Reporting More Than One Donor

FormsNet3 application: Complete questions 31-62 for each donor by adding an additional instance in the FormsNet application.

Paper form submission: Copy questions 31-62 and complete for each donor.

Question 31: Specify donor

Indicate the donor type for this product.
An **autologous** product has cells collected from the recipient for his/her own use.

If the product was **autologous** (marrow, PBSC, other product), select “autologous” and continue with question 46.

If the product was an **autologous cord blood unit**, select “autologous cord blood unit” and continue with question 35.

An **unrelated donor (allogeneic, unrelated)** is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or stepparents/children. Distinguish if the product in an NMDP product or a non-NMDP product. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank, Anthony Nolan, and StemCyte International Cord Blood Center.

If the product was an **NMDP unrelated cord blood unit**, select “NMDP unrelated cord blood unit” and continue with question 32.

If the product was from an **NMDP unrelated donor** (marrow, PBSC, other product), select “NMDP unrelated donor” and continue with question 33.

If the product was from a **non-NMDP unrelated donor** and was facilitated through another registry, select “non-NMDP unrelated donor” and continue with question 34.

If the product was a **non-NMDP cord blood unit**, select “non-NMDP cord blood unit” and continue with question 35.

A **related donor (allogeneic or syngeneic, related)** is a blood-related relative. This includes monozygotic (identical twins), non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc.

If the product was from a **related donor** (marrow, PBSC, other product), select “related donor” and continue with question 40.

If the product was a **related cord blood unit**, select “related cord blood unit” and continue with question 35.

**Question 32: NMDP cord blood unit ID**

Report the NMDP Cord Blood Unit ID. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation. The ID is always numeric and begins with “9” (e.g., 9000-0000-0). If the product ID does not begin with a “9,” the product may not be
an NMDP cord blood unit and the source of the product should be double-checked. Enter the NMDP cord blood unit ID and continue with question 46.

**Question 33: NMDP donor ID**

Report the NMDP Donor ID (e.g., 0000-0000-0). This ID is unique for each donor and is assigned by NMDP. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation. Enter the NMDP Donor ID (e.g., 0000-0000-0) and continue with question 46.

**Question 34: Non-NMDP unrelated donor ID (not applicable for related donors)**

Report the non-NMDP unrelated donor ID. Examples of non-NMDP donor registries include, but are not limited to: Anthony Nolan, Australia Bone Marrow Donor Registry, and REDOME. This ID is often located on the product label, the paperwork accompanying the product, and registry-specific search/product documentation. Enter the non-NMDP unrelated donor ID and continue with question 38.

**Question 35: Non-NMDP cord blood unit ID (include related and autologous CBUs)**

Report the non-NMDP cord blood unit ID. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank and StemCyte International Cord Blood Center. This ID is often located on the product label, the paperwork accompanying the product, and registry-specific search/product documentation. Enter the non-NMDP cord blood ID. Note that some cord blood banks can ship their units either through the NMDP or directly to the transplant center. Carefully review the accompanying documentation to determine which is appropriate for your unit. You may wish to consult with your center’s Transplant Coordinator, as he or she will have insight as to how the product was acquired.

**Question 36: Is the CBU ID also the ISBT DIN number?**

Report “yes” if the non-NMDP CBU ID is the same as the International Society of Blood Transfusion (ISBT) Donation Identification Number (DIN) and continue with question 38. If the product has an ISBT label on it, the ISBT DIN number is in the upper-left-hand corner and consists of a letter followed by 12 numbers, two sideways numbers, and a letter in a box. Example below:

![Example ISBT DIN number]

Please find additional information regarding the ISBT DIN numbers and traceability at [http://www.iccbba.org/](http://www.iccbba.org/)
Question 37: Specify the ISBT DIN number:

Report the ISBT DIN number using the letter, 12 digits, 2 sideways numbers, and the letter in the box.

Questions 38: Registry or UCB Bank ID:

Specify the registry used to obtain the adult donor or umbilical cord blood unit. The Bone Marrow Donors Worldwide (BMDW) codes have been adopted to avoid submitting the entire name and address of the donor registry.

The registry code for NMDP donors is USA1 and for NMDP cord units is U1CB.

Some common banks that do not list with BMDW have been added to the FormsNet list, including St Louis Cord Blood Bank (SLCBB) and Viacord (VIAC).

If the donor was found through DKMS, report the registry that facilitated the HCT. Some registries may be listed more than once with BMDW (one way for marrow/PBSC products and differently for cord blood products). Ensure that the appropriate code for the product was selected because distribution of data depends on the code.

If the registry code cannot be determined using the BMDW website, select “other registry” and continue to question 39.

Question 39: Specify other Registry or UCB Bank

If the BMDW website does not list a match code for the adult donor registry or cord blood bank, provide the registry’s official name in the “specify other registry” field.

Please ensure that the registry you are entering under “other” is not already listed in the pull-down list for question 38. For example, NMDP adult donors, NMDP cords, and New York Cord Bank each have their own
entries above in the registry or UCB Bank ID drop down menu.

**Question 40: Specify the related donor type:**

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**Haploidentical Donors**

A HLA-haploidentical donor is one who shares, by common inheritance, exactly one HLA haplotype with the recipient and is mismatched for a variable number of HLA genes, ranging from zero to five, on the unshared haplotype. Potential HLA-haploidentical donors include biological parents; biological children; full or half siblings; and even extended family donors such as aunts, uncles, nieces, nephews, cousins, or grandchildren. Indicate “HLA-mismatched relative” for question 40 if a haploidentical donor was used for the HCT.

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Indicate the relationship and match between the recipient and the donor.

**Syngeneic:**

*Includes:* Monozygotic (identical) twins. Occurs when a single egg is fertilized to form one zygote, which then divides into two separate embryos.

*Does not include:* Other types of twins or HLA-identical siblings (see below).

**HLA-identical sibling:**

*Includes:* Non-monozygotic (dizygotic, fraternal, non-identical) twins. Occurs when two eggs are fertilized by two different sperm cells at the same time. This category also includes siblings who aren’t twins, but have identical HLA types.

*Does not include:* Half-siblings (report as “HLA matched other relatives” if their HLA is a match, or “mismatched relative” if it does not match).

**HLA-matched other relative:**

*Includes:* All blood-related relatives, other than siblings, who are HLA matched (e.g., parents, aunts, uncles, children, cousins, half-siblings).

*Does not include:* Adoptive parents/children or stepparents/children who are HLA matched.

**HLA-mismatched relative:**

*Includes:* Siblings who are not HLA-identical and all other blood-related relatives who have at least one HLA mismatch (e.g., parents, aunts, uncles, children, cousins, half-siblings). This includes haploidentical donors.

*Does not include:* Adoptive parents/children or stepparents/children
Questions 41-42: Date of birth: (donor/infant)

Report if the donor’s/infant’s date of birth is “known” or “unknown.” If the donor’s/infant’s date of birth is “known,” report the date of birth (YYYY-MM-DD) and continue with question 45. If the donor’s/infant’s date of birth is “unknown,” continue with question 43.

Questions 43-44: Age: (donor/infant)

Report if the donor’s/infant’s age is “known” or “unknown.” If the donor’s/infant’s age is known, report the donor’s/infant’s age at the time of product collection in question 44. Report the age in months if the donor is less than 1 year old, otherwise report the age in years. If the donor’s/infant’s age at collection is unknown, continue with question 45.

Question 45: Sex: (donor/infant)

Indicate the donor’s biological sex as “male” or “female.” For cord blood units, report the infant’s sex.

Questions 46-50: Specify product type:

Indicate “yes” or “no” for each product type listed for the donor specified in question 31.

Examples of “other product” type include, but are not limited to the following:

- Supplemental infusion of NK Cells
- Supplemental infusion of T-regulatory cells
- Supplemental infusion of mesenchymal cells

If “other product” is indicated, report the product type in “specify other product type.” If your center has a protocol where using “other products” is common, you should be consistently reporting the same text in the specify field so that the like products can be grouped together.

Question 51: Specify number of products infused from this donor:

Report the number of products infused from the donor specified in question 31.

Single Product: CIBMTR defines a single product (i.e., cellular product) as **cells collected from a single**
donor using the same mobilization cycle and collection method regardless of the number of collection days.

**Example 1 (multiple bags):** A G-CSF-stimulated donor had two PBSC collections on subsequent days. The products collected over the two days were divided into four bags. Although the product is contained in multiple bags, this collection is considered a single product, as there was no change in mobilization technique or collection method.

**Multiple Products:** For the purposes of this manual, the CIBMTR defines *multiple products* as cells collected using more than one mobilization technique and/or collection method.

**Example 2 (multiple collection methods):** A G-CSF-stimulated donor had a PBSC collection and the product was cryopreserved. One month later the donor had a marrow collection; both products were infused at the time of transplant. Each collection is considered a separate product because different collection methods were used.

**Example 3 (change in mobilization):** A G-CSF-stimulated donor had a PBSC collection, but the cell count was poor. GM-CSF was administered and the donor was re-collected. Each collection is considered a separate product due to the change in mobilization.

**Example 4 (re-mobilization):** A G-CSF-stimulated donor had a PBSC collection, but the cell count was poor. The donor was re-mobilized with G-CSF and a second PBSC collection was performed. Each collection is considered a separate product due to the re-mobilization of the donor.

**Example 5 (two different product types):** A cord blood unit is infused at the same time as marrow. Each collection is considered a separate product.

**Question 52: Specify the number of these products intended to achieve hematopoietic engraftment:**

If infusions of additional cells (not intended to produce engraftment) were given prior to the HCT being reported (i.e., prior to clinical day 0), the cells must be reported as a product on the Pre-TED Form (Form 2400, question 51) and on a separate Cellular Therapy Product Form (Form 4003). If the additional cells were infused post-HCT, for any reason other than a subsequent HCT, they should be reported as a DCI on the appropriate follow-up form. Reporting the additional cells (given pre-HCT and not intended to produce engraftment) on the Form 4003 is the only mechanism the CIBMTR has in place to collect this data and ensure that the quality assurance data is reported to cord blood banks, if applicable.

Report the number of products administered to achieve hematopoietic engraftment.
Question 53: Did the recipient have more than one mobilization event to acquire cells for HCT?

Stem cells do not typically circulate in the bloodstream. Therefore, in order to increase the quantity of cells for collection, an agent is frequently given to the autologous recipient. The purpose of the agent is to move the stem cells from the bone marrow into the peripheral blood. This practice is often referred to as mobilization or priming. Occasionally, a bone marrow product may be primed using a growth factor.

For the purposes of this manual, the CIBMTR defines a mobilization event as the planned administration of growth factors or systemic therapy designed to enhance stem cell collection. If the donor requires an additional mobilization at a later date to collect an additional product, this should be considered an additional mobilization event. Additionally, if the mobilization methods change (e.g., plerixafor is required starting on Day 3 of collection) this would be considered an additional mobilization event.

Example 1: An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. Since the collection and mobilization methods remained the same over the duration of the collection, this is considered one mobilization event.

Example 2: An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection, but the cell count was poor. GM-CSF was administered and the autologous recipient was re-collected. This is considered two mobilization events due to the change in mobilization.

Example 3: An autologous recipient was mobilized with G-CSF and underwent a one-day PBSC collection, but the cell count was poor. The recipient then received plerixafor to enhance the mobilization. This is considered two mobilization events due to the change in mobilization.

Question 54: Specify the total number of mobilization events performed for this HCT (regardless of number of collections or which collections were used for this HCT):

Report the total number of mobilization events performed for this HCT. Include all mobilization events, even if a product from the mobilization event for this HCT was not used during the transplant.

Questions 55-60: Specify all agents used in the mobilization reported above:

Report if any of the following products were used in the mobilization event(s) reported in questions 53-54. Select "yes" or “no” for each question.

G-CSF: granulocyte colony-stimulating factor, filgrastim, Neupogen®
GM-CSF: granulocyte macrophage colony-stimulating factor, sargramostim, Leukine®

Pegylated G-CSF: pegfilgrastim, Neulasta®

Plerixafor: Mozobil®

Other CXCR4 inhibitor: examples include POL6326 and AMD3465. Report experimental and other CXCR4 inhibitors used to mobilize the donor here.

Combined with chemotherapy: Systemic therapies used to enhance the stem cell product may include cyclophosphamide or ICE chemotherapy (Ifosfamide, carboplatin, and etoposide) with or without rituximab.

**Question 61: Was this donor used for any prior HCTs?**

Indicate if the donor reported in question 31 was used for prior HCTs for this recipient. If this is the recipient’s first HCT select “no.” If this is an autologous infusion, select “no.”

**Question 62: Donor CMV-antibodies (IgG or Total) (Allogeneic HCTs only)**

CMV is a common virus that infects 50-80% of adults worldwide, and is transmitted from person to person through bodily fluids. The virus that causes CMV is part of the herpes virus family and, like other herpes viruses, CMV may be dormant for a period of time before the virus is activated in the host. CMV infections are usually harmless in a healthy immune system and typically cause only mild symptoms, if any. However, if a person’s immune system is seriously weakened (as in an immunosuppressed stem cell recipient) the virus can have serious consequences such as pneumonia, liver failure, and even death.

Most laboratory reports indicate a positive result as reactive, and a negative result as non-reactive. Occasionally, laboratory reports show a specific antibody titer. In this case, compare the laboratory result to the reported standards to determine if the result was reactive or non-reactive.

If the laboratory reports a CMV IgM antibody only, not total IgG/IgM or CMV IgG antibody; report the result as “not done.”

If the laboratory reports the results as “inconclusive” or “equivocal,” select “not done.”

If the laboratory reports CMV testing by PCR (DNA detection), report the result as “not done.” CMV testing by PCR is used to detect the presence of the CMV virus and does not test for prior exposure.

Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” “not done,” or “not applicable (cord blood unit)."
Question 63: Was plerixafor (Mozobil) given at any time prior to the preparative regimen? (Related HCTs only)

Stem cells do not typically circulate in the bloodstream. Therefore, in order to increase the quantity of cells for collection, an agent is frequently given to the allogeneic donor or autologous recipient. The purpose of the agent is to move the stem cells from the bone marrow into the peripheral blood. This practice is often referred to as mobilization or priming. Indicate if the donor received plerixafor at any time prior to the start of stem cell collection.
Q64-71: Consent

To be compliant with Federal Regulations for human research subject protection, centers must obtain IRB-approved informed consent from recipients and donors (if applicable, for the related donor sample repository) to allow data submitted to the CIBMTR to be used for observational research. Informed consent must also be obtained from recipients and donors prior to submitting blood samples to the Research Sample Repository. The NMDP/CIBMTR has written protocols and informed consent documents for the Observational Database and Research Sample Repository. All centers must have local IRB approval for the Observational Database protocol. All centers that are NMDP member centers must also have local IRB approval for the Research Sample Repository protocol. With the exception of some selected sites (participating in the related sample repository), centers performing only related donor transplants and/or autologous transplants will not be submitting research samples and do not need to obtain local IRB approval for the repository protocol. The NMDP IRB has approved these protocols and consent forms, and the documents are provided to participating sites to include with their local IRB submissions.

International Centers must obtain consent of each patient participating in the Observational Database in a manner consistent with the laws and regulations of that country.

Under federal legislation, U.S. centers are required to submit outcomes data on all allogeneic transplants, related and unrelated. Data submitted without informed consent from the recipient should be reported on the TED Forms and will only be used for federally required research such as the center-specific outcomes analysis.

**Question 64: Has the recipient signed an IRB-approved consent form for submitting research data to the NMDP/CIBMTR?**

When a recipient consents to participate in the Observational Database, their data are contained in the CIBMTR’s Observational Database and used for research. The database includes recipient baseline and outcome data for related and unrelated allogeneic transplants from any cell source, and for autologous transplants. Data are also collected on unrelated donors and their donation experiences.

The primary purpose of the Observational Database is to have a comprehensive source of data that can be used to study hematopoietic cellular transplantation. Studies using these data include:

- How well recipients recover from their transplants.
- How recovery after transplantation can be improved.
- What the long-term outcomes are after transplantation.
- How access to transplantation for different groups of recipients can be improved.
• How well donors recover from collection procedures.
• The application and success of transplantation in the management of marrow-toxic injuries.

Indicate if the recipient has signed an IRB-approved consent form to participate in the Observational Database. If “yes (patient consented),” continue with question 64. If “no (patient declined)” or “not applicable (patient not approached),” continue with question 68.

When to use the “Not Approached” option for the Research Database Consent
CIBMTR expects all transplant centers to approach all patients for the Research Database consent. The “not approached” option should only be used in the rare event when the physician feels it would be in the best interest of the patient not to be consented.

Recipients who transfer to another facility for a subsequent HCT
Any time a recipient transfers to another transplant center, an IRB approved research database consent would need to be obtained at the new center before data could be reported to the CIBMTR.

See the table below for additional information regarding how to report consent status for those with planned tandem or previous transplants.

<table>
<thead>
<tr>
<th>Transplant Types</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tandem Autologous Transplants</td>
<td>Most transplant centers would consider tandem autologous transplants as part of the same treatment plan and would consent the patient prior to the 1st HCT only. If that's the case, the center should report “yes” to the consent question for the 2nd HCT and provide the date when the consent was first obtained.</td>
</tr>
<tr>
<td>Tandem Autologous-Allogeneic Transplants</td>
<td>Most transplant centers would consider tandem autologous-allogeneic transplants as part of the same treatment plan and would consent the patient prior to the 1st HCT only. If the center has one IRB approved consent covering both the autologous and allogeneic transplants, then the center should report “yes” to the consent question for the 2nd HCT and provide the date when the consent was first obtained. In the case where a center has separate research database consents for autologous and allogeneic HCTs, the center should obtain both consents from the patient prior to the 1st HCT. The center should then report “yes” to the consent question for the 2nd HCT &amp; provide the date when the consent was first obtained.</td>
</tr>
<tr>
<td>Autologous HCT followed by subsequent autologous HCTs (not a)</td>
<td>In this scenario, CIBMTR does not require an additional consent form to be signed. The only consent required would be the one obtained at the time of the first autologous HCT. The center should report “yes” to the consent question for the subsequent HCT and provide the date when the consent was first obtained. However, a center’s IRB may require a second database consent form to be signed in this situation, and centers should refer to the higher standard set by their IRB.</td>
</tr>
<tr>
<td>tandem autologous HCT</td>
<td>Allogeneic HCT followed by subsequent allogeneic HCTs (not a tandem allogeneic HCT)</td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>In this scenario, CIBMTR does not require an additional consent form to be signed. The only consent needed would be the one obtained at the time of the first allogeneic HCT. The center should report “yes” to the consent question for the subsequent HCT and provide the date when the consent was first obtained. However, centers must follow their own institutional policy as well, which may require the patient be re-consented to the Research Database for a subsequent HCT.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Autologous HCT followed by subsequent allogeneic HCTs (not a tandem autologous HCT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>If the center has one IRB approved consent form covering both autologous and allogeneic transplants, then the center should report “yes” to the consent question for the 2nd HCT and provide the date when the consent was first obtained. In the case where a center has separate research database consent forms for autologous and allogeneic HCTs, the patient would need to be re-approached prior to the subsequent allogeneic transplant and asked to sign the appropriate consent form. If the patient was not asked to sign a 2nd consent form, then “not approached” must to be reported on the Pre-TED.</td>
</tr>
</tbody>
</table>

**Question 65: Date form was signed:**

Report the date the research database consent form was signed by the recipient. Do not report the date that the witness or health care professional signed the consent form.

**Question 66: Did the recipient give permission to be directly contacted for future research?**

Indicate if the recipient has given permission to be directly contact by the NMDP/CIBMTR for future research as documented on the research database consent form. If “yes (patient provided permission),” continue with question 67. If “no (patient declined)” or “not approached,” continue with question 68.

Below is an example of this permission found in the NMDP/CIBMTR Research Database for Hematopoietic Cell Transplantation and Cellular Therapy Consent Form.

**VIII. PERMISSION TO CONTACT FOR FUTURE CIBMTR RESEARCH STUDIES**

Do you agree to give the CIBMTR permission to contact you in the future to tell you about research studies for which you are eligible? These studies are different from the studies that use your medical data. These studies would involve you directly, for example, asking you to complete a survey. You may decide if you want to participate in a specific study when you are contacted. By checking the “AGREE” box below, you are only agreeing that the CIBMTR can contact you to tell you about the study. Due to the need to follow up with you after your transplant, please tell your transplant center if your contact information changes. If the contact information on file is no longer valid, it might be necessary to
use an internet-based search service to find you. By agreeing to be contacted for future studies, you authorize the CIBMTR to use such a service to search public and non-public information only for the purpose of trying to locate you.

☐ I AGREE to allow CIBMTR to contact me about future studies.

☐ I DO NOT want CIBMTR to contact me about future studies.

If the recipient declined to take part in the CIBMTR Research Database (as indicated in question 64) but gave permission to be contacted for future CIBMTR studies, ensure that there is documentation before selecting “yes.”

**Question 67: Date form was signed:**

Report the date the research database consent form was signed by the recipient. Do not report the date that the witness or health care professional signed the consent form.

**Question 68: Has the recipient signed an IRB-approved consent form for submitting research blood samples to the NMDP/CIBMTR?**

The Research Sample Repository contains blood samples from unrelated recipients and/or their adult volunteer donors or cord blood units. Related allogeneic recipients and/or donors will participate at selected transplant centers.

The primary objective of the Research Repository is to make blood samples available for research studies related to histocompatibility and hematopoietic cellular transplantation.

Studies in which these data may be used include:

- Improving the understanding of tissue matching for hematopoietic cellular donors and recipients.
- Determining and evaluating the factors that affect transplant outcomes.
- Studying the distribution of HLA tissue types in different populations (e.g., study tissue typing differences between different racial and ethnic populations to help develop methods to improve tissue matching between donors and recipients, including testing of rare HLA types).

Indicate if the recipient signed an IRB-approved consent form to donate research blood samples to the NMDP/CIBMTR. If “yes (patient consented),” continue with question 69. If “no (patient declined),” “not approached,” or “not applicable (center not participating),” continue with question 70.

Blood samples are not submitted for subsequent transplants, however, this question is asked for
subsequent transplants. If the recipient previously consented to submit research blood samples to NMDP/CIBMTR, select “yes (patient consented).”

**Question 69: Date form was signed:**

Report the date the research sample consent form was signed by the recipient. Do not report the date that the witness or health care professional signed the consent form.

**Question 70: Has the donor signed an IRB-approved consent form for submitting research blood samples to the NMDP/CIBMTR? (Related donors only)**

Indicate if the donor signed an IRB-approved consent form to donate research blood samples to the CIBMTR. If “yes (donor consented),” continue with question 71. If “no (donor declined),” “not approached,” or “not applicable (center not participating),” continue with question 72.

**Question 71: Date form was signed:**

Report the date the research sample consent form was signed by the donor. Do not report the date that the witness or health care professional signed the consent form.
Q72-90: Product Processing/Manipulation

**Question 72: Was the product manipulated prior to infusion?**

If any part of the product was manipulated in any way prior to infusion at the transplant center, select "yes."

Do not report cryopreservation (including plasma removal as part of cryopreservation) as a method of manipulation; cryopreservation of the product(s) is reported on the 2006 form, if applicable.

If the product was shipped to your facility, do not report manipulation of the product performed at the collection center.

If the product was not manipulated, select “no” and continue with question 91.

**Question 73: Specify portion manipulated:**

Indicate the portion of the product that was manipulated. If the entire product was manipulated, select “entire product” and continue with question 74. If a portion of the product was removed and manipulated, select “portion of product” and continue with question 75.

If different portions of the product were manipulated in different ways, select “portion of product” to indicate that the manipulation were not performed on the entire product.

**Questions 74-90: Specify all methods used to manipulate the product:**

Indicate the method(s) of stem cell manipulation. Answer each question as “yes” or “no” and do not leave any questions blank.

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**Steps in Manipulation**

If the manipulation consists of several steps, individual steps do not need to be reported as separate manipulations. For example, washing that is part of CD34+ expansion does not need to be reported as a separate manipulation. Similarly, T-cell depletion that is part of expansion does not need to be reported.

In the cases above, if T-cell depletion and/or washing are done as stand-alone manipulations, they should be reported.

- **Washed:** Washing is performed to remove cryoprotectant (such as DMSO) from the product.

- **Diluted:** Dilution is performed to reduce the cell concentration.
**Buffy coat enriched**: Buffy coat enrichment is performed to reduce/remove mature erythrocytes and plasma.¹

**B-cell reduced**: B cell reduction is performed to reduce/remove the quantity of B cells in the product.¹

**CD8 reduced**: CD8 reduction is performed to reduce/remove the population of CD8 cells in the product.¹ The removal of CD8 cells may mitigate the risk of GVHD.

**Plasma reduced (removal)**: Plasma reduction is performed to remove plasma via sedimentation or centrifugation.¹

Plasma reduction may be done in order to minimize the risks associated with ABO mismatched products or to prevent volume overload. Previous versions of the Form 2006 made a distinction between plasma removal and volume reduction; for the purpose of this form, both volume reduction and plasma removal should be reported here.

Plasma reduction/removal that is part of the cryopreservation process should not be reported as manipulation.

**RBC reduced**: RBC reduction is performed to reduce/remove mature erythrocytes from the product.¹

**Cultured (ex-vivo expansion)**: Ex-vivo expansion is a method of culturing cells to “activate, expand, or promote development of a specified cell population in the presence of specific additive(s).”¹

**Genetic manipulation (gene transfer/transduction)**: Gene manipulation refers to any method used to modify the genes in the product cells. Gene transduction refers to the transfer of genes from one cell to another. Genetic manipulation is still in the early investigative phase of research.

**PUVA treated**: Product treated with psoralen and ultraviolet light (PUVA).¹

**CD34 enriched (CD34+ selection)**: CD34+ selection is a manipulation method also known as “positive selection.” This method identifies and selects stem cells that have a CD34+ marker on the cell surface.

**CD133 enriched**: CD133 enrichment identifies and selects stem cells that have a CD133 marker on the cell surface.

**Monocyte enriched**: Monocyte enrichment identifies and selects monocytes.
**Mononuclear cells enriched**: Mononuclear cell enrichment identifies and selects mononuclear cells.

**T-cell depletion**: T-cell depletion removes some or all of the T-cells in an effort to minimize GVHD. Methods of T-cell depletion include antibody affinity column, antibody-coated plates, antibody-coated plates and soybean lectin, antibody + toxin, immunomagnetic beads, and CD34 affinity column plus sheep red blood cell resetting.

If a method of manipulation was performed on the product, but is not listed above, select “yes” for question 89 and specify using question 90. Do not report cryopreservation (or processing used in the cryopreservation process) as manipulation.

Q91-94: Clinical Status of Recipient Prior to the Preparative Regimen (Conditioning)

Question 91: What scale was used to determine the recipient's functional status?

The CIBMTR uses the Karnofsky/Lansky scale to determine the functional status of the recipient immediately prior to the start of the preparative regimen. The Karnofsky Scale is designed for recipients aged 16 years and older, and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. If the recipient is less than one year old, leave questions 91-93 blank.

Questions 92-93: Performance score prior to the preparative regimen:

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. The CIBMTR uses the Karnofsky/Lansky scale to determine the functional status of the recipient immediately prior to the start of the preparative regimen. For the purposes of this manual, the term “immediately prior” represents the pre-HCT work-up phase, or approximately one month prior to the start of the preparative regimen. In cases where the pre-transplant work-up occurs in months prior to transplant (i.e., the pre-transplant workup occurs more than one month prior to transplant), a documented performance score may be submitted if the recipient does not have a score closer to the start of the preparative regimen, the recipient receives no additional treatment after the date of assessment, and the recipient’s status does not clearly decline.

Select the appropriate performance scale, Karnofsky or Lansky, based on the recipient’s age. Using this scale, select the score (10-100) that best represents the recipient’s activity status immediately prior to the start of the preparative regimen. For an example of the Karnofsky/Lansky scale, see Appendix L.

If a Karnofsky/Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician’s clinic note), data management professionals should not assign a performance score based on analysis of available documents. Rather, a physician or mid-level health care provider (NPs and PAs) should provide documentation of the performance score.

The CIBMTR recognizes that some transplant centers prefer to collect and use the ECOG performance score as opposed to the Karnofsky/Lansky score. Although the ECOG and Karnofsky/Lansky performance score systems are based on similar principles, the scales are not the same. For example, the Karnofsky/Lansky scale is described in 11 categories, whereas the ECOG performance status is reported in six categories. Due to the overlap between the two systems, an ECOG score of “one” can represent either “80” or “90” on the Karnofsky/Lansky scale. For centers that collect only an ECOG performance score, CIBMTR
will make the following accommodations when auditing the source data:

• Centers collecting ECOG scores should do so using standard practices to ensure accuracy.
• For the purposes of CIBMTR reporting, conversion of ECOG to Karnofsky/Lansky should follow a standard and consistent practice. This practice should be clear and reproducible.

For more information regarding converting an ECOG score to a Karnofsky/Lansky score, see Appendix L.

**Question 94: Recipient CMV-antibodies (IgG or Total):**

Report the cytomegalovirus (CMV) status of the recipient immediately prior to the start of the preparative regimen. For the purposes of this manual, the term “immediately prior” represents the pre-HCT work-up phase, or approximately one month prior to the start of the preparative regimen. An exception to this definition would apply to a recipient with a documented history of a “reactive” CMV test result. In this case, the CMV test may not be repeated during the pre-HCT work-up phase. Therefore a timeframe of greater than one month prior to the start of the preparative regimen is acceptable. In cases where the pre-transplant work-up occurs in months prior to transplant (i.e., the pre-transplant workup occurs more than one month prior to transplant), a CMV assessment may be submitted if the recipient does not have an assessment closer to the start of the preparative regimen.

CMV is a common virus that infects 50-80% of adults worldwide, and is transmitted from person to person through bodily fluids. The virus that causes CMV is part of the herpes virus family and, like other herpes viruses, CMV may be dormant for a period of time before the virus is activated in the host. CMV infections are usually harmless in a healthy immune system and typically cause only mild symptoms, if any. However, if a person’s immune system is seriously weakened (as in an immunosuppressed stem cell recipient) the virus can have serious consequences such as pneumonia, liver failure, and even death.

Most laboratory reports indicate a positive result as reactive, and a negative result as non-reactive. Occasionally, laboratory reports show a specific antibody titer. In this case, compare the laboratory result to the reported standards to determine if the result was reactive or non-reactive.

If the laboratory reports a CMV IgM antibody only, not total IgG/IgM or CMV IgG antibody, report the result as “not done”.

If the laboratory reports the results as “inconclusive” or “equivocal,” select “not done.”

Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” or “not done.”
Additional Considerations:

- **Recipients < 6 months**: If the recipient is less than 6 months old, report any positive CMV antibody results as “not done” due to the presence of maternal antibodies. However, in infants greater than 6 months old, positive CMV PCR results indicate a CMV infection and the results may be reported as “reactive.”

- **Exposure to IVIG**: Exposure to IVIG may result in a false positive CMV antibody result. If the recipient has been exposed to IVIG leading up to HCT (within 3-6 months), indicate the CMV antibody results using the following guidelines:
  - If the recipient had a non-reactive CMV antibody result prior to IVIG therapy and then routine CMV PCR results showed no copies of CMV, the CMV antibody may be reported as “non-reactive,” even if the CMV antibody became reactive during IVIG treatment.
  - If CMV PCR results quantified copies of CMV DNA (i.e., was positive) during IVIG treatment, the results may be reported as “reactive.”
  - If the recipient did not have a CMV antibody test prior to the initiation of IVIG, but had a positive antibody test during the IVIG therapy, report “not done.”
  - “Not done” should be reported if no CMV antibody tests were done prior to the initiation of IVIG therapy, even if CMV PCR testing was negative during IVIG treatment (because CMV PCR only detects active infection, not prior exposure).

- **Documented history of “reactive” CMV**: In cases where a recipient has a documented history of a “reactive” CMV test and does not have a history of IVIG or blood transfusions from a CMV positive donor, “reactive” should be reported for the CMV status even if the CMV test is repeated during the pre-HCT work-up phase and is “non-reactive”.

- **CMV testing by PCR**: If the laboratory reports CMV testing by PCR (DNA detection) but no CMV antibody testing is done during the pre-transplant work-up or within one month prior to transplant, report the result as “not done.” CMV testing by PCR is used to detect the presence of the CMV virus and does not test for prior exposure.
Q95-155: Comorbid Conditions

Question 95: Is there a history of mechanical ventilation?

A history of mechanical ventilation may impact the recipient’s pulmonary function post-HCT. Mechanical ventilation is any assisted ventilation on behalf of the recipient. Mechanical ventilation can occur as both an endotracheal tube and ventilator, or as a BIPAP machine with a tight fitting mask in continuous use. The one exception to BIPAP is CPAP used for sleep apnea, which generally involves overnight use only for patients with documented sleep apnea. Therefore, do not report a CPAP used for sleep apnea, as it does not have the same implications as other forms of mechanical ventilation.

Indications for mechanical ventilation include, but are not limited to:

- Apnea with respiratory arrest (excludes sleep apnea)
- Acute lung injury
- Vital capacity < 15 mL/kg
- Chronic obstructive pulmonary disease (COPD)
- Clinical deterioration
- Respiratory muscle fatigue
- Obtundation or coma
- Hypotension
- Tachypnea or bradypnea

If the recipient was placed on mechanical ventilation at any time prior to this HCT event (excluding mechanical ventilation during surgery) check “yes.” If the recipient does not have a history of mechanical ventilation, check “no.”

Question 96: Is there a history of proven invasive fungal infection?

Fungal infections play a major role in the clinical outcome of transplant recipients. For the purposes of this manual, the term “proven” is defined as a pathologic specimen or culture that yields a positive result. For example, a chest x-ray that reveals a nodule is not considered a “proven” diagnosis of aspergillus. A biopsy of a specimen with a positive culture for aspergillus is a proven diagnosis.

If the recipient has a history of proven invasive fungal infection at any time prior to this HCT, check “yes.” If the recipient has not had a history of a proven invasive fungal infection, check “no.” For a subsequent HCT, report any documented significant fungal infections in the recipient’s medical history, starting with the preparative regimen of the previous HCT to the time prior to the preparative regimen for the current HCT.
Examples of proven invasive fungal infections include, but are not limited to: invasive aspergillosis, zygomycosis and other molds, invasive candidiasis, cryptococcosis, endemic mycosis, other yeasts, and pneumocystosis.

Non-invasive fungal infections such as thrush and nail fungus should not be reported.

For assistance with reporting fungal infections, consult a transplant physician.

Questions 97-134
Prior to answering question 97, review the list of co-existing disease(s) and/or organ impairments listed under questions 98-134.

Question 97: Were there clinically significant co-existing disease or organ impairment at the time of patient assessment prior to preparative regimen?

Hepatic and Renal Comorbidities

In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities

Hepatic Comorbidity: The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

Renal (Moderate/Severe) Comorbidity: Serum creatinine > 2 mg/dL or > 177 μmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.


Report “yes” to question 97 if the recipient has a documented history and/or current diagnosis of any of the following:

<table>
<thead>
<tr>
<th>Documented Medical History</th>
<th>Question Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrythmia</td>
<td>98</td>
</tr>
<tr>
<td>Cardiac^2</td>
<td>99</td>
</tr>
</tbody>
</table>
Cerebrovascular disease 100
Heart valve disease\(^3\) 102
Inflammatory bowel disease 106
Peptic ulcer 108

<table>
<thead>
<tr>
<th>Current Diagnosis at the Time of Pre-HCT Evaluation</th>
<th>Question Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatologic</td>
<td>113</td>
</tr>
<tr>
<td>Solid tumor, prior(^4)</td>
<td>114</td>
</tr>
<tr>
<td>Diabetes</td>
<td>101</td>
</tr>
<tr>
<td>Hepatic, mild(^5)</td>
<td>103</td>
</tr>
<tr>
<td>Hepatic, moderate/severe</td>
<td>104</td>
</tr>
<tr>
<td>Infection</td>
<td>105</td>
</tr>
<tr>
<td>Obesity</td>
<td>107</td>
</tr>
<tr>
<td>Psychiatric disturbance</td>
<td>109</td>
</tr>
<tr>
<td>Pulmonary, moderate</td>
<td>110</td>
</tr>
<tr>
<td>Pulmonary, severe</td>
<td>111</td>
</tr>
<tr>
<td>Renal, moderate/severe(^6)</td>
<td>112</td>
</tr>
<tr>
<td>Other (specify)</td>
<td>133 and 134</td>
</tr>
</tbody>
</table>

\(^2\) Ejection fraction (EF) \(\leq 50\%) should be reported only if present on most recent test

\(^3\) Excluding asymptomatic mitral valve prolapse

\(^4\) Excluding non-melanoma skin cancer, leukemia, lymphoma, or multiple myeloma

\(^5\) Including any history of hepatitis B or hepatitis C infection

\(^6\) Including renal transplantation at any time in the patient’s history

* Report all comorbidities including those that are considered complications of the primary disease for transplant. See examples below.

Examples of complications of the primary disease for transplant that should be reported as comorbidities.
• A patient with sickle cell had a stroke prior to HCT, the comorbidity to report would be “cerebrovascular disease”.
• A toddler with Hurler Syndrome has cardiomyopathy, cardiac valvular disease and an ejection fraction of 45%, the comorbidities to report would be “cardiac” & “heart valve disease”.

The intent of this question is to identify serious pre-existing conditions that may have an effect on the outcome of the HCT. For the purposes of this manual, the term “clinically significant” refers to conditions that are being treated at the time of pre-HCT evaluation, or are in the recipient’s medical history and could cause complications post-HCT. Conditions listed in the recipient’s medical history that have been resolved (e.g., appendectomy), and/or that would not pose a concern during or after the HCT should not be reported.

Additionally, for the purposes of this manual, the term “at the time of patient assessment” is defined as the pre-HCT evaluation period prior to the start of the preparative regimen. If the recipient does not have a documented history of clinically significant disease(s) or organ impairment(s), check “no” and continue with question 135.

For information regarding reporting clinically significant co-existing disease or organ impairment, see Appendix J.

Questions 98-134: Co-existing diseases or organ impairments

For each listed co-existing disease or organ impairment, check “yes,” “no,” or “unknown.” The definitions for each of the categories below are taken from Sorror, M. L. (2013). How I assess comorbidities before hematopoietic cell transplantation. Blood, 121(15), 2854-2863.

Arrhythmia: Any history of any type of arrhythmia that has necessitated the delivery of a specific antiarrhythmic agent. Examples include, but are not limited to, atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmias.

Cardiac: Any history of coronary artery disease (one or more vessel coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, and / or ejection fraction ≤ 50% (shortening fraction < 26% for pediatric recipients) on the most recent test.

Cerebrovascular disease: Any history of transient ischemic attack, subarachnoid hemorrhage, and / or cerebral thrombosis embolism, or hemorrhage.

Diabetes: Diabetes or steroid-induced hyperglycemia requiring continuous treatment with insulin or oral hypoglycemics in the last 4 weeks.
**Heart valve disease**: Moderate or severe valve stenosis or insufficiency (mitral, aortic, tricuspid, or pulmonary) as determined by echocardiogram, prosthetic mitral or aortic valve, and / or symptomatic mitral valve prolapse.

**Hepatic (mild)**: Chronic hepatitis, bilirubin > upper limit of normal to 1.5x upper limit of normal, or AST/ALT > upper limit of normal to 2.5x upper limit of normal, or any history of hepatitis B or hepatitis C infection. See note in question 97.

**Hepatic (moderate/severe)**: Liver cirrhosis, bilirubin > 1.5x upper limit of normal, or AST/ALT > 2.5x upper limit of normal. See note in question 97.

**Infection**: Documented infection, fever of unknown origin, or pulmonary nodules requiring continuation of antimicrobial treatment after day 0.

**Inflammatory bowel disease**: Any history of Crohn's disease or ulcerative colitis requiring treatment.

**Obesity**: Patients with a body mass index > 35 kg/m$^2$ or BMI-for-age ≥ 95% (pediatric recipients only) during pre-transplant work-up period.

**Peptic ulcer**: Any history of peptic ulcer confirmed by endoscopy and requiring treatment.

**Psychiatric disturbance**: The presence of any mood, anxiety, or other psychiatric disorder requiring continuous treatment during the last four weeks. Examples include, but are not limited to, depression, anxiety, bipolar disorder, and schizophrenia requiring psychiatric consult or treatment in the last 4 weeks.

**Pulmonary (moderate)**: Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 66-80% or dyspnea on slight activity at transplant. Use the Dinakara equation below to determine the DLCOc if only an uncorrected value is provided. For recipients assessed by a postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity.

Dinakara Equation: \[ DLCOc = \frac{\text{uncorrected DLCO}}{0.06965 \times \{\text{hemoglobin g/dL}\}} \]

**Pulmonary (severe)**: Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 ≤ 65% or dyspnea at rest or requiring oxygen at transplant. Use the Dinakara equation above to determine the DLCOc if only an uncorrected value is provided. or recipients assessed by a postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity.
Renal (moderate/severe): Serum creatinine > 2 mg/dL or > 176.8 μmol/L, or on dialysis at transplant, or prior renal transplantation. See note in question 97.

Rheumatologic: Any history of systemic lupus erythematosus, rheumatoid arthritis, polymyositis, mixed connective tissue disease, or polymyalgia rheumatica requiring treatment (do NOT include degenerative joint disease, osteoarthritis)

Solid tumor (prior): Treated at any time point in the patient’s past history, excluding non-melanoma skin cancer, leukemia, lymphoma, or multiple myeloma. For each listed prior solid tumor, check “yes” or “no.” If “yes,” enter the year of diagnosis of the corresponding solid tumor.

Other co-morbid condition: The “other, specify” category should be used to report co-morbid conditions that are of similar clinical concern as the other listed options. Chromosomal abnormalities, impairments and/or disorders associated with the primary disease should not be reported in this section, (e.g., Ph+ for CML/ALL recipients).

The physician performing the recipient’s pre-HCT evaluation may use the HCT Co-Morbidity Index (HCT-CI) to document co-morbid conditions (see Appendix J).

Question 135: Was there a history of malignancy (hematologic or non-melanoma skin cancer) other than the primary disease for which this HCT is being performed?

The intent of this question is to identify other malignancies that may have an effect on the outcome of the HCT. A history of any benign tumor(s) should not be reported in this section. Malignancies reported in the previous solid tumor options should not be reported again here.

If the recipient is transplanted for a disease that has transformed from one disease to another, the original malignancy should not be reported in this section. Details regarding disease transformation will be captured on the Pre-TED Disease Classification form (Form 2402). For more information regarding disease combinations and transformations, refer to the Common Disease Combinations and Common Disease Transformations tables in the Primary Disease for HCT section of the Pre-TED Disease Classification Form (Form 2402).

Indicate if there was a history of malignancy other than the disease for which this HCT is being performed.

Question 136-155: Specify which malignancy(ies) occurred:

For each listed prior malignancy, check “yes” or “no.” If “yes,” enter the year of diagnosis of the corresponding malignancy.

Use questions 153-155 to report any prior hematologic malignancies that were not listed in questions
136-152. Solid tumors should be reported in questions 144-131, not in questions 153-155.
Q156-316: Pre-HCT Preparative Regimen (Conditioning)

Question 156: Height at initiation of pre-HCT preparative regimen:

Report the recipient’s height just prior to the start of the preparative regimen. The intent of this question is to determine the height used when calculating preparative regimen drug doses. This height is usually documented on the transplant orders (for radiation and/or systemic therapy) or admitting orders. Report height to the nearest whole centimeter or inch (round up if 0.5 or greater).

Even if the recipient does not receive a preparative regimen, the height is still required.

Question 157: Actual weight at initiation of pre-HCT preparative regimen:

Report the recipient’s actual body weight just prior to the start of the preparative regimen. The intent of this question is to report the actual weight at the time the preparative regimen starts (which may be different than the weight used to determine preparative regimen doses). This weight is usually documented on the transplant orders (for radiation and/or systemic therapy) or admitting orders. Report weight to the nearest whole kilogram or pound (round up if 0.5 or greater). Do not report adjusted body weight, lean body weight, or ideal body weight.

Even if the recipient does not receive a preparative regimen, the weight is still required.

Question 158: Was a pre-HCT preparative regimen prescribed?

Recipients are generally transplanted under a specific protocol that defines the radiation and/or systemic therapy the recipient is intended to receive as a preparative regimen. This protocol, which may be either a research protocol or standard of care protocol, should be referred to when completing this section.

However, there are instances when a preparative regimen is not given. Examples may include, but are not limited to:

- Primary diagnosis of an immune deficiency.
- Subsequent allogeneic HCT due to loss of, or poor, neutrophil engraftment.

If a preparative regimen is prescribed per protocol, check “yes” and continue with question 159. If a preparative regimen is not prescribed, check “no” and continue with question 317.

For more information regarding the recipient’s preparative regimen, consult a transplant physician or contact
your center’s CIBMTR CRC.

**Question 159: Classify the recipient’s prescribed preparative regimen:**

Myeloablative pre-transplant conditioning destroys bone marrow cells using high-dose radiation and/or systemic therapy. It is used to eliminate the recipient’s immune system and to leave space in the bone marrow niche for the donated cells. A myeloablative regimen is sometimes used for recipients with non-malignant diseases who require HCT for marrow reconstitution (i.e., immunodeficiencies) or to produce a complete donor chimerism.

Non-myeloablative stem cell transplant (NMA or NST) and reduced-intensity conditioning (RIC) preparative regimens generally use lower doses of radiation and/or systemic therapy to prevent graft rejection and to suppress the recipient’s hematopoietic immune system, but not eliminate it completely. Non-myeloablative protocols rely on the immune cells of the donor to destroy the disease (called graft versus tumor or GVT effect), and typically produces mixed chimerism. NST is a common treatment option for recipients who are older or who have other health problems, as the lower radiation and/or systemic therapy doses are easier for the recipient to tolerate.

In general, RIC includes any regimen that does not meet the criteria for either myeloablative or non-myeloablative regimens.

Based on the CIBMTR operational guidelines below, report if the regimen was myeloablative, reduced intensity, or non-myeloablative. The determination of whether the intent of the regimen was reduced intensity or non-myeloablative should be based either on the protocol at your center or the opinion of the physician overseeing the care of the recipient at your center. However, if there’s a protocol utilized at your center that doesn’t fall within CIBMTR operational guidelines for regimen intensity, you may report the regimen intensity based on the protocol intent.

**Examples of Myeloablative, Reduced Intensity, and Non-Myeloablative Regimens**

<table>
<thead>
<tr>
<th>Myeloablative Regimens</th>
<th>Reduced Intensity and Non-Myeloablative Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>• TBI &gt; 500 cGy (single) or &gt; 800 cGy (fractionated)</td>
<td>• TBI ≤ 500 cGy (single) or ≤ 800 cGy (fractionated)</td>
</tr>
<tr>
<td>• <strong>Cyclophosphamide + TBI</strong> (&gt; 500 cGy (single) or &gt; 800 cGy (fractionated))</td>
<td>• ATG + <strong>Cyclophosphamide</strong></td>
</tr>
<tr>
<td>• <strong>Cyclophosphamide + Etoposide + TBI</strong> (&gt; 500 cGy (single) or &gt; 800 cGy (fractionated))</td>
<td>• BEAM (Carmustine [BCNU], Etoposide, Cytarabine [Ara-C], Melphalan)</td>
</tr>
<tr>
<td>• <strong>Busulfan</strong> &gt; 7.2 mg/kg IV or &gt;9.0mg/kg orally</td>
<td>• <strong>Busulfan</strong> ≤ 7.2 mg/kg IV or ≤ 9.0mg/kg orally</td>
</tr>
<tr>
<td>• <strong>Busulfan</strong> &gt;300 mg/m2 IV or &gt;375 mg/m² orally</td>
<td>• <strong>Busulfan</strong> ≤ 300 mg/m² IV or ≤ 375 mg/m² orally</td>
</tr>
<tr>
<td>• <strong>Busulfan</strong> (&gt; 7.2 mg/kg IV or &gt;9.0mg/kg orally) + <strong>Cyclophosphamide</strong></td>
<td>• <strong>Melphalan</strong> ≤ 150 mg/m²</td>
</tr>
<tr>
<td>• <strong>Fludarabine + Cytarabine</strong></td>
<td>• <strong>Fludarabine + Cytarabine</strong></td>
</tr>
</tbody>
</table>
## Indicate whether the intent of the preparative regimen was “myeloablative” (to produce marrow ablation or pancytopenia), “non-myeloablative,” or “reduced intensity.”

**Question 160: Date pre-HCT preparative regimen began (irradiation or drugs):**

Enter the date the preparative regimen began. Use the earliest date from questions 161-167 (radiation) or 168-315 (chemotherapy). All dates reported in the preparative regimen section must be equal to or after the date reported for this question.

**Question 161: Was irradiation planned as part of the pre-HCT preparative regimen?**

If irradiation is planned as part of the preparative regimen, check “yes” and continue with question 162. If irradiation is not planned, check “no” and continue with question 169. Irradiation performed as previous treatment should not be reported in this section. Report irradiation performed as previous treatment on the appropriate Disease Specific Form.

**Question 162: What was the prescribed radiation field?**

Indicate if the planned irradiation was to “total body,” “total body by tomotherapy,” “total lymphoid or nodal regions,” or “thoracoabdominal region.”

**Question 163: Total prescribed dose:**

Enter the total dose of radiation prescribed. If radiation was prescribed as a single dose, the amount of radiation delivered in the single dose constitutes the total dose. If the radiation was prescribed in fractionated doses, multiply the dose per fraction by the total number of fractions to determine the total dose. Enter the total dose of radiation in either grays (Gy) or centigrays (cGy).

**Example:**

- **Busulfan** (>7.2 mg/kg IV or >9.0 mg/kg orally) + **Melphalan** >150 mg/m²
- **Melphalan** >150 mg/m²
- **Thiotepa** ≥ 10 mg/kg
- **Treosulfan** > 30,000 mg/m² or > 30 g/m²
- **Fludarabine** + **Cyclophosphamide**
- **Fludarabine** + **TBI** ≤ 500 cGy (single) or ≤ 800 cGy (fractionated)
- **Thiotepa** < 10 mg/kg
- **Treosulfan** ≤ 30,000 mg/m² or ≤ 30 g/m²
- **Etoposide** + **Cyclophosphamide**

These values represent the total prescribed doses. For example, if a recipient is scheduled to receive Melphalan 100 mg/m² for two days (200 mg/m²), the regimen would be myeloablative because the total prescribed dose is > 150 mg/m².
Radiation Order: TBI, 200 cGy/day for three days (3 doses)
Total dose: 200 cGy x 3 doses = 600 cGy
Report “Total Dose” as: 600 cGy

Question 164: Date started:
Enter the date the single dose or first fraction of radiation was administered.

Question 165: Was the radiation fractionated?
Radiation is either delivered as a single dose or in several treatments (fractions). Radiation is fractionated to increase the loss of diseased cells, as they do not recover as quickly as disease-free cells.

If the radiation was fractionated, check “yes” and continue with question 166. If the radiation was not fractionated, check “no” and continue with question 169.

Question 166: Prescribed dose per fraction:
Enter the prescribed dose per fraction in either grays (Gy) or centigrays (cGy).

The dose per fraction multiplied by the total number of fractions (question 168) must be equal to the total dose reported in question 163.

Question 167: Number of days:
Enter the total number of days radiation therapy was prescribed, including any days of rest between days when therapy was administered. The number of days radiation was administered can be greater than the number of fractions.

Example:
Radiation Order: TBI, 200 cGy/day every other day (Mon-Wed-Fri) x 3 doses
Total dose: 200 cGy x 3 doses = 600 cGy
Report “Number of days” as: 5

Question 168: Total number of fractions:
Enter the total number of fractions (treatments) of radiation that were administered. The recipient may receive more than one fraction per day (hyperfractionation).

The total number of fractions multiplied by the dose per fraction (question 166) must be equal to the total dose reported in question 163.
Preparative Regimen – Drugs

The following questions report the prescribed drug therapy that was part of the preparative regimen. Do not report the dose that was actually given. If the recipient has comprehensive report forms due, the actual dose given will be reported on the Recipient Baseline Form (Form 2000). Do not include drugs that are intended to offset the side effects of the chemotherapy (e.g., corticosteroids for nausea, MESNA for hemorrhagic cystitis, etc.).

Drugs After Transplant

Occasionally, protocols list drugs that may be given before and after transplant. If the drugs are planned to be given before and after transplant, only the doses given before transplant should be quantified in the preparative regimen section. The doses given after transplant should be reported in the Post-HCT Disease Therapy Planned as of Day 0 or GVHD Prophylaxis section. For example, if bortezomib or rituximab is planned to be given on Days -2, +1, +4, and +7, report the Day -2 dose in the preparative regimen section, and the post-transplant doses as planned post-HCT therapy.

ATG or alemtuzumab (Campath) given for GVHD prophylaxis planned prior to Day 0 should be reported in the preparative regimen section of the Pre-TED. If ATG, alemtuzumab or cyclophosphamide is planned after Day 0, it should be reported in the GVHD prophylaxis section (questions 317-343).

In this section, include any intrathecal drugs the recipient received for prophylaxis or treatment of CNS disease within 14 days prior to the start date of the preparative regimen.

The form lists each drug by the generic name. The form also lists some drugs by broad categories, with specific drugs listed individually. For example, anthracycline is listed as the broad drug category, followed by the specific drugs daunorubicin, doxorubicin, and idarubicin. The following website provides the trade names under which generic drugs are manufactured: http://www.rxlist.com/script/main/hp.asp.

Report the total dose of each drug as prescribed in the preparative regimen section of the HCT protocol. Do not report the prescribed daily dose. Drug doses must be reported in whole numbers. If the total dose includes a decimal, round to the nearest whole number. For paper submission, do not modify the number of boxes or include decimal values. The pharmacy record or Medication Administration Record (MAR) should be used for determining the date the drug was started.

Report the dose units as either “mg/m²,” “mg/kg,” “target total AUC (µmol x min/L),” “mCi,” or “MBq.” If the total prescribed dose is reported in a unit other than those listed, convert the dose to the appropriate unit.

See the example below or consult with a transplant pharmacist for the appropriate conversion. If drug doses
cannot be converted to the unit listed (e.g., Campath), leave the unit field blank, override the error (using “unable to answer”), and attach a copy of the source document to the Pre-TED using the attachment feature in FormsNet3.

Example: Calculating Total Drug Doses

Drug doses are calculated either by recipient weight in kilograms (kg) or recipient body surface area (BSA) in m². The HCT protocol will specify “x mg/kg” or “x mg/m²” and the total number of doses to be administered.

For example, if the protocol requires cyclophosphamide at 60 mg/kg x 2 days (i.e., 2 doses), the “total prescribed dose” should be reported as “120 mg/kg.”

Pharmacokinetic testing can be used to determine whether the drug concentration in the bloodstream is appropriate to the dose given. This reflects the speed of absorption and elimination of the drug. These tests are usually performed using the first dose of systemic therapy, or a test dose, where multiple samples are drawn at specific time points following the first dose. The samples are sent to a laboratory that performs the testing to determine the drug concentration. If carboplatin was prescribed, indicate if pharmacokinetic testing was performed to determine the preparative regimen dosing. If it is not known whether or not this testing was performed, consult a transplant physician.

A common example of this situation occurs in the use of busulfan. In some cases, a “test dose” of the drug is given before the actual preparative regimen is started, and this dose is used for acquiring drug levels that are used to adjust the dose that will be used in the preparative regimen. In other situations, the first dose of the drug is given in the usual fashion as part of the preparative regimen. After this first dose, serum drug levels are drawn and sent to a reference lab. The drug is continued at the starting dose until the lab results are reported and adjustment is made to later doses.

When a drug is used for the preparative regimen where pharmacokinetics will be tested, it is important to distinguish whether the testing will be done with a “test dose” before beginning the preparative regimen or using the first dose of the preparative regimen. The reporting of the dosing for the CIBMTR forms depends upon this distinction. This helps distinguish whether the dose is part of the therapeutic regimen, or not.

1. A test dose was given > 24 hours prior to the intended therapeutic dosing.
   • Example: A patient with AML underwent allogeneic HCT from a sibling; busulfan and cyclophosphamide were used as the preparative regimen. The patient presented to clinic 9 days before the HCT, where a dose of busulfan at 0.5 mg/kg was given intravenously. Blood samples were drawn for the next 6 hours, after which the patient left the clinic. His samples were sent to a lab, results were returned the next day, and an adjusted dose of busulfan was calculated. He returned to the hospital 6 days before HCT, and began to receive busulfan at the adjusted dose intravenously for 4 days, followed by cyclophosphamide, and proceeded to receive his cells.
Since he received 0.5 mg/kg as a “test dose,” this would not be reported in his total preparative regimen dose.

If a test dose was given, where the dose was distinct from the therapeutic dosing preparative regimen (often 1-2 or more days prior to the initiation of regular dosing), the following should be reported:

- On the Pre-TED (2400) form, the total prescribed dose per protocol would NOT include the test dose.
- On the Baseline (2000) form, the start date of the chemotherapy agent should be reported as the date the first therapeutic dose was administered. The actual dose received would NOT include the test dose.

2. The first dose of therapeutic dosing is used for monitoring.

- **Example:** A patient with MDS received an allogeneic HCT from an unrelated donor; busulfan and fludarabine were used as the preparative regimen. She was admitted to the hospital 7 days before her HCT, and received a dose of busulfan at 0.8 mg/kg IV at 6:00 AM. Serum samples were drawn every 30 minutes until the next dose of Busulfan at 0.8 mg/kg IV was given at 12:00 noon. Her blood was sent to a reference lab, and she continued to receive busulfan every 6 hours. On day -6, the lab called with her drug levels, and it was determined that the current dose was correct. No adjustment was made, and she completed all 16 doses of busulfan. Since the dose of busulfan (0.8 mg/kg) that was used for drug testing was ALSO her first dose of the preparative regimen, it should be included in the amount of drug that was given for preparative regimen. The total prescribed dose per protocol should be reported as “13 mg/kg.” (0.8 mg/kg x 16 doses = 12.8 mg/kg rounded to 13 mg/kg).

If the first dose of the preparative regimen was used to determine pharmacokinetics, the following should be reported:

- On the Pre-TED (2400) form, the total prescribed dose per protocol would include the dose used for monitoring.
- On the Baseline (2000) form, the start date of the chemotherapy agent should be reported as the date the first dose was administered. The actual dose received would include the dose used for monitoring.

Test doses must be reported consistently at your center. Since most centers follow a consistent approach to pharmacokinetic testing, it should be straightforward for the center to adopt a consistent approach to the reporting of test doses.

The “other, specify” category should be used only if the drug is not one of the listed options. If more than one “other” drug is prescribed, list the name of the drugs in the space provided and attach a copy of the source document using the attachment feature in FormsNet3. Do not report additional sites of radiation (e.g., cranial boost) in the “other” drug category. If the recipient is assigned to the Comprehensive Report Forms by the form selection algorithm, the additional sites of radiation will be reported on the Recipient
Baseline Form (Form 2000). If the recipient is assigned to TED Forms by the form selection algorithm, the additional sites of radiation will not be reported.

If the Pre-TED is being completed for a subsequent HCT, do not report therapy that was given to treat the recipient’s disease (between the previous and current planned HCTs) in the preparative regimen section.

If there is a change to the chemotherapy preparative regimen (e.g., from busulfan + fludarabine to melphalan + fludarabine) after the Form 2400 has been submitted, an error correction must be completed in FormsNet to update the chemotherapy regimen given.
Q317-343: GVHD Prophylaxis

The following GVHD prophylaxis questions are to be completed for allogeneic HCTs only. Autologous and syngeneic HCTs continue with question 344.

Question 317: Was GVHD prophylaxis planned/given?

After allogeneic HCT, specific immunosuppressive therapy may be administered to prevent GVHD or to immunosuppress the host marrow, thereby promoting engraftment of the donor stem cells. Most transplant centers have specific GVHD prophylaxis protocols and graft rejection protocols. Planned agents a recipient received as a result of these protocols should be included in this section.

If GVHD prophylaxis was planned per protocol, check “yes” and continue with question 318. If GVHD prophylaxis was not planned per protocol, check “no” and continue with question 344.

Questions 318-343: Specify:

The prophylactic drug options listed on the form are intended to be administered in a systemic or oral form. If the recipient received one of the listed drugs in a topical form, report the drug in the “other, specify” category.

If doses ALG, ALS, ATG, or ATS are planned to be given after infusion, report the total planned post-infusion dose (in mg / kg) in question 319. Do not include any doses administered prior to infusion.

The Pre-TED Form lists the generic chemotherapy drug names. The following website provides the trade names under which generic drugs are manufactured: http://www.rxlist.com/script/main/hp.asp

If GVHD prophylaxis is used for a syngeneic (monozygotic or identical twin) or autologous HCT, attach a copy of the source document using the attachment feature in FormsNet3.
Q344: Other Toxicity Modifying Regimen

The following other toxicity modifying regimen question is optional for non-U.S. centers.

**Question 344: Was KGF (palifermin, Kepivance) started or is there a plan to use it?**

Check “yes” if KGF was started or planned. Check “no” if KGF was not started or planned.

Check “masked trial” if the recipient is part of a KGF study where the agent the recipient received is not known (e.g., placebo, drug, or other agent). Use the error correction process to update the data field once the trial is over and the agent the recipient was given is known.
Q345-357: Post-HCT Disease Therapy
Planned as of Day 0

Question 345: Is this HCT part of a planned multiple (sequential) graft/HCT protocol?

If the current HCT is part of a planned multiple graft/HCT protocol, check “yes.” The HCT for which the form is being completed could be for any of the transplants within the planned multiple graft/HCT protocol. The word “planned” should not be interpreted as: if the recipient relapses, then the “plan” is to perform a subsequent HCT. If this HCT is not part of a planned multiple graft/HCT protocol, check “no.”

Question 346: Is additional post-HCT therapy planned?

If additional post-HCT therapy is planned according to the protocol or standard of care, check “yes” even if the recipient does not receive the planned therapy. The word “planned” should not be interpreted as: if the recipient relapses, then the “plan” is to treat with additional therapy. If additional post-HCT therapy is not planned per protocol, check “no” and submit the form.

The following post-HCT planned therapy questions are optional for non-U.S. centers.

Questions 347-357: Additional post-HCT planned therapy

Indicate if the options listed on the form are intended to be part of the post-HCT planned therapy according to the protocol or standard of care. Report other planned therapies in the “other, specify” category.
The Disease Classification Form is required for all transplants, including subsequent transplants on the comprehensive report form track.

All transplant centers participating in the CIBMTR must submit a Disease Classification Form (Form 2402) for each allogeneic (related or unrelated) hematopoietic cell transplant (HCT). The Disease Classification Form is a requirement of the SCTOD for all United States transplant centers when either the stem cell donation or the transplant occurs within the United States. For more information regarding the SCTOD, see General Instructions, Stem Cell Therapeutics Outcomes Database.

Although data regarding recipients receiving autologous HCT are not required to be submitted as part of the C.W. Bill Young Transplant Program, the CIBMTR is highly committed to collecting data on these recipients for research studies. Centers choosing to report autologous data to the CIBMTR must report on all autologous transplants performed at their center. For more information regarding data reporting for autologous HCT, see General Instructions, Autologous Hematopoietic Stem Cell Transplant.

The Disease Classification Form may be submitted to the CIBMTR up to two weeks prior to the start of the recipient’s preparative regimen (see Helpful Hint below). The Disease Classification Form is due the day of the HCT (day 0), and is past due if not received by that date.

The Disease Classification Form is designed to capture important details regarding the recipient’s primary disease for which the reported HCT is being given. Key reporting areas differ depending on the disease reported (question 1), but may include disease type, subtype, transformations, cytogenetic and molecular markers, disease-specific laboratory results, staging, and disease status.

**Helpful Hint:**
In order to avoid having to make changes to the HCT date, complete the data for the Pre-TED Disease Classification Form (in FormsNet3SM or on paper), but do not submit the form until the first dose of the preparative regimen is given.

**For recipients receiving a subsequent HCT:**
Transplant centers must submit a Disease Classification Form for all subsequent HCTs; this includes recipients assigned to the TED Forms and the Comprehensive Report Forms by the form selection algorithm.

For the majority of subsequent HCTs, the recipient will remain on the original follow-up form track (TED or
CRF) assigned by the form selection algorithm. For more information regarding center type and the form selection algorithm, see Section 1 in the Center Reference Guide. A recipient may need to change tracks if enrolled on a study that requires comprehensive forms.

For recipients of multiple transplants, transplant centers are not granted access to the new Pre-TED Disease Classification Form in FormsNetSM until the Post-TED (Form 2450) or Post-Infusion Data Form (Form 2100) from the previous transplant has been completed.

Links to Sections of the Form:
Q1-2: Primary Disease for HCT
Q3-89: Acute Myelogenous Leukemia
Q90-151: Acute Lymphoblastic Leukemia
Q152-155: Acute Leukemias of Ambiguous Lineage and Other Myeloid Neoplasms
Q156-166: Chronic Myelogenous Leukemia
Q167-260: Myelodysplastic / Myeloproliferative Diseases
Q261-267: Other Leukemia
Q268-285: Hodgkin and Non-Hodgkin Lymphoma
Q286-317: Multiple Myeloma / Plasma Cell Disorder
Q318-319: Solid Tumors
Q320-321: Severe Aplastic Anemia
Q322-324: Inherited Abnormalities of Erythrocyte Differentiation or Function
Q325-327: Disorders of Immune System
Q328-330: Inherited Abnormalities of Platelets
Q330-331: Inherited Disorders of Metabolism
Q332-333: Histocytic Disorders
Q334-341: Autoimmune Diseases
Q342: Other Disease

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/</td>
<td>2402:</td>
<td>Add</td>
<td>Added (in red below) additional instruction for question 277:</td>
</tr>
<tr>
<td>Date</td>
<td>Action</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
</tbody>
</table>
| 27/19        | Disease    | **Question 277: Was a PET (or combination PET / CT) scan performed? (at last evaluation prior to the start of the preparative regimen / infusion)**
<p>|              | Classification | Report “Yes” and go to question 278 if a PET scan was performed within three months prior to the start of the preparative regimen / infusion. <strong>Combination PET / CT may also be reported, but a CT scan alone should not be captured here.</strong> Centers may report a PET scan performed during the most recent line of therapy so long as it is the most recent scan and was done within noted period. Report “No” and go to question 283 if a PET scan was not performed within this period. |
| 2/27/19      | Add        | Added (in red below) additional instruction for question 165: <em>Indicate the number of times the recipient has been in the disease phase reported in question 163.</em>                                                                                                                                                                                                                                                                  |
| 8/10/18      | Modify     | Modified (red text was added, struck out text was deleted) the instructional blue box for question 212: Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. *<em>The CIBMTR forms capture disease subtype using the WHO classification of myeloid neoplasms and acute leukemia. Secondary myelofibrosis is not included as a separate category per the WHO classification. Therefore, when reporting the disease subtype at the time of transplant for recipients with secondary myelofibrosis, report “Primary Myelofibrosis (PMF)” to accurately capture these cases on the CIBMTR Forms. Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. However, effective immediately, cases of post-essential thrombocythemia myelofibrosis (post-ET MF) or post-polycythemia vera myelofibrosis (post-PV MF) will now be reported as “Primary Myelofibrosis (PMF)” at the time of HCT. In order to capture accurate data, the secondary MF cases need to be lumped in with the PMF cases, since treatment for post-ET MF and post-PV MF is the same as PMF.</em> |
| 8/9/18       | Add        | Added instruction for question 281-282: <em>If the PET scan result is only documented as an ‘X’, report this as “Unknown” for question 281.</em>                                                                                                                                                                                                                                                                                                           |
| 4/10/18      | Modify     | Updated the Common Disease Transformation Table included in the instructions for questions 1 and 2. The CLL section of the form should not be completed for a Richter’s Transformation as of Revision 3 of the Form 2402.                                                                                                                                                                                                                                                                                         |
| 4/9/18       | Modify     | Modified the following instruction for question 317: Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. A PET scan Date of radiographic study (PET, MRI, CT) may be used if the same or previous PET scan radiographic study had previously been obtained and only in limited circumstances (e.g., plasmacytomas, lytic lesions). |
| 3/22/18      | Add        | Added <strong>MDS/MPN</strong> note box below the instructions for question 256 regarding recipients who only received supportive care prior to transplant.                                                                                                           |</p>
<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Action</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/28/18</td>
<td>2402: Disease</td>
<td>Add</td>
<td>Added the following instruction for question 283. <em>When a transformation has occurred (e.g., follicular lymphoma (FL) transformed to DLBCL), count the response number (CR1, REL2, etc.) beginning with the transformed lymphoma (in this case the DLBCL). Do not include the responses to the lymphoma sub-type prior to the transformation.</em></td>
</tr>
<tr>
<td>2/27/18</td>
<td>2402: Disease</td>
<td>Add</td>
<td>Added instruction for questions 281-282. <em>If multiple scores are documented, report the highest.</em></td>
</tr>
<tr>
<td>2/14/18</td>
<td>2402: Disease</td>
<td>Remove</td>
<td>Removed incorrect instruction (struck out below) from question 271. <em>If the histology reported at infusion (question 268) is a transformation from CLL, indicate “Yes,” and go to question 272. Also, complete the disease classification questions for CLL.</em></td>
</tr>
<tr>
<td>1/30/18</td>
<td>2402: Disease</td>
<td>Modify</td>
<td>Version 3 of the 2402: Disease Classification section of the Forms Instruction Manual released. Version 3 corresponds to revision 3 of the Form 2402.</td>
</tr>
</tbody>
</table>
Q1-2: Primary Disease for HCT / Cellular Therapy

Disease Classification Questions
The newest versions of the TED Forms use the World Health Organization (WHO) disease classifications. The Disease Classification questions contain all of the established WHO disease types and subtypes. The “other, specify” category should be used only if the recipient’s disease is not one of the listed options. For more information regarding disease classification, consult a transplant physician, contact your center’s CIBMTR CRC, or visit the WHO website at: http://www.who.int/classifications/icd/en/.

Several of the Disease Classification questions ask for “Status at Transplantation.” Although there are many interpretations of disease response criteria, when reporting data to the CIBMTR, use the guidelines in this manual to determine disease status. A majority of the disease response criteria are established by an international working group. Citations of resources used to define disease responses are included where applicable. If the recipient’s status is unclear, consult with the transplant physician for further information or contact your center’s CIBMTR CRC.

Malignant vs. Non-Malignant
Malignant diseases involve cells dividing without control that can spread to other parts of the body through blood and lymph systems. These diseases are usually characterized by unlimited, aggressive growth, invasion of surrounding tissues, and metastasis. Non-malignant diseases involve cell overgrowth, but lack the malignant properties of cancer.

The CIBMTR database disease codes are represented in parentheses after the disease subtype on the Disease Classification questions and can be helpful in mapping diagnosis [e.g., Myeloid Sarcoma (295)], and determining if the disease is malignant or non-malignant. Disease codes (10-299) indicate a malignant disease, with the exception of Paroxysmal Nocturnal Hemoglobinuria (PNH) (56). A disease code of (300) or above indicates a non-malignant disease, with the exception of disease code (900), which could indicate either a malignant or non-malignant disease.

If the indication for HCT is due to a combination of diseases or a transformation of one disease to another, it may be necessary to report multiple disease classifications. The tables below list how common examples of disease combinations and transformations should be reported using the Disease Classification questions.

Common Disease Combinations
### Disease Combinations

<table>
<thead>
<tr>
<th>Disease Combinations</th>
<th>Report Primary Disease as:</th>
<th>Report disease diagnosis date of:</th>
<th>Complete multiple disease sections of the Disease Classification Form?</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAN or SAA and AML</td>
<td>AML</td>
<td>AML</td>
<td>No</td>
</tr>
<tr>
<td>FAN or SAA and MDS</td>
<td>MDS</td>
<td>MDS</td>
<td>No</td>
</tr>
<tr>
<td>MYE and AMY</td>
<td>MYE</td>
<td>MYE</td>
<td>No</td>
</tr>
</tbody>
</table>

### Common Disease Transformations

<table>
<thead>
<tr>
<th>Disease Transformation</th>
<th>Report primary disease as:</th>
<th>Report disease diagnosis date of:</th>
<th>Complete multiple disease sections of the Disease Classification Form?</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS or MPS to AML</td>
<td>AML</td>
<td>AML</td>
<td>Yes- AML and MDS/MPN</td>
</tr>
<tr>
<td>JMML to AML</td>
<td>AML</td>
<td>AML</td>
<td>Yes- AML and MDS/MPN (select questions only)</td>
</tr>
<tr>
<td>NHL to another NHL</td>
<td>Second NHL diagnosis</td>
<td>Second NHL diagnosis</td>
<td>No</td>
</tr>
<tr>
<td>HL to NHL*</td>
<td>NHL</td>
<td>NHL</td>
<td>No</td>
</tr>
<tr>
<td>CLL to NHL (i.e., Richter’s Syndrome)</td>
<td>NHL</td>
<td>CLL</td>
<td>No</td>
</tr>
</tbody>
</table>

AML=Acute Myelogenous Leukemia; AMY=Amyloidosis; CLL=Chronic Lymphocytic Leukemia; FAN=Fanconi Anemia; MDS=Myelodysplastic Syndrome; MPS=Myeloproliferative Disease; MYE=Multiple Myeloma; NHL=Non-Hodgkin Lymphoma; SAA=Severe Aplastic Anemia.

*Ensure that the disease process is a transformation from Hodgkin lymphoma to Non-Hodgkin lymphoma (typically diffuse large B-cell lymphoma), rather than the distinct entity “B-cell lymphoma, unclassifiable, with features indeterminate between DLBCL and classical Hodgkin Lymphoma.”

#### Question 1: Date of diagnosis for primary disease for HCT:

The date of diagnosis is important because the interval between diagnosis and HCT is often a significant indicator for the recipient’s prognosis post-HCT.

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center, and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.
If the recipient was diagnosed prenatally (*in utero*), report the date of birth as the date of diagnosis.

If the exact pathological diagnosis date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

If this is a subsequent HCT for a new malignancy (or other new indication), report the date of diagnosis of the new malignancy.

**Question 2: What was the primary disease for which the HCT was performed?**

Select the primary disease for which the recipient is receiving the HCT and continue with the appropriate disease classification questions.
**Q3-89: Acute Myelogenous Leukemia**

**Acute Myelogenous Leukemia (AML)** is a cancer of the white blood cells. It is characterized by the rapid proliferation of abnormal, immature myelocytes, known as myeloblasts, in the bone marrow. This accumulation of blasts in the marrow prevents the formation of healthy red blood cells, white blood cells, and/or platelets. Normal myeloblasts develop into neutrophils, basophils, and eosinophils, which are all white blood cells that fight infection. In AML, the leukemic myeloblasts do not fully develop and are unable to fight infection. The symptoms of AML result from a drop in red blood cell, platelet, and normal white blood cell counts caused by the replacement of normal bone marrow with leukemic cells.

Certain prognostic indicators are associated with poorer outcomes. These include advanced age (50+ years of age), AML arising from MDS or secondary/therapy-related AML, and certain genetic mutations that are described in greater detail later in this manual.

**Question 3: Specify the AML classification**

Indicate the disease classification at diagnosis.

Report the most specific entity that applies to the recipient. For example, if the recipient was classified using both cytogenetic data and the M5 FAB classification, the more specific cytogenetic data should be reported for classification purposes.

**Question 4: Did AML transform from MDS or MPN?**

AML often evolves from MDS or MPN. This transformation is typically distinguished by the percentage of blasts in the bone marrow.

AML that transforms from MDS or MPN has a lower survival prognosis because of the association with unfavorable cytogenetic abnormalities.

AML can also evolve from Juvenile Myelomonocytic Leukemia (JMML). JMML is a rare form of chronic leukemia that affects young children, usually before the age of five. JMML results from DNA mutations in cells called monocytes. Normal monocytes attack invading microorganisms and assist lymphocytes in carrying out immune functions. Abnormal monocytes in JMML accumulate in the bone marrow and interfere with the production of normal white blood cells, red blood cells, and platelets.

If AML transformed from MDS or MPN (including JMML), check “Yes” and complete both the AML and MDS/MPN disease classification sections. If AML did not transform from MDS or MPS, check “No.”
If MDS/MPN is suspected, but not confirmed by documented laboratory or pathologic findings, or if there is documentation of MDS/MPN concurrent with AML, check “No.”

**Question 5: Is the disease (AML) therapy related?**

Agents such as radiation or systemic therapy used to treat other diseases (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, or breast cancer) can damage the marrow and lead to a secondary malignancy such as AML. If the diagnosis of AML is therapy-related, check “Yes.”

If the diagnosis of AML is not therapy-related, check “No.”

- If AML was preceded by therapy-related MDS, check “No.”
- If the recipient developed AML after an environmental exposure (e.g., exposure to benzene), check “No.”

If it is unknown whether or not the diagnosis of AML was therapy-related, check “Unknown.”

**Question 6: Did the recipient have a predisposing condition?**

A predisposing condition is a condition that contributes to the susceptibility of developing leukemia. Therefore, diagnosis of the condition increases the likelihood that the recipient will develop leukemia. If the recipient has a documented history of a predisposing condition, check “Yes” and continue with question 7. If there is no history of a predisposing condition or if predisposition is unknown, indicate “No” or “Unknown” and continue with question 9.

**Question 7-8: Specify condition:**

Bloom syndrome is an autosomal recessive genetic disorder characterized by excessive chromosome breakage and corresponding rearrangements, proportional dwarfism, and sun sensitivity. The chromosomal instability seen in Bloom syndrome is generally assumed to be responsible for these individuals’ predisposition to malignancy.

Down syndrome is also a chromosomal disorder (trisomy 21). It is characterized by an additional chromosome 21. Down syndrome patients exhibit a particular set of facial characteristics, growth deficiency, and cognitive impairment. Although Down syndrome patients have a reduced risk of developing many common malignancies, they have an increased risk of developing leukemia.

Fanconi anemia is a rare genetic blood disorder that prevents the body from producing a sufficient number of new blood cells to function properly. Abnormal blood cells may also be produced. These patients are short in stature, exhibit skeletal anomalies, and have an increased risk of developing solid tumors and
leukemias.

Dyskaratosis congenita (DKC), also known as Zinsser-Engman-Cole syndrome, involves progressive bone marrow failure. Patients with DKC experience skin hyperpigmentation, nail dystrophy, and oral leukoplakia (a white patch / plaque that cannot be rubbed off).

Indicate the recipient's predisposing condition prior to the diagnosis of leukemia. If the condition was “Other condition,” specify the condition in question 8.

**At Diagnosis, Last Evaluation, and In Between**
Questions 9-83 ask about testing performed at different time points prior to HCT. For reporting purposes, use the definitions below to determine where to report testing on the Disease Classification Form.

**At Diagnosis:** Any testing performed between the date of diagnosis (question 1) and the start of any treatment for AML.

**In Between:** Any pre-infusion testing which cannot be reported as part of “At Diagnosis” or “Last Evaluation.”

**Last Evaluation:** Testing performed during the recipient’s work-up for HCT or cellular therapy (generally within 30 days of the start of the preparative regimen or infusion).

**Question 9: Were cytogenetics tested (karyotyping or FISH)? (at diagnosis)**

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality which reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C, Cytogenetic Assessments.

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

FISH is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA. These probes are mixed with cells from the recipient’s blood or bone marrow. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells.

**Table 3. Examples of AML Cytogenetic Findings Categorized by Prognosis**
<table>
<thead>
<tr>
<th>Favorable</th>
<th>Intermediate</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(15;17)</td>
<td>Normal</td>
<td>≥ 3 abnormalities</td>
</tr>
<tr>
<td>t(8;21)</td>
<td>+8</td>
<td>5- or 5q-</td>
</tr>
<tr>
<td>inv(16) or t(16;16)</td>
<td>t(9;11)</td>
<td>7- or 7q-</td>
</tr>
<tr>
<td>All other abnormalities</td>
<td></td>
<td>t(9;22)</td>
</tr>
</tbody>
</table>

Indicate whether cytogenetic studies were performed at diagnosis. Do not report any testing performed after treatment for AML has started. If cytogenetic studies were obtained at diagnosis, check “Yes” and go to question 10. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate “No” or “Unknown” respectively and go to question 21.

**Question 10-11: Were cytogenetics tested via FISH?**

If FISH studies were performed at diagnosis (see note box above question 9), report “Yes” for question 10 and indicate whether clonal abnormalities were detected in question 11. Do not report any testing performed after treatment for AML has started. If FISH studies were not performed at this time point, report "No" for question 10 and go to question 15. Examples of this include: no FISH study performed or FISH sample was inadequate.

**Question 12-14: Specify cytogenetic abnormalities (FISH)**

Report the number of abnormalities detected by FISH at diagnosis (see note box above question 9) in question 12. After indicating the number of abnormalities in question 12, select all abnormalities detected in questions 13-14.

If a clonal abnormality is detected, but not listed as an option in question 13, select “Other abnormality” and specify the abnormality in question 14. If multiple “Other abnormalities” were detected, report “see attachment” in question 14 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 15-16: Were cytogenetics tested via karyotyping?**

If karyotyping was performed at diagnosis (see note box above question 9), report “Yes” for question 15 and indicate whether clonal abnormalities were detected in question 16. Do not report any testing performed after treatment for AML has started. If karyotyping was not performed at this time point, indicate “No” and go to question 20. Examples of this include: karyotyping was not performed or karyotyping sample was inadequate.

**Question 17-19: Specify cytogenetic abnormalities (karyotyping)**

Report the number of abnormalities detected by karyotyping at diagnosis (see note box above question 9) in
question 17. After indicating the number of abnormalities in question 17, select all abnormalities detected in questions 18-19.

If a clonal abnormality is detected, but not listed as an option in question 18, select “Other abnormality” and specify the abnormality in question 19. If multiple “Other abnormalities” were detected, report “see attachment” in question 19 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 20: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 9-19. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 21: Were tests for molecular markers performed (e.g., PCR, NGS)? (at diagnosis)**

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient’s primary disease. Testing for these sequences is often performed using PCR based methods; however, lower sensitivity testing, including FISH, may also be used to detect molecular markers. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include chromosomal microarray / chromosomal genomic array, Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

If testing for molecular markers was performed at diagnosis (see note box above question 9), report “Yes” and go to question 22.

If molecular marker testing was not performed at diagnosis or it is not known if testing was done, report “No” or “Unknown” respectively and go to question 34.

**Question 22-33: Specify results**

For each molecular marker in questions 22-31, report whether testing was “Positive,” “Negative,” or “Not done” at diagnosis (see note box above question 9). If tests identified a molecular marker other than those listed in questions 22-31, report the result in question 32 and specify the marker in question 33.

If multiple “Other molecular marker[s]” were tested, report one instance (i.e., copy) of question 32-33 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” were tested, do the following:
• report one instance of question 32-33; and
• report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
• report “see attachment” in question 33; and
• attach any / all reports documenting the results of testing for “Other molecular marker[s].”

If CEBPA is reported as “Positive” (question 22) question 23 must be completed. If the lab report does not specify whether the detected marker was biallelic / homozygous or monoallelic / heterozygous, confirm with the laboratory whether this information can be determined prior to reporting “Unknown.”

If FLT3-ITD is reported as “Positive” (question 25) questions 26 and 27 must be completed. If the allelic ratio is known, report “Known” for question 26 and report the value in question 27. If the lab report does not specify the allelic ratio, confirm with the laboratory whether this information can be determined prior to reporting “Unknown.”

### Table 4. Common Molecular Markers Associated with AML

<table>
<thead>
<tr>
<th>Molecular Abnormality</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEBPA</td>
<td>CEBPA, aka CCAAT/enhancer binding protein α, is a transcription factor required for the differentiation of granulocytes. Numerous CEBPA mutations have been identified in relation to AML, with the majority of patients displaying biallelic mutations ultimately resulting in the down regulation of gene activity. Decreased gene activity results in decreased differentiation potential for immature granulocytes. An estimated 7-15% of AML patients have CEBPA mutations and CEBPA mutations are generally found in M1 and M2 subtypes in conjunction with intermediate-risk cytogenetics. Studies show an association with more favorable outcomes.¹</td>
</tr>
<tr>
<td>FLT3-D835 point mutation</td>
<td>FLT3 encodes a receptor tyrosine kinase. The FLT3-D835 point mutation, aka FLT3-TKD, is an activating mutation impacting tyrosine-kinase domains. FLT3 mutations are found in up to 1/3 of all AML patients. The clinical significance of TKD activation remains unclear. FLT3-D385 mutations are often found in conjunction with other mutations. Overall, FLT3-D385 is not considered a favorable or poor prognostic indicator. However, in certain combinations with other mutations, there are associations with both improved and diminished survival.²³</td>
</tr>
<tr>
<td>FLT3-ITD mutation</td>
<td>FLT3 encodes a receptor tyrosine kinase. The FLT3-ITD (internal tandem duplication) interferes with certain down regulation functions within receptor tyrosine kinases, leading to activation of TK activity. FLT3 mutations are found in up to 1/3 of all AML patients. FLT3-ITD is considered a poor prognostic factor. Sorafenib (Nexavar) has been shown to initially improve disease response in FLT3-ITD-positive AML.⁴</td>
</tr>
<tr>
<td>IDH1</td>
<td>Isocitrate Dehydrogenase (IDH) is an oxidative enzyme involved in the citric acid cycle. IDH1 mutations result in incorrect catalytic activity, leading to increased levels of an oncometabolite, 2-hydroxyglutarate. The pathologic activity of IDH1 mutations is still being studied, but it has been suggested that IDH mutations may be a distinct mechanism in AML pathogenesis;</td>
</tr>
<tr>
<td><strong>IDH2</strong></td>
<td>Isocitrate Dehydrogenase (IDH) is an oxidative enzyme involved in the citric acid cycle. IDH2 is a mitochondrial homolog to IDH1. Much like IDH1 mutations, IDH2 mutations result in incorrect catalytic activity, leading to increased levels of (D)-2-hydroxyglutarate. The pathologic activity of IDH2 mutations are still being studied, but it has been suggested that IDH mutations may be a distinct mechanism in AML pathogenesis; research models show they may cause an accumulation of hematopoietic progenitor cells. Early research suggests IDH2 mutation may be a more favorable prognostic indicator, unlike IDH1 mutation, though there may be differences based on where the IDH2 mutation occurs in gene.</td>
</tr>
<tr>
<td><strong>KIT</strong></td>
<td>KIT encodes a receptor tyrosine kinase. The KIT mutations at exons 8 and 17 are associated with activation of encoded proteins, resulting in activation impacting tyrosine-kinase domains. Patients with t(8;21) and inv(16) cytogenetics are frequently screened for KIT mutations, which adversely affect prognosis in these patients.</td>
</tr>
<tr>
<td><strong>NPM1</strong></td>
<td>NPM1 encodes a protein responsible for multiple cellular functions, including the regulation of the ARF-p53 tumor suppressor pathway. Mutations in NPM1 result in gene over-expression and subsequent inactivation of ARF-p53 tumor suppression pathway. NPM1 mutations are one of the most common molecular markers seen in AML and are associated with improved survival.</td>
</tr>
<tr>
<td><strong>Other molecular marker</strong></td>
<td>Assessments for other molecular markers known or believed to be associated with AML may be performed. If these studies are performed, indicate “positive” or “negative” and specify the marker in question 56.</td>
</tr>
</tbody>
</table>

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2 Mead AJ, Linch DC, Hills RK, Wheatley K, Burnett AK, Gale RE. (2007). FLT3 tyrosine kinase domain mutations are biologically distinct from and have a significantly more favorable prognosis than FLT3 international tandem duplications in patient with acute myeloid leukemia. *Blood*, 110, 1262-70.


**Question 34: Were cytogenetics tested (karyotyping or FISH)? (between diagnosis and last evaluation)**

See question 9 for a description of cytogenetic tests. Indicate whether cytogenetic studies were performed between diagnosis and the last evaluation prior to HCT / cellular therapy (see note above question 9). If cytogenetic studies were obtained during this time, check “Yes” and go to question 15. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate “No” or “Unknown” respectively and go to question 46.

**Question 35-36: Were cytogenetics tested via FISH?**

If FISH studies were performed between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 9), report “Yes” for question 35 and indicate whether clonal abnormalities were detected in question 36. If multiple FISH assessments were performed, report “Abnormalities Identified” if any testing showed clonal abnormalities during this period. If FISH studies were not performed during this period, report “No” for question 35 and go to question 40. Examples of this include: no FISH study performed or all FISH samples were inadequate.

**Question 37-39: Specify cytogenetic abnormalities (FISH)**

Report the number of abnormalities detected by FISH between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 9) in question 37. If FISH studies showed different clonal abnormalities during this time, report the total number of clonal abnormalities detected. After indicating the number of clonal abnormalities in question 37, select all clonal abnormalities detected during this period in questions 38-39. This includes all clonal abnormalities detected any FISH assessment performed during this period.

If a clonal abnormality is detected, but not listed as an option in question 38, select “Other abnormality” and specify the abnormality in question 39. If multiple “Other abnormalities” were detected, report “see attachment” in question 39 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.
**Question 40-41: Were cytogenetics tested via karyotyping?**

If karyotyping was performed between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 9), report “Yes” for question 40 and indicate whether clonal abnormalities were detected in question 41. If multiple karyotypes were performed, report “Abnormalities Identified” if any testing showed clonal abnormalities during this period. If karyotyping was not performed during this period, report “No” for question 40 and go to question 45. Examples of this include: no karyotyping performed or all karyotype samples were inadequate.

**Question 42-44: Specify cytogenetic abnormalities (karyotyping)**

Report the number of abnormalities detected by karyotyping between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 9) in question 42. If karyotype studies showed different clonal abnormalities during this time, report the total number of clonal abnormalities detected. After indicating the number of clonal abnormalities in question 42, select all clonal abnormalities detected during this period in questions 43-44. This includes all clonal abnormalities detected any karyotype performed during this period.

If a clonal abnormality is detected, but not listed as an option in question 38, select “Other abnormality” and specify the abnormality in question 39. If multiple “Other abnormalities” were detected, report “see attachment” in question 39 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 45: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 34-44. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 46: Were tests for molecular markers performed (e.g., PCR, NGS)? (between diagnosis and last evaluation)**

See question 21 for a description of testing for molecular markers. Indicate whether testing for molecular markers was performed between diagnosis and the last evaluation prior to HCT / cellular therapy (see note above question 9). If testing for molecular markers was performed during this time, check “Yes” and go to question 47. If cytogenetic studies were not obtained during this period or it is not known whether testing for molecular markers was performed, indicate “No” or “Unknown” and go to question 59.

**Question 47-58: Specify results**

For each molecular marker in questions 47-56, report whether testing was “Positive,” “Negative,” or “Not
done” between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 9). If tests identified a molecular marker other than those listed in questions 47-56, report the result in question 57 and specify the marker in question 58.

If multiple “Other molecular marker[s]” were tested, report one instance (i.e., copy) of question 57-58 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” were tested, do the following:

- report one instance of question 57-58; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 58; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”

If CEBPA is reported as “Positive” (question 47) question 48 must be completed. If the lab report does not specify whether the detected marker was biallelic / homozygous or monoallelic / heterozygous, confirm with the laboratory whether this information can be determined prior to reporting “Unknown.”

If FLT3-ITD is reported as “Positive” (question 50) questions 51 and 52 must be completed. If the allelic ratio is known, report “Known” for question 51 and report the value in question 52. If the lab report does not specify the allelic ratio, confirm with the laboratory whether this information can be determined prior to reporting “Unknown.”

**Question 59: Were cytogenetics tested (karyotyping or FISH)? (at last evaluation)**

See question 9 for a description of cytogenetic testing. Indicate whether cytogenetic studies were performed at the last evaluation prior to HCT / cellular therapy (see note box above question 9). If cytogenetic studies were obtained at this time point, check “Yes” and go to question 60. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate “No” or “Unknown” respectively and go to question 71.

**Questions 60-61: Were cytogenetics tested via FISH?**

If FISH studies were performed at the last evaluation prior to HCT / cellular therapy (see note box above question 9), report “Yes” for question 60 and indicate whether clonal abnormalities were detected in question 61. If FISH studies were not performed at this time point, report “No” for question 60 and go to question 65. Examples of this include: no FISH study performed or FISH sample was inadequate.
**Question 62-64: Specify cytogenetic abnormalities (FISH)**

Report the number of abnormalities detected by FISH at the last evaluation prior to HCT / cellular therapy (see note box above question 9) in question 62. After indicating the number of abnormalities in question 62, select all abnormalities detected in questions 63-64.

If a clonal abnormality is detected, but not listed as an option in question 63, select “Other abnormality” and specify the abnormality in question 64. If multiple “Other abnormalities” were detected, report “see attachment” in question 64 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 65-66: Were cytogenetics tested via karyotyping?**

If karyotyping was performed at the last evaluation prior to HCT / cellular therapy (see note box above question 9), report “Yes” for question 65 and indicate whether clonal abnormalities were detected in question 66. If karyotyping was not performed at this time point, indicate “No” and go to question 71. Examples of this include: karyotyping was not performed or karyotyping sample was inadequate.

**Question 67-69: Specify cytogenetic abnormalities (karyotyping)**

Report the number of abnormalities detected by karyotyping at the last evaluation prior to HCT / cellular therapy (see note box above question 9) in question 67. After indicating the number of abnormalities in question 67, select all abnormalities detected in questions 68-69.

If a clonal abnormality is detected, but not listed as an option in question 68, select “Other abnormality” and specify the abnormality in question 69. If multiple “Other abnormalities” were detected, report “see attachment” in question 69 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 70: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 59-69. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 71: Were tests for molecular markers performed (e.g., PCR, NGS)? (at last evaluation)**

See question 21 for a description of testing for molecular markers. If testing for molecular markers was performed at the last evaluation prior to HCT / cellular therapy (see note box above question 9), report “Yes” and go to question 72. If molecular marker testing was not performed at this time point or it is not known if testing was done, report “No” or “Unknown” respectively and go to question 84.
**Question 72-83: Specify results**

For each molecular marker in questions 72-81, report whether testing was “Positive,” “Negative,” or “Not done” at the last evaluation prior to HCT / cellular therapy (see note box above question 9). If tests identified a molecular marker other than those listed in questions 72-81, report the result in question 82 and specify the marker in question 83.

If multiple “Other molecular marker[s]” were tested, report one instance (i.e., copy) of question 82-83 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” were tested, do the following:

- report one instance of question 82-83; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 83; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”

If CEBPA is reported as “Positive” (question 72) question 73 must be completed. If the lab report does not specify whether the detected marker was biallelic / homozygous or monoallelic / heterozygous, confirm with the laboratory whether this information can be determined prior to reporting “Unknown.”

If FLT3-ITD is reported as “Positive” (question 75) questions 76 and 77 must be completed. If the allelic ratio is known, report “Known” for question 76 and report the value in question 77. If the lab report does not specify the allelic ratio, confirm with the laboratory whether this information can be determined prior to reporting “Unknown.”

**Question 84: Did the recipient have central nervous system leukemia at any time prior to the start of the preparative regimen / infusion?**

Central nervous system (CNS) involvement by leukemia may be detected via pathologic examination of cerebrospinal fluid or tumor tissue as well as by radiological examinations (e.g., MRI, PET/CT, MIBG, etc.). If the recipient had documented involvement of AML in the CNS, report “Yes” for question 84. If all CNS testing was negative since the time of diagnosis, report “No.” If testing for CNS involvement was not performed from the time of diagnosis to the time of HCT / cellular therapy, report “Unknown.”

**Question 85: What was the disease status (based on hematologic test results)?**

Indicate the disease status of AML at the last assessment prior to the start of the preparative regimen. Refer to the AML Response Criteria section of the Forms Instructions Manual for definitions of each response. For reporting purposes, consider complete remission with incomplete hematologic recovery (CRi) a complete
remission (CR1, CR2, or CR3+).

If the recipient did not receive any treatment for AML from the time of diagnosis to the start of the preparative regimen / infusion, report “No treatment” and go to question 89.

If the recipient’s disease status is primary induction failure at the time of HCT / cellular therapy, go to question 89.

If the recipient’s disease status is CR / CRi at the time of HCT / cellular therapy, go to question 86.

If the recipient’s disease status is relapse at the time of HCT / cellular therapy, go to question 88.

**Question 86: How many cycles of induction therapy were required to achieve 1st complete remission (CR)? (includes CRi)**

Chemotherapy is initially given as induction therapy intended to bring the disease into remission. Recipients usually have one to two cycles of induction therapy; disease prognosis is considered less favorable if the patient fails to achieve remission with the first induction therapy and even poorer if patients fail two or more induction therapies. An example of a common induction therapy for all AML subtypes (except M3) is a combination of an anthracycline and cytarabine, commonly known as “7+3.” In this regimen, cytarabine is typically administered for seven days at a dose of 100 mg/m\(^2\)/day. The anthracycline (usually daunorubicin at 45 to 60 mg/m\(^2\)/day or idarubicin at 12 mg/m\(^2\)/day) is generally given on the first three days the cytarabine is given.

The second phase of chemotherapy is known as consolidation therapy. The goal of consolidation therapy is to destroy any remaining leukemia cells and sustain remission. An example of a common consolidation therapy for all AML subtypes (except M3) is high-dose cytarabine, commonly referred to as “HiDAC.” In this regimen, cytarabine is typically administered at a dose exceeding 10 g/m\(^2\) per cycle.

Maintenance chemotherapy may follow consolidation therapy. Maintenance chemotherapy is given in lower doses and is intended to prolong a remission. Maintenance therapy is used less commonly for the treatment of AML than other malignancies. Treatment may also be administered for relapsed disease. Much like induction therapy, treatment for relapse is intended to bring the disease back into remission. Systemic therapeutic agents used to induce remission following relapse often differ from those used in the initial induction, since the disease is often resistant to many of the agents used earlier in the disease course and is considered high-risk with a poor prognosis. Allogeneic HCT is often considered the only potential “cure” for relapsed disease.

Indicate the number of cycles of induction therapy that were required to achieve the first CR.
This question is optional for international centers.


**Question 87: Was the recipient in remission by flow cytometry?**

Question 87 will only be answered if CR has been reported for question 85. Flow cytometry assessment is a method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics. Its primary clinical purpose in the setting of leukemias is to quantify blasts in the peripheral blood or bone marrow, or to identify unique cell populations through immunophenotyping. Flow cytometry assessment may also be referred to as “MRD,” or minimal residual disease, testing.

Flow cytometric remission is a treatment response in which no blasts can be detected.

If flow cytometric abnormalities associated with the recipient’s disease were identified previously, but the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate “yes.”

If flow cytometric abnormalities associated with the recipient’s disease were identified at the last evaluation prior to the start of the preparative regimen, indicate “no.”

Indicate “unknown” if flow cytometric abnormalities associated with the recipient’s disease were identified previously and no flow cytometry assessment was performed prior to the start of the preparative regimen.

Indicate “not applicable” if one of the following applies:

- No flow cytometry assessments were performed at any time prior to the start of the preparative regimen.
- Flow cytometric abnormalities were not identified on previous testing and no flow cytometric abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

This question is optional for international centers.

**Question 88: Date of most recent relapse:**

Enter the date of the most recent relapse prior to the start of the preparative regimen / infusion. If reporting a pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear), enter the date the sample was collected. If extramedullary disease was detected by radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place. If the physician determines cytogenetic or molecular relapse, enter the date the sample was collected for...
cytogenetic or molecular evaluation. If the physician determines evidence of relapse following a clinical
assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in
General Instructions, General Guidelines for Completing Forms.

**Question 89: Date assessed**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen.
The date reported should be that of the most disease-specific assessment within the pre-transplant work-up
period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g.,
bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory
assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical
examination. Enter the date the sample was collected for pathological and laboratory evaluations; enter the
date the imaging took place for radiographic assessments.

If the exact date is not known, use the process for reporting partial or unknown dates as described in
General Instructions, Guidelines for Completing Forms.

This question is optional for international centers.
**Q90-151: Acute Lymphoblastic Leukemia**

**Acute Lymphoblastic Lymphoma**

Due to the aggressive nature of precursor T- and precursor B-cell lymphoblastic lymphoma (or lymphoma/leukemia), the primary disease reported for recipients with these malignancies should be acute lymphoblastic leukemia (T-cell lymphoblastic leukemia/lymphoma or B-cell ALL, NOS {L1/L2}).

**Acute Lymphoblastic Leukemia (ALL)** is a cancer of the white blood cells. It is characterized by the rapid proliferation of abnormal, immature lymphocytes, known as lymphoblasts, in the bone marrow. This accumulation of blasts in the marrow prevents the formation of healthy red blood cells, white blood cells and/or platelets. Normal lymphoblasts develop into B and T lymphocytes that fight infection. In ALL, the leukemic lymphoblasts do not fully develop and therefore cannot fight infection. The symptoms of ALL are caused by the replacement of normal bone marrow with leukemic cells, resulting in a drop in red blood cells, platelets, and normal white blood cells. It is estimated that 80-85% of ALL cases occur in children, with peak incidence of pediatric ALL at age 5. Biologically, adult and pediatric ALL are very different. Pediatric cases are more often characterized by favorable prognostic indicators including a precursor B-cell population, TEL / AML1 fusion gene, and/or hyperdiploidy; adult cases are more often characterized by poor prognostic indicators including a precursor T-cell population and / or BCR / ABL fusion gene.1


**Question 90: Specify ALL classification**

Indicate the disease classification at diagnosis.

Due to the aggressive nature of precursor T- and precursor B-cell lymphoblastic lymphoma (or lymphoma / leukemia), the primary disease reported for recipients with these malignancies should be acute lymphoblastic leukemia.

If the cytogenetic or molecular abnormalities present at diagnosis are listed on the Pre-TED form, check the sub-type rather than “B-cell ALL, NOS” option.

**Question 91: Did the recipient have a predisposing condition?**

A predisposing condition is a condition that contributes to the susceptibility of developing leukemia. Therefore, diagnosis of the condition increases the likelihood that the recipient will develop leukemia. If the
recipient has a documented history of a predisposing condition, check “Yes” and continue with question 92. If there is no history of a predisposing condition or if predisposition is unknown, indicate “No” or “Unknown” and continue with question 94.

**Question 92-93: Specify condition:**

Aplastic anemia is an acquired or inherited disorder of the bone marrow characterized by pancytopenia, where the body does not produce a sufficient number of new blood cells. Inherited aplastic anemias include Fanconi anemia (specified separately on this form), Shwachman-Diamond anemia, Diamond-Blackfan anemia, and dyskeratosis congenita. Acquired aplastic anemia may develop after exposures to toxins, radiation, and/or chemotherapy, or may result from an autoimmune condition such as systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA). The majority of presenting signs and symptoms in aplastic anemia patients are directly related to their low blood counts and include fatigue, dizziness, shortness of breath, abnormal bleeding or bruising, and frequent infections.

Bloom syndrome is an autosomal recessive genetic disorder characterized by excessive chromosome breakage and corresponding rearrangements, proportional dwarfism, and sun sensitivity. The chromosomal instability seen in Bloom syndrome is generally assumed to be responsible for these individuals’ predisposition to malignancy.

Down syndrome is also a chromosomal disorder (trisomy 21). It is characterized by an additional chromosome 21. Down syndrome patients exhibit a particular set of facial characteristics, growth deficiency, and cognitive impairment. Although Down syndrome patients have a reduced risk of developing many common malignancies, they have an increased risk of developing leukemia.

Fanconi anemia is a rare genetic blood disorder that prevents the body from producing a sufficient number of new blood cells to function properly. Abnormal blood cells may also be produced. These patients are short in stature, exhibit skeletal anomalies, and have an increased risk of developing solid tumors and leukemias.

**Question 94: Were tyrosine kinase inhibitors (i.e., imatinib mesylate) given for pre-HCT therapy at any time prior to the start of the preparative regimen?**

Report whether the recipient received any tyrosine kinase inhibitor from the diagnosis of ALL to the start of the preparative regimen / infusion. Examples include: Imatinib mesylate is also known as Gleevec, Glivec, STI-571, or CGP57148B.

This question is optional for international centers.
Question 95: Were cytogenetics tested (conventional or FISH)? (at diagnosis)

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality which reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C, Cytogenetic Assessments.

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

FISH is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA. These probes are mixed with cells from the recipient’s blood or bone marrow. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells.

Table 5. Examples of ALL Cytogenetic Findings Categorized by Prognosis (Adult Precursor B-cell ALL)

<table>
<thead>
<tr>
<th>Favorable</th>
<th>Intermediate</th>
<th>Poor</th>
<th>Very Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>High hyperdiploidy (51-65 chromosomes)</td>
<td>Normal 11q abnormalities del(6q) del(17p) del(9p) del(12p) -13/del(13q) t(14q32) t(10;14) Low hyperdiploidy (47-50)</td>
<td>-7/del(7p) +8 11q23 abnormalities/MLL t(1;19) t(17;19) t(5;14) t(9;22)</td>
<td>≥ 5 abnormalities t(4;11) t(8;14)</td>
</tr>
</tbody>
</table>
Indicate whether cytogenetic studies were performed at diagnosis. Do not report any testing performed after treatment for AML has started. If cytogenetic studies were obtained at diagnosis, check “Yes” and go to question 96. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate “No” or “Unknown” respectively and go to question 106.

**Question 96-97: Were cytogenetics tested via FISH?**

If FISH studies were performed at diagnosis (see note box above question 95), report “Yes” for question 96 and indicate whether clonal abnormalities were detected in question 97. Do not report any testing performed after treatment for ALL has started. If FISH studies were not performed at this time point, report “No” for question 96 and go to question 97. Examples of this include: no FISH study performed or FISH sample was inadequate.

**Question 98-100: Specify cytogenetic abnormalities (FISH)**

Report the number of abnormalities detected by FISH at diagnosis (see note box above question 95) in question 98. After indicating the number of abnormalities in question 98, select all abnormalities detected in questions 99-100.

If a clonal abnormality is detected, but not listed as an option in question 99, select “Other abnormality” and specify the abnormality in question 100. If multiple “Other abnormalities” were detected, report “see attachment” in question 100 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3 SM, refer to the Training Guide.

**Question 101-102: Were cytogenetics tested via karyotyping?**

If karyotyping was performed at diagnosis (see note box above question 95), report “Yes” for question 101 and indicate whether clonal abnormalities were detected in question 102. Do not report any testing performed after treatment for ALL has started. If karyotyping was not performed at this time point, indicate “No” and go to question 107. Examples of this include: karyotyping was not performed or karyotyping sample was inadequate.
**Question 103-105: Specify cytogenetic abnormalities (karyotyping)**

Report the number of abnormalities detected by karyotyping at diagnosis (see note box above question 95) in question 103. After indicating the number of abnormalities in question 103, select all abnormalities detected in questions 104-105.

If a clonal abnormality is detected, but not listed as an option in question 104, select “Other abnormality” and specify the abnormality in question 105. If multiple “Other abnormalities” were detected, report “see attachment” in question 105 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 106: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 95-105. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 107: Were tests for molecular markers performed (e.g., PCR)? (at diagnosis)**

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient’s primary disease. Testing for these sequences is often performed using PCR based methods; however, lower sensitivity testing, including FISH, may also be used to detect molecular markers. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include chromosomal microarray / chromosomal genomic array, Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

If testing for molecular markers was performed at diagnosis (see note box above question 95), report “Yes” and go to question 108.

If molecular marker testing was not performed at diagnosis or it is not known if testing was done, report “No” or “Unknown” respectively and go to question 113.

**Table 6. Common Molecular Markers Associated with ALL**

<table>
<thead>
<tr>
<th>Molecular Abnormality</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCR-ABL</td>
<td>BCR-ABL, aka Philadelphia chromosome, refers to the tyrosine kinase gene fusion resulting from the translocation of material from chromosome 9 (ABL) onto chromosome 22 (BCR).</td>
</tr>
</tbody>
</table>
Molecular weight varies depending on exact location of the translocation; isoform p190 is typically seen in ALL. Tyrosine kinase inhibitor therapies such as imatinib mesylate (Gleevec) target and block ABL from fusing with BCR. Presence of BCR-ABL gene fusion is associated with poorer outcomes.  

TEL-AML1, *aka* ETV6-RUNX1, is a fusion gene resulting from the translocation of chromosomes 12 and 21. It is the most common fusion gene seen in childhood precursor B-cell ALL. Research in murine models shows that cell lines expressing TEL-AML1 proliferate more slowly than the non-expressing cell lines, but evade inhibition of proliferation typically regulated by tissue growth factor β (TGF-β), ultimately leading to the growth of the leukemic cell population. TEL-AML1 is considered a favorable prognostic indicator.

Other molecular marker

Assessments for other molecular markers known or believed to be associated with ALL may be performed. If these studies were performed, indicate “positive” or “negative” and specify the marker in question 99.

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**Question 108-111: Specify results**

For each molecular marker in questions 108-109, report whether testing was “Positive,” “Negative,” or “Not done” at diagnosis (see note box above question 95). If tests identified a molecular marker other than those listed in questions 108-109, report the result in question 110 and specify the marker in question 111.

If multiple “Other molecular marker[s]” were tested, report one instance (i.e., copy) of question 110-111 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” were tested, do the following:

- report one instance of question 110-111; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 111; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”
**Question 112: Were cytogenetics tested (karyotyping or FISH)? (between diagnosis and last evaluation)**

See question 95 for a description of cytogenetic tests. Indicate whether cytogenetic studies were performed between diagnosis and the last evaluation prior to HCT / cellular therapy (see note above question 95). If cytogenetic studies were obtained during this time, check “Yes” and go to question 113. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate “No” or “Unknown” respectively and go to question 124.

**Question 113-114: Were cytogenetics tested via FISH?**

If FISH studies were performed between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 95), report “Yes” for question 113 and indicate whether clonal abnormalities were detected in question 114. If multiple FISH assessments were performed, report “Abnormalities Identified” if any testing showed clonal abnormalities during this period. If FISH studies were not performed during this period, report “No” for question 113 and go to question 118. Examples of this include: no FISH study performed or all FISH samples were inadequate.

**Question 115-117: Specify cytogenetic abnormalities (FISH)**

Report the number of abnormalities detected by FISH between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 95) in question 115. If FISH studies showed different clonal abnormalities during this time, report the total number of clonal abnormalities detected. After indicating the number of clonal abnormalities in question 115, select all clonal abnormalities detected during this period in questions 116/117. This includes all clonal abnormalities detected any FISH assessment performed during this period.

If a clonal abnormality is detected, but not listed as an option in question 116, select “Other abnormality” and specify the abnormality in question 117. If multiple “Other abnormalities” were detected, report “see attachment” in question 117 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 118-119: Were cytogenetics tested via karyotyping?**

If karyotyping was performed between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 95), report “Yes” for question 118 and indicate whether clonal abnormalities were detected in question 119. If multiple karyotypes were performed, report “Abnormalities Identified” if any testing showed clonal abnormalities during this period. If karyotyping was not performed during this period, report “No” for question 118 and go to question 124. Examples of this include: no karyotyping performed or all karyotype samples were inadequate.
Question 120-122: Specify cytogenetic abnormalities (karyotyping)

Report the number of abnormalities detected by karyotyping between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 95) in question 120. If karyotype studies showed different clonal abnormalities during this time, report the total number of clonal abnormalities detected. After indicating the number of clonal abnormalities in question 120 select all clonal abnormalities detected during this period in questions 121-122. This includes all clonal abnormalities detected any karyotype performed during this period.

If a clonal abnormality is detected, but not listed as an option in question 121, select “Other abnormality” and specify the abnormality in question 122. If multiple “Other abnormalities” were detected, report “see attachment” in question 122 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 123: Was documentation submitted to the CIBMTR?

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 112-122. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 124: Were tests for molecular markers performed (e.g., PCR)? (between diagnosis and last evaluation)

See question 107 for a description of testing for molecular markers. Indicate whether testing for molecular markers was performed between diagnosis and the last evaluation prior to HCT / cellular therapy (see note above question 95). If testing for molecular markers was performed during this time, check “Yes” and go to question 125. If cytogenetic studies were not obtained during this period or it is not known whether testing for molecular markers was performed, indicate “No” or “Unknown” respectively and go to question 129.

Question 125-128: Specify results

For each molecular marker in questions 125-126, report whether testing was “Positive,” “Negative,” or “Not done” between diagnosis and the last evaluation prior to HCT / cellular therapy (see note box above question 95). If tests identified a molecular marker other than those listed in questions 125-126, report the result in question 127 and specify the marker in question 128.

If multiple “Other molecular marker[s]” were tested, report one instance (i.e., copy) of question 127-128 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” were tested, do the following:

• report one instance of question 127-128; and
• report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;”
and
• report “see attachment” in question 128; and
• attach any / all reports documenting the results of testing for “Other molecular marker[s].”

Question 129: Were cytogenetics tested (karyotyping or FISH)? (at last evaluation)

See question 95 for a description of cytogenetic testing. Indicate whether cytogenetic studies were performed at the last evaluation prior to HCT / cellular therapy (see note box above question 95). Do not report any testing performed after treatment for ALL has started. If cytogenetic studies were obtained at this time point, check “Yes” and go to question 130. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate “No” or “Unknown” respectively and go to question 141.

Question 130-131: Were cytogenetics tested via FISH?

If FISH studies were performed at the last evaluation prior to HCT / cellular therapy (see note box above question 95), report “Yes” for question 130 and indicate whether clonal abnormalities were detected in question 131. If FISH studies were not performed at this time point, report “No” for question 130 and go to question 135. Examples of this include: no FISH study performed or FISH sample was inadequate.

Question 132-134: Specify cytogenetic abnormalities (FISH)

Report the number of abnormalities detected by FISH at the last evaluation prior to HCT / cellular therapy (see note box above question 95) in question 132. After indicating the number of abnormalities in question 132, select all abnormalities detected in questions 133-134.

If a clonal abnormality is detected, but not listed as an option in question 133, select “Other abnormality” and specify the abnormality in question 134. If multiple “Other abnormalities” were detected, report “see attachment” in question 134 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 135-136: Were cytogenetics tested via karyotyping?

If karyotyping was performed at the last evaluation prior to HCT / cellular therapy (see note box above question 95), report “Yes” for question 135 and indicate whether clonal abnormalities were detected in question 136. If karyotyping was not performed at this time point, indicate “No” and go to question 141. Examples of this include: karyotyping was not performed or karyotyping sample was inadequate.
**Question 137-139: Specify cytogenetic abnormalities (karyotyping)**

Report the number of abnormalities detected by karyotyping at the last evaluation prior to HCT / cellular therapy (see note box above question 95) in question 137. Only consider clonal abnormalities associated with the recipient's AML when completing questions 137-139. After indicating the number of abnormalities in question 137, select all abnormalities detected in questions 138-139.

If a clonal abnormality is detected, but not listed as an option in question 138, select “Other abnormality” and specify the abnormality in question 139. If multiple “Other abnormalities” were detected, report “see attachment” in question 139 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 140: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 129-139. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 141: Were tests for molecular markers performed (e.g., PCR)? (at last evaluation)**

See question 107 for a description of testing for molecular markers. If testing for molecular markers was performed at the last evaluation prior to HCT / cellular therapy (see note box above question 95), report “Yes” and go to question 142. If molecular marker testing was not performed at this time point or it is not known if testing was done, report “No” or “Unknown” respectively and go to question 146.

**Question 142-145: Specify results**

For each molecular marker in questions 142-145, report whether testing was “Positive,” “Negative,” or “Not done” at the last evaluation prior to HCT / cellular therapy (see note box above question 95). If tests identified a molecular marker other than those listed in questions 142-143, report the result in question 144 and specify the marker in question 145.

If multiple “Other molecular marker[s]” were tested, report one instance (i.e., copy) of question 144-145 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” were tested, do the following:

- report one instance of question 144-145; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 145; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”
Question 146: Did the recipient have central nervous system leukemia at any time prior to the start of the preparative regimen / infusion?

Central nervous system (CNS) involvement by leukemia may be detected via pathologic examination of cerebrospinal fluid or tumor tissue as well as by radiological examinations (e.g., MRI, PET/CT, MIBG, etc.). If the recipient had documented involvement of ALL in the CNS, report “Yes” for question 84. If all CNS testing was negative since the time of diagnosis, report “No.” If testing for CNS involvement was not performed from the time of diagnosis to the time of HCT / cellular therapy, report “Unknown.”

Question 147: What was the disease status (based on hematological test results)?

Indicate the disease status of ALL at the last evaluation prior to the start of the preparative regimen. Refer to the ALL Response Criteria section of the Forms Instructions Manual for definitions of each response. For reporting purposes, consider complete remission with incomplete hematologic recovery (CRi) a complete remission (CR1, CR2, or CR3+).

If the recipient did not receive any treatment for ALL from the time of diagnosis to the start of the preparative regimen / infusion, report “No treatment” and go to question 151.

If the recipient’s disease status is primary induction failure at the time of HCT / cellular therapy, go to question 151.

If the recipient’s disease status is CR / CRi at the time of HCT / cellular therapy, go to question 148.

If the recipient’s disease status is relapse at the time of HCT / cellular therapy, go to question 150.

Question 148: How many cycles of induction therapy were required to achieve CR?

Chemotherapy is initially given as induction therapy intended to bring the disease into remission. Recipients usually have one to two cycles of induction therapy. An example of a common induction therapy for precursor B-cell ALL in children with higher-risk prognostic indicators is a combination of vincristine, prednisone, an anthracycline, and L-asparaginase given over 4-6 weeks. Patients with a rapid response, defined as < 5% blasts within 7 to 14 days of starting induction, have improved outcomes.¹


The second phase of chemotherapy is known as consolidation therapy. The goal of consolidation therapy is to destroy any remaining leukemia cells and sustain remission. An example of a consolidation therapy for
precursor B-cell ALL in children is daunorubicin and cytarabine; several studies support the use of consolidation therapy in ALL.

Maintenance therapy typically involves daily doses of mercaptopurine and weekly doses of methotrexate. Treatment continues for 2-3 years for most children with ALL. Treatment may also be administered for relapsed disease. Much like induction therapy, treatment for relapse is intended to bring the disease back into remission. Systemic therapeutic agents used to induce remission following relapse often differ from those used during initial induction, since the disease is considered high-risk with a poor prognosis and is often resistant to many of the agents used earlier in the disease course. Allogeneic HCT is often considered the only potential “cure” for relapsed disease, if the patient has not already been transplanted.

Indicate the number of cycles of induction therapy that were required to achieve the first CR.

Question 149: Was the recipient in remission by flow cytometry?

Question 149 will only be answered if CR has been reported for question 147. Flow cytometry assessment is a method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics. Its primary clinical purpose in the setting of leukemias is to quantify blasts in the peripheral blood or bone marrow, or to identify unique cell populations through immunophenotyping. Flow cytometry assessment may also be referred to as “MRD,” or minimal residual disease, testing.

Flow cytometric remission is a treatment response in which no blasts can be detected.

If flow cytometric abnormalities associated with the recipient’s disease were identified previously, but the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate “yes.”

If flow cytometric abnormalities associated with the recipient’s disease were identified at the last evaluation prior to the start of the preparative regimen, indicate “no.”

Indicate “unknown” if flow cytometric abnormalities associated with the recipient’s disease were identified previously and no flow cytometry assessment was performed prior to the start of the preparative regimen.

Indicate “not applicable” if one of the following applies:

- No flow cytometry assessments were performed at any time prior to the start of the preparative regimen.
- Flow cytometric abnormalities were not identified on previous testing and no flow cytometric abnormalities were identified at the last evaluation prior to the start of the preparative regimen.
**Question 150: Date of most recent relapse:**

Enter the date of the most recent relapse prior to the start of the preparative regimen. If reporting a pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear), enter the date the sample was collected. If extramedullary disease was detected by radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place. If the physician determines cytogenetic or molecular relapse, enter the date the sample was collected for cytogenetic or molecular evaluation. If the physician determines evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 151: Date assessed**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant work-up period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
Q152-155: Acute Leukemias of Ambiguous Lineage and Other Myeloid Neoplasms

**Questions 152-153: Specify other acute leukemia classification**

Indicate the other acute leukemia disease classification at diagnosis. If the subtype is not listed, report as “other leukemia” and specify the reported disease.

- Acute undifferentiated leukemia is a type of AML characterized by immature predominating cells that cannot be classified.
- Biphenotypic, bilineage, or hybrid leukemias have characteristics representative of both myeloid and lymphoid lineages.
- Mast cell leukemia is characterized by an increased number of tissue mast cells in the peripheral blood.

**Question 154: What was the disease status (based on hematological test results)?**

Indicate the disease status of acute leukemia at the last evaluation prior to the start of the preparative regimen.

### Table 7. Disease Status of Acute Leukemia

<table>
<thead>
<tr>
<th>Disease Status</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Induction Failure (PIF)</td>
<td>The patient received treatment for acute leukemia but never achieved complete remission at any time. PIF is not limited by the number of unsuccessful treatments; this disease status only applies to recipients who have never been in complete remission.</td>
</tr>
<tr>
<td>Complete Remission (CR)</td>
<td>Hematologic complete remission is defined as meeting all of the following response criteria for at least four weeks.</td>
</tr>
<tr>
<td></td>
<td>• &lt; 5% blasts in the bone marrow</td>
</tr>
<tr>
<td></td>
<td>• Normal maturation of all cellular components in the bone marrow</td>
</tr>
<tr>
<td></td>
<td>• No extramedullary disease (e.g., CNS, soft tissue disease)</td>
</tr>
<tr>
<td></td>
<td>• Neutrophils ≥ 1,000/µL</td>
</tr>
<tr>
<td></td>
<td>• Platelets ≥ 100,000/µL</td>
</tr>
<tr>
<td></td>
<td>• Transfusion independent</td>
</tr>
<tr>
<td></td>
<td>In some cases, there may not be a four-week interval between completion of therapy and the pre-transplant disease assessment; in this case, CR should still be reported as</td>
</tr>
</tbody>
</table>
the status at transplant, since it represents the “best assessment” prior to HCT. This is an exception to the criteria that CR be durable beyond four weeks; the pre-transplant disease status should not be changed based on early relapse or disease assessment post-transplant.

Include recipients with persistent cytogenetic or molecular abnormalities who meet the above CR criteria for hematologic CR.

Include recipients meeting the above CR criteria regardless of how many courses of therapy were required to achieve CR.

The number of this complete remission can be determined by using the following guidelines:

- 1st CR: no prior relapse
- 2nd CR: one prior relapse
- 3rd or higher: two or more prior relapses

<table>
<thead>
<tr>
<th>Relapse (REL)</th>
<th>Relapse is defined as the recurrence of disease after CR, meeting the following criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• ≥ 5% blasts in the marrow or peripheral blood</td>
</tr>
<tr>
<td></td>
<td>• Extramedullary disease</td>
</tr>
<tr>
<td></td>
<td>• Reappearance of cytogenetic and/or molecular abnormalities associated with diagnosis that, in the judgment of a physician, are at a level representing relapse</td>
</tr>
<tr>
<td></td>
<td>• Disease presence determined by a physician upon clinical assessment</td>
</tr>
<tr>
<td></td>
<td>The number of this relapse can be determined by using the following guidelines:</td>
</tr>
<tr>
<td></td>
<td>• 1st relapse: one prior CR</td>
</tr>
<tr>
<td></td>
<td>• 2nd relapse: two prior CR</td>
</tr>
<tr>
<td></td>
<td>• 3rd or higher: three or more CRs</td>
</tr>
</tbody>
</table>

Do not include a partial response (PR) when determining number of relapse. Recipients who achieve a PR to treatment should be classified as either PIF or relapse; PR in acute leukemia is generally of short duration and is unlikely to predict clinical benefit.

| No Treatment | The recipient was diagnosed with acute leukemia and never received therapeutic agents; include patients who have received only supportive therapy, including growth factors and/or blood transfusions. |

**Question 155: Date assessed**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant work-up period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments.
If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
Q156-166: Chronic Myelogenous Leukemia

Chronic myelogenous leukemia (CML) is a slow-progressing cancer of the myeloid white blood cells. It is characterized by increased proliferation of immature white blood cells (granulocytes) with damaged DNA, or blasts, which accumulate in the blood and bone marrow. Normal blasts develop into white blood cells that fight infection. The symptoms of CML are caused by the replacement of normal bone marrow with leukemic cells, resulting in fewer red blood cells, platelets, and normal white blood cells.

**Question 156: Was therapy given prior to this HCT?**

If the recipient received therapy to treat CML prior to this HCT, check “yes” and go to question 157. Do not report a prior HCT or cellular therapy as these are captured separately on the Pre-TED Form (Form 2400). If the recipient did not receive therapy to treat CML, check “no” and go to question 163.

**Question 157-162: CML treatment**

Indicate the therapy the recipient received to treat CML prior to this HCT. If the recipient’s treatment consisted of a combination of chemotherapeutic agents, check the “combination chemotherapy” box and each drug included in the combination from the list provided. The “other, specify” category should only be used if the drug is not one of the listed options. For example, if the recipient received a combination of interferon and cytarabine, check all of the following: “combination chemotherapy,” “interferon,” and “other, specify: cytarabine.”

**Question 163: What was the disease status?**

Indicate the disease status of CML at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen was given). Refer to the CML Response Criteria section for a description of each disease response.

If the recipient is in complete hematologic response or chronic phase at the start of the preparative regimen, go to question 164. Otherwise, go to question 165.

**Question 164: Specify level of response**

If the recipient’s disease status (question 163) is “complete hematologic remission” or “chronic phase,” specify the cytogenetic / molecular response. Refer to the below definitions of cytogenetic and molecular responses.

**Definitions of Cytogenetic and Molecular Responses to Therapy**
<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete molecular remission</td>
<td>0% BCR / ABL transcripts detected in peripheral blood or bone marrow</td>
</tr>
<tr>
<td>(most favorable)</td>
<td></td>
</tr>
<tr>
<td>Major molecular remission</td>
<td>&gt; 0 – 0.1% BCR / ABL transcripts detected in peripheral blood or bone</td>
</tr>
<tr>
<td></td>
<td>marrow</td>
</tr>
<tr>
<td>Complete cytogenetic response</td>
<td>0% Ph+ cells detected in bone marrow</td>
</tr>
<tr>
<td>Partial cytogenetic response</td>
<td>&gt; 0 – 35% Ph+ cells in bone marrow</td>
</tr>
<tr>
<td>Minor cytogenetic response</td>
<td>&gt; 35 – 65% Ph+ cells in bone marrow</td>
</tr>
<tr>
<td>Minimal cytogenetic response</td>
<td>&gt; 65 – 95% Ph+ cells in bone marrow</td>
</tr>
<tr>
<td>No cytogenetic response</td>
<td>&gt; 95% Ph+ cells in bone marrow.</td>
</tr>
<tr>
<td>(least favorable)</td>
<td></td>
</tr>
</tbody>
</table>


The above responses are listed from most favorable (complete molecular remission) to least favorable (no cytogenetic response). Centers should report the most favorable response achieved. For example, if a recipient has achieved a major molecular remission by PCR testing as well as a complete cytogenetic response by karyotyping / FISH, the center should report “major molecular remission” for question 164.

**Question 165: Number**

Indicate the number of times the recipient has been in the disease phase reported in question 163.

**Question 166: Date assessed**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant work-up period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
The myelodysplastic syndromes (MDS) are a group of clonal hematopoietic stem cell diseases characterized by cytopenia(s), dysplasia (abnormal growth or development leading to an alteration in size, shape, and organization of the cell) in one or more of the major myeloid cell lines (WBC, RBC, and/or platelets), ineffective hematopoiesis, and an increased risk of developing acute myelogenous leukemia (AML). MDS occurs primarily in older adults, with a median age of 70 years. The majority of patients present with symptoms related to cytopenias. Most patients present with anemia requiring RBC transfusions.

Primary or de novo MDS occurs without a known history of chemotherapy or radiation exposure. Some inherited hematologic disorders, such as Fanconi anemia, dyskeratosis congenita, Shwachmann-Diamond syndrome, and Diamond-Blackfan syndrome are associated with an increased risk of MDS.

Myeloproliferative Neoplasms (MPN) are characterized by the overproduction of blood cells (red blood cells, white blood cells, and/or platelets) or collagen in the bone marrow. Often the MPN will be identified because of a blood test for another condition, as some patients are asymptomatic. Common symptoms found in the array of myeloproliferative disorders include fatigue and the enlargement of the spleen (splenomegaly).

Question 167: What was the MDS/MPN subtype?

Please indicate the MDS/MPN subtype at diagnosis. For a list of MDS/MPN subtypes and their diagnostic criteria, see Appendix H.
If the MDS/MPN subtype at diagnosis was “atypical chronic myeloid leukemia,” continue to the signature line.

**Question 168: Was the disease (MDS/MPN) therapy-related?**

Agents such as radiation or systemic therapy used to treat other diseases (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, or breast cancer) can damage the marrow and lead to a secondary malignancy, such as MDS/MPN. If the diagnosis of MDS/MPN is therapy-related, select “yes.” If the diagnosis of MDS/MPN is not therapy-related, select “no.” If it is unknown if the MDS/MPN is therapy-related, select “unknown.”

Do not answer this question “yes” if the recipient developed MDS/MPN after an environmental exposure (e.g., exposure to benzene).

**Question 169: Did the recipient have a predisposing condition?**

A predisposing condition is a condition that contributes to the susceptibility of developing MDS/MPN. If the recipient has a documented history of a predisposing condition, select “yes” and continue with question 170. If there is no history of a predisposing condition or if predisposition is unknown, indicate “no” or “unknown” and continue with question 172.

**Question 170-171: Specify condition:**

Aplastic anemia may progress to MDS and/or AML. Aplastic anemia is a broad classification referring to bone marrow failure characterized by pancytopenia and marrow hypoplasia.

Bloom syndrome is an autosomal recessive genetic disorder characterized by excessive chromosome breakage, with corresponding rearrangements. It is characterized by proportional dwarfism and sun sensitivity. The chromosomal instability seen in Bloom syndrome is generally assumed to be responsible for these individuals’ predisposition to malignancy.

Down syndrome is also a chromosomal disorder. It is characterized by an additional chromosome 21, also referred to as trisomy 21. Down syndrome patients exhibit a particular set of facial characteristics, growth deficiency, and cognitive impairment. Although Down syndrome patients have a reduced risk of developing many common malignancies, they have an increased risk of developing leukemia.

Fanconi anemia is a rare genetic blood disorder that prevents the body from producing a sufficient number of new blood cells to function properly. Abnormal blood cells may also be produced. These patients are short in stature, exhibit skeletal anomalies, and have an increased risk of developing solid tumors and leukemias.

If the recipient had a predisposing condition not listed above, select “other condition” and specify the
condition in question 171.

**Question 172-173: WBC**

Indicate whether the white blood cell (WBC) count was “known” or “unknown” at diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 173. If “unknown,” continue with question 174.

**Question 174-175: Hemoglobin**

Indicate whether the hemoglobin was “known” or “unknown” at diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 175. If “unknown,” continue with question 177.

**Question 176: Were RBCs transfused ≤ 30 days before the date of test?**

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

Indicate if red blood cells were transfused less than or equal to 30 days prior to the testing reported in question 175.

**Question 177-178: Platelets**

Indicate whether the platelet count was “known” or “unknown” at diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 178. If “unknown,” continue with question 180.

**Question 179: Were platelets transfused ≤ 7 days before date of test?**

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support the counts.

Indicate if platelets were transfused less than or equal to 7 days prior to the testing reported in question 178.

**Question 180-181: Neutrophils**

Indicate whether the neutrophil percentage in the blood was “known” or “unknown” at diagnosis. If “known,” report the value documented on the laboratory report in question 181. If “unknown,” continue with question 182.
**Question 182-183: Blasts in bone marrow**

* If the bone marrow pathology report states a range for blasts, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
* If the report indicates “sheets of blasts” or “packed marrow,” report 100%.
* If the report states > n% blasts, enter (n +1)% on the form. For example, if the laboratory report indicates > 90% blasts, report 91%.
* If the report states < n% blasts, enter (n -1)% on the form. For example, if the laboratory report indicates < 5% blasts, report 4%.

Indicate whether the percentage of blasts in the bone marrow was “known” or “unknown” at diagnosis. If “known,” report the percentage documented on the laboratory report in question 183. If “unknown,” continue with question 184.

**Question 184: Were cytogenetics tested (conventional or FISH)?**

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at diagnosis. If cytogenetic studies were obtained, select “yes” and continue with question 185.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select “no” or “unknown” and continue with question 212.

**Question 185: Results of test:**

If cytogenetic studies identified abnormalities, indicate “abnormalities identified” and continue with question 186.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified, continue with question 212.

**Question 186: Specify the number of distinct cytogenetic abnormalities:**

Indicate the total number of abnormalities at diagnosis.
Questions 187-211: Specify abnormalities identified at diagnosis:

Report all abnormalities identified by all methods of cytogenetic assessment at diagnosis by selecting “yes” or “no” for each question. Do not leave any response blank. If one or more abnormalities are best classified as “other abnormality,” select “yes” for question 210 and specify the abnormality in question 211.

Question 212: Did the recipient progress or transform to a different MDS/MPN subtype between diagnosis and the start of the preparative regimen?

Transformation to Myelofibrosis
Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. The CIBMTR forms capture disease subtype using the WHO classification of myeloid neoplasms and acute leukemia. Secondary myelofibrosis is not included as a separate category per the WHO classification. Therefore, when reporting the disease subtype at the time of transplant for recipients with secondary myelofibrosis, report “Primary Myelofibrosis (PMF)” to accurately capture these cases on the CIBMTR Forms.

Indicate if the recipient’s disease progressed to AML or transformed into a different MDS/MPN subtype between initial diagnosis and the start of the preparative regimen. Approximately one third of MDS cases transform into AML, signifying a poorer prognosis. Progression to AML is defined by an increase in blood or bone marrow blasts equal to or greater than 20%.

MDS/MPN subtypes may also transform/progress from one into another. A progression from one subtype of MDS to another indicates that the number of cytopenias, number of blasts, and/or morphology of marrow sufficiently qualified them for a higher grade (i.e., more severe) MDS. For example, an MDS classified as RCUD at diagnosis whose blast count rises to 8% as documented on bone marrow aspirate would have progressed to RAEB-1.

Conversely, do not report a progression/transformation if the recipient's assessments after diagnosis show that they qualify for a lower grade (i.e., less severe MDS). For example, a recipient who is diagnosed with RAEB-2, but whose assessments show that they meet the criteria for RAEB-1 as a response to treatment, would not qualify as a progression or transformation. In this example, the disease is lower grade (i.e., less severe), rather than a higher grade (i.e., more severe) so it should not be reported as a progression/ transformation. See the table below for guidance in determining the severity of MDS/MPN progressions and transformations.

Grade of MDS Progression/Transformations
Indicate if the recipient's disease progressed to AML or transformed from one MDS/MPN subtype to another. If the recipient's disease did transform or progress, select “yes” and continue with question 213. If there was no documented transformation or progression, select “no” and continue with question 216.

If there was no documented transformation or progression and the disease subtype is JMML, continue to the signature line.

**Question 213: Specify the MDS/MPN subtype after transformation:**

Indicate the recipient’s current MDS/MPN subtype after transformation. If the recipient experienced more than one transformation after diagnosis, report the most recent subtype. For a list of MDS/MPN subtypes and their diagnostic criteria, see Appendix H.

Unless the recipient transformed to AML, continue with question 214.

If the disease transformed to AML, go to question 215.

**Question 214: Specify the date of the most recent transformation:**

Report the date of assessment that determined the most recent disease transformation (i.e., if there were multiple transformations, report the most recent). Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
Question 215: Date of MDS Diagnosis

If the recipient’s MDS / MPN transformed to AML prior to HCT, report the date of diagnosis of MDS / MPN. If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Ensure the date of diagnosis for AML has been reported in question 1, AML is reported as the primary disease for HCT in question 2, and the AML section of the Disease Classification Form has been complete appropriately. Go to the signature line.

Question 216-217: WBC

Indicate whether the white blood cell (WBC) count was “known” or “unknown” at the last evaluation prior to the start of the preparative regimen. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 217. If “unknown,” continue with question 218.

Question 218-219: Hemoglobin

Indicate whether the hemoglobin was “known” or “unknown” at the last evaluation prior to the start of the preparative regimen. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 219. If “unknown,” continue with question 221.

Question 220: Was RBCs transfused < 30 days before the date of test?

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

Indicate if red blood cells were transfused less than or equal to 30 days prior to the testing reported in question 219.

Question 221-222: Platelets

Indicate whether the platelet count was “known” or “unknown” at the last evaluation prior to the start of the preparative regimen. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 222. If “unknown,” continue with question 224.

Question 223: Were platelets transfused < 7 days before date of test?

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support the counts.

Indicate if platelets were transfused less than or equal to 7 days prior to the testing reported in question
Questions 224-225: Neutrophils

Indicate whether the neutrophil percentage in the blood was “known” or “unknown” at the last evaluation prior to the start of the preparative regimen. If “known,” report the value documented on the laboratory report in question 225. If “unknown,” continue with question 226.

Questions 226-227: Blasts in bone marrow:

If the bone marrow pathology report states a range for blasts, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
If the report indicates “sheets of blasts” or “packed marrow,” report 100%.
If the report states > n% blasts, enter (n+1)% on the form. For example, if the laboratory report indicates > 90% blasts, report 91%.
If the report states < n% blasts, enter (n-1)% on the form. For example, if the laboratory report indicates < 5% blasts, report 4%.

Indicate whether the percentage of blasts in the bone marrow was “known” or “unknown” at the last evaluation prior to the start of the preparative regimen. If “known,” report the percentage documented on the laboratory report in question 227. If “unknown,” continue with question 228.

Question 228: Were cytogenetics tested (conventional or FISH)?

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at the last evaluation prior to the start of the preparative regimen. If cytogenetic studies were obtained, select “yes” and continue with question 229.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select “no” or “unknown” and continue with question 256.

Question 229: Results of test:

If cytogenetic studies identified abnormalities, indicate “abnormalities identified” and continue with question 230.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified,
continue with question 256.

**Question 230: Specify the number of distinct cytogenetic abnormalities:**

Indicate the total number of abnormalities at the last evaluation prior to the start of the preparative regimen.

**Question 231-255: Specify abnormalities identified at the last evaluation prior to the start of the preparative regimen:**

Report all abnormalities identified by all methods of cytogenetic assessment at the last evaluation prior to the start of the preparative regimen by selecting “yes” or “no” for each question. Do not leave any response blank. If one or more abnormalities are best classified as “other abnormality” select “yes” for question 254 and specify the abnormality in question 255.

**Question 256: What was the disease status?**

Indicate the disease status of MDS/MPN at the last assessment prior to the start of the preparative regimen. Refer to the MDS/MPN Response Criteria section of the Forms Instructions Manual for definitions of each disease response.

*“Never Treated” is not an option choice on the current revision of the Pre-TED: Disease Classification Form. When completing this form, centers should report “No Response (NR) / Stable Disease (SD)” for recipients who have only received supportive care prior to transplant.*

**Question 257: Specify the cell line examined to determine HI status:**

Indicate the cell line examined to determine hematologic improvement. To determine the cell line, review the Hematologic Improvement criteria listed in the MDS/MPN Response Criteria section of the Forms Instructions Manual.

**Question 258: Date of progression**

Enter the assessment date that progression from hematologic improvement was established prior to the start of the preparative regimen. Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations. If extramedullary disease was detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
**Question 259: Date of relapse:**

Enter the assessment date that relapse from complete remission was established prior to the start of the preparative regimen. Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations. If extramedullary disease was detected on radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 260: Date assessed:**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant work-up period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
**Q261-267: Other Leukemia**

**CLL**, or chronic lymphocytic leukemia, is characterized by $\geq 5 \times 10^9/L$ monoclonal lymphocytes with a CLL phenotype (usually co-expressed CD5 and CD23). The term SLL, or small lymphocytic lymphoma is used for non-leukemic cases with the tissue morphology and immunophenotype of CLL.

**Hairy cell leukemia** is characterized by the presence of abnormal B-lymphocytes in the bone marrow, peripheral blood, and spleen.

**PLL**, or prolymphocytic leukemia, is a type of CLL and is characterized by increased presence of immature prolymphocytes in the bone marrow and peripheral blood.

**Question 261-262: Specify the other leukemia classification**

Indicate the other leukemia disease classification at diagnosis. If the subtype is not listed, report as “other leukemia” and specify the reported disease.

**Question 263: Was any 17p abnormality detected?**

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies detected any 17p abnormality at any time prior to the start of the preparative regimen.

If “yes” and the disease classification is CLL, continue with question 264. If “yes” and the disease classification is PLL, continue with question 266.

If cytogenetic studies did not detect any 17p abnormality at any time prior to the start of the preparative regimen, select “no” and continue with question 264.

**Question 264: Did a histologic transformation to diffuse large B-cell lymphoma (Richter syndrome) occur at any time after CLL diagnosis?**

Histologic transformation may occur after CLL diagnosis. Indicate if CLL transformed into diffuse large B-cell lymphoma (known as Richter’s transformation or Richter’s syndrome). If CLL transformed, select “yes” and continue with question 271. If CLL did not transform, select “no” and continue with question 266.
**Question 265: What was the disease status? (Atypical CML)**

Indicate the disease status for atypical CML at the last evaluation prior the start of the preparative regimen (or infusion of no preparative regimen was given). If no treatment was given prior to HCT, go to the signature line. Otherwise, continue with question 267.

**Disease Status of Atypical CML**

*Primary Induction Failure (PIF)*

The patient received treatment for atypical CML but never achieved complete remission at any time. PIF is not limited by the number of unsuccessful treatments; this disease status only applies to recipients who have never been in complete remission._

*Complete Remission (CR)*

All of the following criteria are met and maintained for four or more weeks:

- Marrow with normal maturation of all cellular components
- \( \leq 5\% \) blasts in the marrow
- No signs or symptoms of the disease
  
  If the timeframe between achieving CR and the start date of the HCT (i.e., day 0) is less than four weeks, and the recipient is believed to be in CR, report the status at transplantation as CR.

*Important: if within four weeks following transplant the recipient’s status is determined to not be CR, an Error Correction Form must be submitted to change the pre-HCT status.*

Include recipients with persistent cytogenetic abnormalities who otherwise meet all the criteria of CR.

Report that the recipient is in CR at the time of transplant no matter how many courses of therapy it may have taken to achieve that CR.

The number of this complete remission can be determined by using the following guidelines:

- 1st CR: no prior relapse
- 2nd CR: one prior relapse
- 3rd or higher: two or more prior relapses

*Relapse (REL)*

Recurrence of disease after CR. Relapse is defined as:
• > 5% blasts in the marrow
• Extramedullary disease
• Reappearance of cytogenetic abnormalities and/or molecular markers associated with the diagnosis at levels that, as determined by a physician, represent relapse.

The number of this relapse can be determined by using the following guidelines:

• 1st relapse: one prior CR
• 2nd relapse: two prior CRs
• 3rd or higher: three or more CRs

No treatment
The recipient was diagnosed with atypical CML and never treated.

Question 266: What was the disease status? (CLL, PLL, Hairy cell leukemia)

Indicate the disease status for CLL/SLL, PLL, or hairy cell leukemia at the last evaluation prior the start of the preparative regimen (or infusion if no preparative regimen was given) and continue with question 267.

If reporting CLL / SLL or PLL, refer to the CLL Response Criteria section of the Forms Instructions Manual for definitions of each response.

Disease Status of Hairy Cell Leukemia

Untreated
The recipient was diagnosed with hairy cell leukemia and never treated.

Complete Remission (CR)
Disappearance of all evidence of disease.
Requires all of the following:

• Neutrophils ≥ 1.5 × 10^9
• Hemoglobin ≥ 12.0 g/dL
• Platelets ≥ 100 × 10^9/L
• Absence of hairy cells on peripheral blood smear
• No palpable lymphadenopathy or hepatosplenomegaly
**Partial Remission (PR)**
Requires all of the following:

- ≥ 50% reduction in the absolute hairy cell count in the peripheral blood and the bone marrow
- ≥ 50% improvement of all cytopenias
- ≥ 50% reduction in abnormal lymphadenopathy or hepatosplenomegaly

**Stable Disease (SD)**
Not applicable for hairy cell leukemia.

**Progressive Disease**
Not applicable for hairy cell leukemia.

**Relapse (untreated)**
Relapse after CR:

- Reappearance of hairy cells in the peripheral blood smear and/or bone marrow (regardless of the degree of infiltration)
- Development of peripheral blood cytopenias
- Splenomegaly

Relapse after PR:

- ≥ 50% increase of residual hairy cells in the marrow
- Development of cytopenias
- Splenomegaly insufficient to qualify as PR
  OR
  - Reappearance of hairy cells in the bone marrow of those patients who had been classified as partial responders based on residual splenomegaly only


**Other leukemia:**
To determine the disease status, use the criteria for the leukemia that most closely resembles the disease for which this form is being completed. For questions, contact your transplant center’s CIBMTR CRC.
**Question 267: Date assessed:**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant work-up period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments.

If the exact date is not known, use the process for reporting partial or unknown dates as described in [General Instructions, Guidelines for Completing Forms](https://CIBMTR.org/forms-instructions).
Hodgkin lymphoma (HL or Hodgkin disease) is a cancer of the immune system that is marked by the presence of a type of cell called the Reed-Sternberg cell. The two major types of Hodgkin lymphoma are classical Hodgkin lymphoma (90-95% of cases) and nodular lymphocyte-predominant Hodgkin lymphoma (5-10% of cases).

Classical Hodgkin lymphoma can be further subdivided into four histologic subtypes: nodular sclerosis (NS), mixed cellularity (MC), lymphocyte deplete (LD), and lymphocyte rich (LR). Symptoms include the painless enlargement of lymph nodes, spleen, or other immune tissue. Generalized pruritus is also common and may precede the diagnosis by months. The most common sites of involvement include cervical, supraclavicular, and mediastinal lymph nodes. Central nervous system involvement may occur in rare cases. Other symptoms include fever, weight loss, fatigue, and/or night sweats.

Non-Hodgkin lymphoma (NHL) is a large group of cancers derived from lymphocytes (white blood cells). Non-Hodgkin lymphomas can occur at any age and are often marked by enlarged lymph nodes, fever, night sweats and weight loss. There are many different types of non-Hodgkin lymphoma. These types can be divided into aggressive (fast-growing), intermediate, or indolent (slow-growing) and can develop from either B-cells or T-cells. See Table 10.

Lymphomas that occur after bone marrow or stem cell transplantation are usually B-cell non-Hodgkin lymphomas and are collectively known as post-transplant lymphoproliferative disorders (PTLD).

Acute Lymphoblastic Leukemia / Lymphoma
Due to the aggressive nature of precursor B- and precursor T-cell lymphoblastic lymphoma (or lymphoma / leukemia), the primary disease to report for recipients with these malignancies should be acute lymphoblastic leukemia (B-cell lymphoblastic leukemia/lymphoma or early T-cell precursor lymphoblastic leukemia).

Hodgkin Lymphoma (HL) and non-Hodgkin Lymphoma (NHL) are WHO disease classification subtypes of lymphoma. HL and NHL can transform into other disease subtypes. NHL can transform into other NHL subtypes, or into HL subtypes, but HL will rarely transform into NHL. Additionally, HL and NHL can occur at the same time and most likely classified as “B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma".
In order to complete the correct Disease Classification questions for a recipient who has a history of both HL and NHL, it is important to determine which disease is active prior to the start of the preparative regimen. A physician must make this determination.

The following two scenarios are examples of the data reporting practice for recipients with a combination of HL and NHL.

**Scenario 1:** A recipient is being transplanted for active NHL, but has a history of HL that is in remission at the start of the preparative regimen. Report the active NHL on the Disease Classification questions, and report HL as a prior malignancy on the Pre-TED Form (Form 2400).

**Scenario 2:** A recipient is being transplanted for both active NHL and active HL. Report this as NHL using “Other B-cell Lymphoma” and specify in question 269. Complete the Disease Classification questions for NHL. This only applies when the NHL and HL have been diagnosed at different times (i.e., two primaries).

**Question 268-269: Specify the lymphoma histology (at infusion)**

Indicate the histology for which the recipient is receiving a transplant or cellular therapy. If the histology is “Other B-cell lymphoma” or “Other T-cell / NK-cell lymphoma,” specify the histology in question 269.

Go to question 270 if either of the following histologies were reported in question 268:

- Diffuse, large B-cell lymphoma – Activated B-cell type (non-GCB)
- Diffuse, large B-cell lymphoma – Germinal center B-cell type

Otherwise, go to question 271.

**Question 270: Assignment of DLBCL subtype:**

DLBCL subtypes may be identified using different techniques including immunohistochemistry (IHC) and gene expression profiling. IHC involves staining a tissue sample and determining the presence of cell surface markers via microscopy. Gene expression profiling utilized molecular techniques.

Report the method used to determine the DLBCL subtype. Indicate “Unknown” if the method cannot be determined from the available source documentation.

**Question 271: Is the lymphoma histology reported at transplant a transformation from CLL?**

In some cases, CLL may evolve to a more aggressive diffuse large B-cell lymphoma (DLBCL). This is
commonly referred to as Richter’s syndrome or Richter’s transformation. In a sub-set of CLL cases, the transformation may be to Hodgkin lymphoma (HL).

If the histology reported at infusion (question 268) is a transformation from CLL, indicate “Yes,” and go to question 272.

If the histology reported at infusion is not a transformation from CLL, indicate “No” and go to question 273.

**Question 272: Was any 17p abnormality detected?**

Report “Yes” if an abnormality was ever detected (by any method) on the short arm of chromosome 17 since the date of diagnosis of CLL. This includes any 17p abnormality detected after transformation to lymphoma and go to question 277. Report “No” if a 17p abnormality was not detected and go to question 277.

**Question 273: Is the lymphoma histology reported at transplant a transformation from a different lymphoma histology (not CLL)?**

Transformation may occur when a slow-growing lymphoma with an indolent clinical history changes to a more aggressive lymphoma histologically and clinically. An example of a common transformation would include follicular lymphoma evolving to a diffuse large B-cell lymphoma (DLBCL).

If a histologic transformation occurred after or concurrently with diagnosis, indicate “Yes” and go to question 274. If a histologic transformation did not occur, indicate “No” and go to question 277.

**Question 274-275: Specify the original lymphoma histology (prior to transformation)**

Report the histology of the recipient’s primary disease at diagnosis. If the histology is “Other B-cell lymphoma” or “Other T-cell / NK-cell lymphoma,” specify the histology in question 275.

**Question 276: Date of original lymphoma diagnosis**

Report the date of diagnosis for the histology specified in questions 274-275. If the exact pathological diagnosis date is not known, use the process described in General Instructions, [General Guidelines for Completing Forms](#).

**Question 277: Was a PET (or combination PET / CT) scan performed? (at last evaluation prior to the start of the preparative regimen / infusion)**

Report “Yes” and go to question 278 if a PET scan was performed within three months prior to the start of the preparative regimen / infusion. Combination PET / CT may also be reported, but a CT scan alone should not be captured here. Centers may report a PET scan performed during the most recent line of therapy so long as it is the most recent scan and was done within noted period. Report “No” and go to question 283 if a
PET scan was not performed within this period.

**Question 278: Was the PET (or PET / CT) scan positive for lymphoma involvement at any disease site?**

Report “Yes” if the most recent PET scan prior to the start of the preparative regimen / infusion detected the recipient’s primary disease. Otherwise, report “No.”

**Question 279-280: Date of PET scan**

Questions 279-280 refer to the PET scan used to answer question 278. If the date of this PET scan is known, report “Known” and specify the date in question 280. If the date is only partially known (e.g., the month and year are known, but not the day) report “Known”, and use the process described in General Instructions, General Guidelines for Completing Forms to complete question 280. If the date cannot be determined / estimated, report “Unknown” and go to question 281.

**Question 281-282: Deauville (five-point) score of the PET (or PET/CT) scan**

Questions 281-282 refer to the PET scan used to answer question 278. Report whether the five-point PET score is known. This information is typically documented in the PET report. Consult the appropriate transplant physician if the results are unclear. If “Known,” report the score in question 282. Otherwise, report “Unknown” for question 281 and go to question 283. If the PET scan result is only documented as an ‘X’, report this as “Unknown” for question 281.

If multiple scores are documented, report the highest.

**Question 283: What was the disease status?**

The recipient’s pre-HCT disease status may be evaluated by a PET scan, CT scan, or both. If possible, complete question 283 using the metabolic (PET) criteria provided in the Lymphoma Response Criteria section of the manual. If it is not possible to use metabolic criteria to report the recipient’s disease (e.g., insufficient PET scan(s), non-PET-avid disease), use the radiographic criteria instead.

Indicate the disease status at the last evaluation prior to the start of the preparative regimen. When determining the disease status, compare the restaging assessments immediately prior to the preparative regimen to the assessments at baseline. “Baseline” is defined as the disease at diagnosis or at relapse/progression. When a transformation has occurred (e.g., follicular lymphoma (FL) transformed to DLBCL), count the response number (CR1, REL2, etc.) beginning with the transformed lymphoma (in this case the DLBCL). Do not include the responses to the lymphoma sub-type prior to the transformation.

**Question 284: Total number of lines of therapy received (between diagnosis and HCT / infusion)**

A single line of therapy refers to any agents administered during the same time period with the same intent.
(induction, consolidation, etc.). If a recipient’s disease status changes resulting in a change to treatment, this should be considered a new line of therapy. Additionally, if therapy is changed because a favorable disease response was not achieved, this should be considered a new line of therapy.

Indicate how many lines of therapy the recipient received prior to the start of the preparative regimen / infusion.

**Question 285: Date assessed:**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. Report the date imaging took place for the radiographic assessment (CT, MRI, PET, or PET/CT). Report the date the sample was collected for pathological evaluation (e.g., bone marrow biopsy). If no radiographic or pathologic assessment was performed within one month prior to transplant, report the most recent office visit in which the physician evaluated the recipient’s disease status.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, [General Guidelines for Completing Forms](#).
Q286-317: Multiple Myeloma / Plasma Cell Disorder

One kind of white blood cell, the plasma cell (also called plasma B cells, plasmocytes, or effector B cells), produces proteins called antibodies or immunoglobulins (Igs) that are part of our defense system against foreign substances (called antigens). Antibodies are produced in response to such things as viruses, bacteria, and other infectious agents.

Multiple myeloma is a cancer that leads to the proliferation of malignant plasma cells (myeloma cells). Myeloma cells usually proliferate in the bone marrow. When myeloma cells grow into isolated masses in other sites, these masses are called plasmacytomas. Health problems caused by multiple myeloma can affect the bones, immune system, kidneys, and red blood cell count.

The immunoglobulins (antibodies) produced by healthy plasma cells are composed of pairs of heavy chains and light chains (see graphic below). Healthy plasma cells create many different kinds of immunoglobulins that are classified by their heavy chain type into five categories (IgG, IgA, IgM, IgD, or IgE). The light chain types are designated kappa (κ) or lambda (λ). The whole Ig molecule is then labeled IgG kappa, IgG lambda, IgA kappa, IgA lambda, etc. These protein levels can be measured in blood serum and/or urine.

Structure of an Immunoglobulin (Antibody)

Secretory Multiple Myeloma:
Healthy plasma cells make immunoglobulins (antibodies) of all types. With the proliferation of malignant plasma cells, the level of one immunoglobulin type increases in the blood and/or urine. This abnormal immunoglobulin type is called the monoclonal immunoglobulin, monoclonal protein (M-protein/M-spike/M-component), or paraprotein. In most cases, the normal immunoglobulins are reciprocally depressed.
Patients with this condition are said to have *secretory myeloma*.

Some myeloma patients make only an excess of the light chain portion of the immunoglobulin molecule (i.e., only monoclonal kappa or lambda light chains). The light chain is also called Bence Jones protein. In most patients whose myeloma cells only make light chains, this paraprotein may not be detectable in the blood, but only in the urine. These patients are said to have *light-chain-only disease*. Ninety-seven percent of patients diagnosed with multiple myeloma have a detectable paraprotein in the blood serum and/or urine.

**Distribution of Monoclonal Proteins in Secretory Multiple Myeloma**

<table>
<thead>
<tr>
<th>Monoclonal Proteins at Diagnosis</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Source of monoclonal proteins</strong></td>
<td></td>
</tr>
<tr>
<td>Serum monoclonal proteins</td>
<td>80%</td>
</tr>
<tr>
<td>Urine monoclonal proteins</td>
<td>75%</td>
</tr>
<tr>
<td><strong>Type of monoclonal proteins</strong></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>50-54%</td>
</tr>
<tr>
<td>IgA</td>
<td>20%</td>
</tr>
<tr>
<td>Monoclonal light chain (light-chain-only disease)</td>
<td>20%</td>
</tr>
<tr>
<td>IgD</td>
<td>2%</td>
</tr>
</tbody>
</table>


**Nonsecretory Multiple Myeloma:**

In some myeloma patients, the malignant plasma cells do not produce an excess of the heavy chain or light chain portion of the immunoglobulin molecule; therefore, a paraprotein is not detectable in the serum or urine. These patients are said to have nonsecretory myeloma (i.e., the absence of a paraprotein on immunofixation). Immunofixation detects the specific immunoglobulins after separating the proteins into bands on an electrophoresis gel. Nonsecretory myeloma accounts for 3% of myeloma cases.

**Amyloidosis:**

Amyloidosis is a disease in which abnormally folded proteins build up in different tissues of the body. In the most common amyloidosis, AL amyloidosis, the abnormally folded protein is the light chain component of an
immunoglobulin. These light chains may build up in a variety of tissues, but the most common sites of build-up are the heart, kidneys, liver and nerves. According to the Amyloidosis Foundation, AL Amyloidosis is a relatively rare disorder, with 1200-3200 new cases reported each year in the United States. The disease mostly impacts men and people over 40.

Accessibility verified on October 21, 2013.

Question 286-287: Specify the multiple myeloma/plasma cell disorder (PCD) classification:

Indicate the multiple myeloma/plasma cell disorder (PCD) disease classification at diagnosis. If the subtype is not listed, report as “other plasma cell disorder” and specify the reported disease.

Plasma Cell Disorders and Characteristics

Multiple Myeloma (symptomatic)
Diagnostic criteria for symptomatic multiple myeloma requires clonal bone marrow plasma cells in ≥ 10% or biopsy proven bony or extramedullary plasmacytoma and any one or more of the following myeloma-defining events:

1. Evidence of end organ damage (i.e., CRAB features) that can be attributed to the underlying plasma cell proliferative disorder, specifically:
   - Hypercalcemia: serum calcium >1 mg/dL (> 0.25 mmol/L) higher than the ULN or > 11 mg/dL (> 2.75 mmol/L)
   - Renal insufficiency: creatinine clearance < 40 ml/min or serum creat >2 mg/dL (> 177 μmol/L)
   - Anemia: hemoglobin > 2 g/dL (> 20 g/L) below the LLN or a hemoglobin <10 g
   - Bone lesions: one or more osteolytic lesions on skeletal x-ray, CT or PET-CT

2. Any one or more of the following biomarkers of malignancy:
   - Clonal bone marrow plasma percentage ≥ 60%
   - Involved : uninvolved serum free light chain ratio ≥ 100
   - > 1 focal lesion on MRI studies (each lesion must be ≥ 5 mm in size)

Plasma Cell Leukemia

- Peripheral blood absolute plasma cell count of at least $2.0 \times 10^9$/L (2,000 cells/mm$^3$)
- ≥ 20% plasma cells in the peripheral differential white blood cell count.

Solitary Plasmacytoma (in absence of bone marrow findings diagnostic for multiple myeloma or plasma cell leukemia)

**Extramedullary:**

- No M-protein in serum and/or urine
- Extramedullary tumor of clonal plasma cells
- Normal bone marrow
- Normal skeletal survey
- No related organ or tissue impairment (end organ damage including bone lesions)

**Bone Derived**

- No M-protein in serum and/or urine
- Single area of bone destruction due to clonal plasma cells
- Bone marrow not consistent with multiple myeloma
- Normal skeletal survey (and MRI of spine and pelvis if done)
- No related organ or tissue impairment (no end organ damage other than solitary bone lesion)

*Note: if the recipient has greater than one plasmacytoma, but has not been diagnosed with another plasma cell disorder, select “other plasma cell disorder” and specify how many plasmacytomas are present and if each is bone derived or extramedullary.*

Amyloidosis

Amyloidosis is the buildup of abnormally folded proteins in various tissues of the body. Affected tissues may include the kidneys, heart, liver, gastrointestinal tract, etc. In the most common type of amyloidosis, “AL amyloidosis,” light chains from antibodies function as the amyloid protein, building up within organs and disrupting organ function. Serum and urine tests are useful for evaluating amyloidosis, but a tissue biopsy is the best way to diagnose the condition.

Osteosclerotic myeloma/ POEMS Syndrome

POEMS syndrome is poorly understood, but generally refers to polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes. Diagnosis may be made using the presence of the major
criteria and one minor criteria below:

**Major Criteria (both of the following):**

- Polyneuropathy
- Monoclonal plasmaproliferative disorder

**Minor Criteria (at least one of the following):**

- Sclerotic bone lesions
- Castleman disease
- Organomegaly (splenomegaly, hepatomegaly, lymphadenopathy)
- Edema (edema, pleural effusion, or ascites)
- Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic)
- Skin changes (hyperpigmentation, hypertrichosis, plethora, hemangiomata, white nails)
- Papilledema

**Light Chain Deposition Disease**

Similar to amyloidosis, light chain deposition disease is characterized by the overproduction and deposition of light chains in organs throughout the body; however, the organ most often affected is the kidneys. Under microscopy, the pattern of deposition and the use of staining techniques help pathologists differentiate between amyloidosis and light chain deposition disease.

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6 Osteosclerotic lesion or Castleman disease is usually present.


For recipients diagnosed with more than one PCD, either sequentially or concurrently, ensure that all
applicable questions are completed.

If the recipient’s disease classification is one of the following, continue with question 288.

- Multiple myeloma – IgG
- Multiple myeloma – IgA
- Multiple myeloma – IgD
- Multiple myeloma – IgE
- Multiple myeloma – IgM (not Waldenstrom macroglobulinemia)
- Multiple myeloma – light chain only

If the recipient’s disease classification is the following, neither kappa nor lambda light chains will be present; therefore, continue with question 289.

- Multiple myeloma – non-secretory

If the recipient’s disease classification is one of the following, continue with question 294.

- Plasma cell leukemia
- Solitary plasmacytoma (no evidence of myeloma)
- Amyloidosis
- Osteosclerotic myeloma/POEMS syndrome
- Light chain deposition disease

If the recipient’s disease classification is the following, continue with question 287.

- Other Plasma Cell Disorder

**Question 288: Light Chain**

Indicate the presence of light chains as either kappa or lambda.

**Question 289-290: What was the Durie-Salmon staging (at diagnosis)?**

Indicate Durie-Salmon stage and sub-classification at diagnosis. If this is not documented in the medical record, see the table below to determine the appropriate stage and sub-classification. If “unknown,” continue with question 291.
## Durie-Salmon Staging System for Multiple Myeloma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| I     | All of the following:  
• Hemoglobin > 10 g/dL  
• Serum calcium normal (< 10.5 mg/dL)  
• On radiograph, normal bone structure or solitary bone plasmacytoma only  
• Low M-component production rate (IgG < 5 g/dL, IgA < 3 g/dL), Urinary light chain M-component on electrophoresis (< 4 g/24 hr) |
| II    | Fitting neither stage I nor stage III |
| III   | One or more of the following:  
• Hemoglobin < 8.5 g/dL  
• Serum calcium > 12 mg/dL  
• Advanced lytic bone lesions (three or more lytic lesions)  
• High M-component product rate (IgG > 7 g/dL, IgA > 5 g/dL), Urinary light chain M-component on electrophoresis (> 12 g/24 hr) |

**Sub-classification** (either A or B)  
A: Relatively normal renal function (serum creatinine < 2.0 mg/dL)  
B: Abnormal renal function (serum creatinine ≥ 2.0 mg/dL)

\[8\] Adapted from Durie BG, Salmon SE: A clinical staging system for multiple myeloma: Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. *Cancer*. 1975;36:842-54.

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## I.S.S. Staging System for Multiple Myeloma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Serum β2-microglobulin &lt; 3.5 mg/L and serum albumin ≥ 3.5 g/dL</td>
</tr>
<tr>
<td>II</td>
<td>Serum β2-microglobulin &lt; 3.5 mg/L and serum albumin &lt; 3.5 g/dL OR Serum β2-microglobulin 3.5 to &lt;5.5 mg/dL irrespective of serum albumin level</td>
</tr>
<tr>
<td>III</td>
<td>Serum β2-microglobulin ≥ 5.5 mg/L irrespective of serum albumin level</td>
</tr>
</tbody>
</table>

International staging system for multiple myeloma. *Journal of Clinical Oncology*, 23(15), 3412-3420.

**Question 294: Were cytogenetics tested (conventional or FISH)?**

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at any time prior to the start of the preparative regimen. If cytogenetic studies were obtained, select “yes” and continue with question 295.

If no cytogenetic studies were obtained or if it is unknown if chromosome studies were performed, select “no” or “unknown” and continue with question 316.

**Question 295: Results of test:**

If cytogenetic studies identified abnormalities, indicate “abnormalities identified” and continue with question 296.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified, continue with question 316.

**Question 296-315: Specify abnormalities identified at any time prior to the start of the preparative regimen:**

Report all abnormalities identified by all methods of cytogenetic assessment at any time prior to the start of the preparative regimen by selecting “yes” or “no” for each question. Do not leave any response blank. If one or more abnormalities are best classified as “other abnormality” select “yes” for question 314 and specify the abnormality in question 315.

**Question 316: What was the disease status?**

*Amyloidosis*

If the recipient’s primary disease is amyloidosis (without evidence of myeloma), report Complete Remission (CR) if the CR criteria for all involved organs are met (see Amyloidosis Response Criteria). If the disease status at transplant is anything other than CR, report “Not applicable.” This is a change from the previous instruction which asked centers to report “Not applicable” for all amyloidosis cases, regardless of disease response.

Indicate the disease status of the PCD at the last evaluation prior to the start of the preparative regimen. If
the primary disease is POEMS, report “Not applicable” and go to the signature line. See the Multiple Myeloma Response Criteria section for multiple myeloma and solitary plasmacytoma disease status definitions. See Plasma Cell Leukemia Response Criteria for plasma cell leukemia disease status definitions.

**Question 317: Date Assessed:**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. Date of radiographic study (PET, MRI, CT) may be used *if* the same radiographic study had previously been obtained and *only* in limited circumstances (e.g., plasmacytomas, lytic lesions).

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
Q318-319: Solid Tumors

Question 318-319: Specify the solid tumor classification:

Indicate the solid tumor disease classification at the time of diagnosis. Germ cell tumors that originate in the ovary or testes should be reported as ovarian or testicular, respectively. If the subtype is not listed, report as “Other solid tumor” and specify the reported malignancy in question 310. If a certain disease becomes a common indication for HCT, the CIBMTR will add the disease as a separate category.
Questions 320-321: Specify the severe aplastic anemia classification:

Indicate the severe aplastic anemia disease classification at diagnosis. If the subtype is not listed, report as “other acquired cytopenic syndrome” and specify the reported disease. If a certain disease becomes a common indication for HCT, the CIBMTR will add the disease as a separate category.
Q322-324: Inherited Abnormalities of Erythrocyte Differentiation or Function

Questions 322-324: Specify the inherited abnormalities of erythrocyte differentiation or function classification

Indicate the inherited abnormalities of erythrocyte differentiation or function disease classification at diagnosis. If the subtype is not listed, report as "other constitutional anemia" or "other hemoglobinopathy" and specify the reported disease. If a certain disease becomes a common indication for HCT, the CIBMTR will add the disease as a separate category.
Q325-327: Disorders of Immune System

Questions 325-327: Specify disorder of immune system classification:

Indicate the disorder of the immune system's disease classification at diagnosis. If the subtype is not listed, report as "other SCID" or "other immunodeficiency" and specify the reported disease. If a certain disease becomes a common indication for HCT, the CIBMTR will add the disease as a separate category.
Questions 328-329: Specify inherited abnormalities of platelets classification:

Indicate the inherited abnormalities of platelets disease classification at diagnosis. If the subtype is not listed, report as "other inherited platelet abnormality" and specify the reported disease. If a certain disease becomes a common indication for HCT, the CIBMTR will add the disease as a separate category.
Q330-331: Inherited Disorders of Metabolism

Questions 330-331: Specify inherited abnormalities of metabolism classification:

Indicate the inherited abnormalities of metabolism disease classification at diagnosis. If the subtype is not listed, report as "inherited metabolic disorder, not otherwise specified" and specify the reported disease. If a certain disease becomes a common indication for HCT, the CIBMTR will add the disease as a separate category.
Q332-333: Histocytic Disorders

Questions 332-333: Specify the histiocytic disorder classification:

Indicate the histiocytic disorder disease classification at diagnosis. If the subtype is not listed, report as “other histiocytic disorder” and specify the reported disease in question 333. If a certain disease becomes a common indication for HCT, the CIBMTR will add the disease as a separate category.
Questions 334-341: Specify autoimmune disease classification:

Indicate the autoimmune disease classification at diagnosis. If the subtype is not listed, report as “other arthritis,” “other connective tissue disease,” “other vasculitis,” “other autoimmune neurological disorder,” “other autoimmune cytopenia,” or “other autoimmune bowel disorder,” and specify the reported disease. If a certain disease becomes a common indication for HCT, the CIBMTR will add the disease as a separate category.
Q342: Other Disease

Question 342: Specify other disease:

Before using this category, check with a transplant physician to determine whether the disease can be classified as one of the listed options in the Disease Classification questions. Examples include: erythropoietic protoporphyrin (EPP), and dystrophic epidermolysis bullosa (DEB).
Transplant centers participating in the CIBMTR must submit a Post-TED Form for recipients who meet any of the following criteria:

- Recipient receives a transplant at a United States center designated as a TED-only center.
- Recipient receives a transplant at a United States center designated as Comprehensive Report Form center and has been assigned to the TED track by the Form Selection Algorithm.
- Recipient receives an allogeneic transplant at a United States center designated as Comprehensive Report Form center, but has not consented to participate in research.
- Recipient receives a transplant at an international center, has consented to participate in research, and has been assigned to the TED track by the Form Selection Algorithm.

The Post-TED fulfills the requirements of the SCTOD for recipients meeting any of the above criteria. For more information regarding the SCTOD, see General Instructions, Stem Cell Therapeutics Outcomes Database.

For more information, including information on the TED and Comprehensive Report Form Selection Algorithm, see Section 1 in the Center Reference Guide.

The Post-TED must be completed at the following time points: 100 days, six months, and annually post-HCT. These forms should be completed as closely to these time points as possible. The structure of the TED Forms is such that each form should fit on a timeline with distinct start and stop dates that do not overlap any other forms, except in the case of a subsequent HCT. The Post-TED is considered past due 120 days after each of these time points.

If the Post-TED form is being completed for a six-month or annual evaluation, the answers to all questions should reflect the clinical status of the recipient since the last report.

Subsequent HCT:
If a recipient receives a subsequent HCT between Post-TED time points (100 day, six months, annually), the TED form sequence will start over again with another Pre-TED.

However, if the recipient receives an autologous HCT as a result of a poor graft or graft failure, the TED form sequence will not start over again. Generally this type of infusion (autologous rescue) is used to treat the recipient’s poor graft response, rather than to treat the recipient’s disease.
Contact your center’s CIBMTR CRC if the subsequent Pre-TED does not come due automatically.

If the recipient received a subsequent transplant (excluding an autologous rescue), the answers to all questions should reflect the clinical status of the recipient the day prior to the start of the preparative regimen or, if no preparative regimen was given, the answers to all questions should reflect the clinical status of the recipient the day prior to HCT infusion.

Non-Malignant Diseases
If the HCT being reported was given to treat a non-malignant disease (as reported on the Pre-TED Disease Classification Form {Form 2402}), do not complete the following sections of the Post-TED Form:

- Q75-97: Disease Assessment at the Time of Best Response to HCT
- Q98-160: Post-HCT Therapy
- Q235-238: Current Disease Status

Questions 161-163 will also be left blank if the HCT being reported was given to treat a non-malignant disease.

Lost to Follow-Up:
Occasionally, centers may lose contact with recipients for a variety of reasons, including the recipient’s moving, changing physicians, or death. If contact with a recipient appears lost, please consider calling the recipient at home or work, sending a letter, communicating with the treating or referring physician, or contacting the hospital billing department. If your center receives documented information that a recipient is alive or dead, the form should be filled out with the recipient survival status. If no documentation exists and several unsuccessful attempts have been made to contact the recipient, they are considered lost to follow-up and the form may be marked as such using the Lost to Follow-Up tool in FormsNet3 for each reporting period in which no contact exists.

Select TED
Select TED recipients are required to answer a limited subset of questions on the Post-TED form. These questions include:

- Key fields;
- Survival, questions 1-6;
- Subsequent transplant, questions 7-11; and
- New malignancy, questions 49-56
Instruction for reporting in these data fields does not differ from that provided for all recipients on the TED form. Refer to the applicable sections of the Forms Instructions Post-TED Manual for further information on completing these fields.

Links to Sections in Manual:
Q1-6: Survival
Q7-13: Subsequent Transplant
Q14-16: Initial ANC Recovery
Q17-18: Initial Platelet Recovery
Q19-38: Graft-Versus-Host Disease
Q39-45: Liver Toxicity Prophylaxis
Q46-47: Veno-occlusive disease (VOD) / Sinusoidal obstruction syndrome (SOS)
Q48-55: New Malignancy, Lymphoproliferative or Myeloproliferative Disorder
Q56-74: Chimerism Studies
Q75-97: Disease Assessment at the Time of Best Response to HCT
Q98-160: Post-HCT Therapy
Q161-234: Relapse or Progression Post-HCT
Q235-238: Current Disease Status

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/19/19</td>
<td>2450: Post-TED</td>
<td>Add</td>
<td>Added the following red warning box instruction (in red below) below question 75 to clarify when to use the CCR option in the Disease Assessment at the Time of Best Response to HCT section of the Post-TED (2450) form: Continued Complete Remission (CCR) should be reported for all patients who were already in CR at the start of the preparative regimen.</td>
</tr>
<tr>
<td>12/21/18</td>
<td>2450: Post-TED</td>
<td>Remove</td>
<td>Removed the following blue note box instruction (struck out below) above question 82 regarding Flow Cytometry reporting for Lymphoma and Myeloma. These assessments can now be reported in the same way as all other disease assessments. Myeloma and Lymphoma Flow cytometry assessments performed to detect myeloma or lymphoma should not be reported if negative (&lt; 5% malignant cells detected). If flow cytometry was performed to detect myeloma or lymphoma and showed less than 5% malignant</td>
</tr>
<tr>
<td>Date</td>
<td>Code</td>
<td>Action</td>
<td>Description</td>
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<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>8/10/18</td>
<td>2450</td>
<td>Modify</td>
<td><strong>Modified</strong> (added text in red and deleted text is struck-out) the instructions for reporting the “date assessed” for questions 80, 83, 87, 90, 96, and 98: If the best response is “not in complete remission,” report the date of the most recent testing performed during the reporting period and prior to relapse or progression treatment for relapsed, progressive, or persistent disease, if applicable. If no treatment for relapsed, progressive, or persistent disease was given, report the date of the most recent disease-specific testing performed within approximately 30 days of the follow-up date.</td>
</tr>
<tr>
<td>8/10/18</td>
<td>2450</td>
<td>Remove</td>
<td>Removed the following instruction from questions 157 and 231: Reporting the administration of a cellular therapy / donor cellular infusion in question 231 will generate additional cellular therapy forms which are used to capture important details regarding the infusion(s).</td>
</tr>
<tr>
<td>4/30/18</td>
<td>2450</td>
<td>Add</td>
<td>Added the following instruction for question question 34. Please note, questions 35 and 36 must still be answered if question 34 is reported as “unknown.”</td>
</tr>
<tr>
<td>4/30/18</td>
<td>2450</td>
<td>Modify</td>
<td>Updated language on how to report the “Date of most recent disease assessment” for questions 237-238.</td>
</tr>
<tr>
<td>3/19/18</td>
<td>2450</td>
<td>Add</td>
<td>Added the following instruction for question 235. The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.</td>
</tr>
<tr>
<td>3/5/18</td>
<td>2450</td>
<td>Modify</td>
<td>Updated language on what to capture as a molecular assessment for questions 75-97.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>2450</td>
<td>Add</td>
<td>Added <strong>Amyloidosis</strong> note box above the instructions for question 75.</td>
</tr>
<tr>
<td>8/31/17</td>
<td>2450</td>
<td>Add</td>
<td>Added text (in red below) to the description of stage 4 gut GVHD provided in the Acute GVHD Grading and Staging Table located below the instructions for question 22. Severe abdominal pain, with or without ileus, and/or grossly bloody stool.</td>
</tr>
<tr>
<td>8/1/17</td>
<td>2450</td>
<td>Add</td>
<td>Added the text below to the instructions for question 22. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic).</td>
</tr>
<tr>
<td>8/1/17</td>
<td>2450</td>
<td>Add</td>
<td>Added the text below to the instructions for questions 23-28. Report the stage of each organ at diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic).</td>
</tr>
<tr>
<td>7/26/18</td>
<td>2450</td>
<td>Add</td>
<td>Added text (in red) to instructions for question 36 to clarify intent of question. Report the date of maximum chronic GVHD involvement, based on clinical grade.</td>
</tr>
<tr>
<td>Date</td>
<td>Action</td>
<td>Description</td>
<td></td>
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</tr>
<tr>
<td>7/26/17</td>
<td>Modify</td>
<td>Modified instructions for question 34 to clarify intent of question. Added text in red and removed text which is struck out. Report the maximum chronic GVHD involvement, based on clinical grade, since the date of the last report, as documented by the recipient’s primary care provider.</td>
<td></td>
</tr>
<tr>
<td>7/11/17</td>
<td>Add</td>
<td>Added the following text to the description of lower GI GVHD provided in the instructions for questions 23-28: Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.</td>
<td></td>
</tr>
<tr>
<td>7/10/17</td>
<td>Add</td>
<td>Added Intervention Reporting Scenarios A, B, C, and D below the instructions for question 172.</td>
<td></td>
</tr>
<tr>
<td>7/10/17</td>
<td>Modify</td>
<td>Added (in red) and removed (crossed out) text to / from the instructions for question 172 as indicated below. Report the date of earliest administration of therapy for relapsed, persistent, or progressive disease or decreasing / loss of donor chimerism within the report period therapy was started for the reason specified in question 165; if multiple instances, cycles, or lines of therapy are administered, report the date of the first treatment. If treatment was started in a prior reporting period and continued into the current reporting period, report the original therapy start date (prior to the start of the current reporting period) and override the validation error in FormsNet3SM using the code “verified correct.” If therapy was stopped in a prior reporting period and restarted (or a new therapy was started) during the current reporting period, report the earliest date treatment was administered during the current reporting period. See the intervention reporting scenarios provided below for further clarification.</td>
<td></td>
</tr>
<tr>
<td>7/10/17</td>
<td>Add</td>
<td>Added (in red) text to the instructions for questions 166-171 as indicated below. Indicate the methods detecting the reason for which therapy for persistent disease, relapsed / progressive disease, or for decreased / loss of donor chimerism was given (as reported in question 165). For each option, select “yes” if the last assessment by that method was performed prior to the start of the intervention(s) and was consistent with the rationale reported in question 165. … If multiple therapies were given during the reporting period for different reasons (e.g., the recipient initially receives treatment for decreased chimerism and subsequently receives different treatment for relapse during the same reporting period), report “yes” for any methods of detection confirming the reason in question 165. See the intervention reporting scenarios provided below for further clarification.</td>
<td></td>
</tr>
<tr>
<td>7/10/17</td>
<td>Add</td>
<td>Added (in red) text to the instructions for question 165 as indicated below. Indicate whether therapy was given for persistent disease, relapsed / progressive disease, or for decreased / loss of donor chimerism. In some instances, therapy may be given to treat disease and decrease / loss of chimerism. In these cases, report the indication pertaining to the recipient’s disease status (i.e., “persistent disease” or “relapsed / progressive disease”). If therapy continued from a prior reporting period and a new therapy was started for a different reason during the current reporting period, report the reason the new therapy was started. See the</td>
<td></td>
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<tr>
<td>Date</td>
<td>Version</td>
<td>Action</td>
<td>Comment</td>
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</tr>
<tr>
<td>7/10/17</td>
<td>2450: Post-TED</td>
<td>Add</td>
<td>Added Liver Toxicity Prophylaxis warning box above question 39.</td>
</tr>
<tr>
<td>6/8/17</td>
<td>2450: Post-TED Data</td>
<td>Remove</td>
<td>Removed unnecessary text from the following instruction for question 31 to clarify instructions. Report “no” if chronic GVHD was not clinically diagnosed – initially or as a flare – in the reporting period; this includes instances where chronic GVHD persists from a prior reporting period. without flare in the current reporting period.</td>
</tr>
<tr>
<td>5/25/17</td>
<td>2450: Post-TED</td>
<td>Add</td>
<td>Added Steroids and Non-Steroid Immunosuppression for GVHD warning box to the instructions for question 37 and 38.</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2450: Post-TED</td>
<td>Add</td>
<td>Added the following information regarding Non-Malignant Diseases to the Post-TED Title Page: <strong>Non-Malignant Diseases</strong> If the HCT being reported was given to treat a non-malignant disease (as reported on the Pre-TED Disease Classification Form (Form 2402)), do not complete the following sections of the Post-TED Form: • Q75-97: Disease Assessment at the Time of Best Response to HCT • Q98-160: Post-HCT Therapy • Q235-238: Current Disease Status Questions 161-163 will also be left blank if the HCT being reported was given to treat a non-malignant disease.</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2450: Post-TED Data</td>
<td>Add</td>
<td>Added Therapy Over Multiple Reporting Periods note box to the instructions for question 12.</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2450: Post-TED Data</td>
<td>Add</td>
<td>Added Malignant Diseases Only warning box to the following pages of the Post-TED Manual: • Q75-97: Disease Assessment at the Time of Best Response to HCT • Q98-160: Post-HCT Therapy • Q161-234: Relapse or Progression Post-HCT • Q235-238: Current Disease Status</td>
</tr>
<tr>
<td>4/19/17</td>
<td>2450: Post-TED Data</td>
<td>Remove</td>
<td>Removed incorrect instruction from question 231. Cellular therapy refers to the infusion of human or animal derived cells, which may or may not be modified or processed to achieve a specific composition. Examples include T-cell, NK cell, and mesenchymal cell infusions as well as donor cellular infusions. Indicate “yes” if the recipient received any form of cellular therapy for reasons other than relapse, persistent, or progressive disease or decreasing / loss of donor chimerism; hematopoietic cell transplantation should not be reported as cellular therapy, as this is captured in questions 7-13 of the Post-TED form.</td>
</tr>
</tbody>
</table>
| 4/14/17    | 2450: Post-TED | Add    | Added the following note box to the instructions for question 164 regarding **Interventions for Decreased / Loss of Chimerism:**
<table>
<thead>
<tr>
<th>Date</th>
<th>Revision</th>
<th>Type</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/7/17</td>
<td>2450: Post-TED Data</td>
<td>Add</td>
<td>Added instructions, in red below, to question 172 regarding treatment which overlaps reporting periods. Report the date of earliest administration of therapy for relapsed, persistent, or progressive disease or decreasing / loss of donor chimerism within the report period; if multiple instances, cycles, or lines of therapy are administered, report the first. If treatment was started in a prior reporting period and continues into the current reporting period, report the original therapy start date (prior to the start of the current reporting period) and override the validation error in FormsNet3SM using the code “verified correct.”</td>
</tr>
<tr>
<td>4/7/17</td>
<td>2450: Post-TED Data</td>
<td>Add</td>
<td>Added instructions to questions 23-28 to clarify how to report transaminitis under “other site” for acute GVHD. <strong>Other site(s) involved with acute GVHD:</strong> Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 28. If reporting transaminitis under “other site,” write in “transaminitis” rather than “liver” when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under “other site.”</td>
</tr>
</tbody>
</table>
| 4/6/17 | 2450: Post-TED Data | Modify | Updated instructions for question 21 to clarify reporting questions. The wording has changed, but the intent of the instructions is the same. Question 21 will only be enabled in FormsNet3SM if the center has reported “no” for question 19 and, therefore, has not reported a date of diagnosis in question 20. If prompted to answer question 21, report “yes” if acute GVHD was diagnosed in a prior reporting period and any of the following conditions are met:  
  • The recipient’s acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).  
  • The recipient’s acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred within 30 days of symptom resolution / quiescence.  
  • The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 19). Report “no” for questions 19 and 21 if the recipient had no active acute GVHD symptoms during the reporting period or all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of |
chronic GVHD (see note above question 19).
Indicate whether acute GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive acute GVHD, or a prior history of GVHD. If “yes,” continue with question 29; questions concerning acute GVHD at the time of diagnosis will be skipped. See question 19 for instructions on reporting an acute GVHD flare or acute GVHD occurring after the onset of chronic GVHD.
If the recipient has no active symptoms during the reporting period, report “no” and continue with question 31.

Updated instructions for question 19 to clarify reporting questions. The wording has changed, but the intent of the instructions is the same. Questions 19 and 21 on the Post-TED Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 19 or question 21 must be answered “yes.” There will not be a situation where “yes” is reported for both question 19 and question 21. If question 19 is answered yes and a diagnosis date has been reported in question 20, question 21 will be disabled in FormsNet3SM. Centers should report “yes” for question 19 to indicate the recipient developed acute GVHD in the following scenarios:
• Acute GVHD is diagnosed for the first time during the reporting period.
• An acute GVHD flare is diagnosed during the current reporting period and all of the following conditions are met:
  ◦ The recipient’s prior acute GVHD symptoms did not persist from the prior reporting period into the beginning of the current reporting period.
  ◦ The flare is diagnosed after at least 30 days without any active acute GVHD symptoms.
  ◦ The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 19).
If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report “no” for question 19 and “yes” for question 21. Question 21 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer
questions 19 and 21.
Report “no” for questions 19 and 21 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 19). Indicate whether a new clinical diagnosis of acute GVHD was documented during the reporting period. If acute GVHD was diagnosed during the reporting period, report “yes” and continue with question 20.
If the recipient had a flare of acute GVHD occurring after at least a 30 day period of symptom quiescence, report “yes” and continue with question 20. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent acute GVHD which is captured in question 21.
Indicate “no” if acute GVHD was not clinically diagnosed—initially or as a flare—in the reporting period; this includes instances where acute GVHD persists from a prior reporting period without flare in the current reporting period.

<table>
<thead>
<tr>
<th>Date</th>
<th>Version</th>
<th>Event</th>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/27/17</td>
<td>2450:</td>
<td>Post-TED Data</td>
<td>Added another example to questions 22 and 29 regarding when to report “Not Applicable” for the grade of acute GVHD. This instruction was previously available in the description of staging acute lower intestinal tract GVHD. * Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description below)</td>
</tr>
<tr>
<td>3/27/17</td>
<td>2450:</td>
<td>Post-TED Data</td>
<td>Added instruction to question 30: If “not applicable” was reported for question 29, question 30 must be left blank.</td>
</tr>
<tr>
<td>3/15/17</td>
<td>2450:</td>
<td>Post-TED Data</td>
<td>Added instruction to question 37 regarding when to use Not Applicable. Instructions for this option choice were not previously available. Indicate “not applicable” in any of the following scenarios: The recipient has never received systemic steroids (&gt; 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD. This form is being completed for a subsequent HCT and the recipient has never received systemic steroids (&gt; 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen is given). The recipient stopped taking systemic steroids (&gt; 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD in a</td>
</tr>
</tbody>
</table>
The recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen was given).

- The recipient stopped taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD in a previous reporting period and did not restart non-steroidal immunosuppressive agents (including PUVA) during the current reporting period.

<table>
<thead>
<tr>
<th>Date</th>
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<th>Action</th>
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</thead>
<tbody>
<tr>
<td>3/15/17</td>
<td>Added instruction to question 38 regarding when to use Not Applicable. Instructions for this option choice were not previously available. Indicate “not applicable” in any of the following scenarios:</td>
<td>Add</td>
</tr>
<tr>
<td>3/30/17</td>
<td>Added Scenario D to Acute GVHD Grading Scenarios under question 29.</td>
<td>Add</td>
</tr>
<tr>
<td>3/14/17</td>
<td>Added the following instruction below to question 29. This instruction was previously provided under question 19, but has been added to question 29 for further clarification. <strong>If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD.</strong> See question 19 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.</td>
<td>Add</td>
</tr>
<tr>
<td>3/14/17</td>
<td>Added scenario B to Acute GVHD Diagnosis Scenarios under question 19.</td>
<td>Add</td>
</tr>
<tr>
<td>3/14/17</td>
<td>Modified the note above question 19 to address questions received. The instructions have not changed, but the wording has been updated to be clearer. <strong>If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 19-30). Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section.</strong> Report any <strong>new or persistent acute GVHD symptoms (persistent or newly diagnosed)</strong> occurring on or after the date of diagnosis of chronic GVHD in the chronic GVHD section of the form (questions 234-323). See the examples included in the instructions for questions 252-301. If chronic GVHD was diagnosed in a prior reporting period, the center should report “no” for questions 19 and 21 in each subsequent reporting period. Any GVHD symptoms occurring</td>
<td>Modify</td>
</tr>
<tr>
<td>Date</td>
<td>Version</td>
<td>Action</td>
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<tr>
<td>3/13/17</td>
<td>2450:</td>
<td>Add</td>
</tr>
<tr>
<td>3/8/17</td>
<td>2450:</td>
<td>Add</td>
</tr>
<tr>
<td>3/2/17</td>
<td>2450:</td>
<td>Modify</td>
</tr>
<tr>
<td>3/1/17</td>
<td>2450:</td>
<td>Modify</td>
</tr>
<tr>
<td>3/1/17</td>
<td>2450:</td>
<td>Modify</td>
</tr>
</tbody>
</table>

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**Notes:**

- Additional details on specific modifications and updates can be found in the [CIBMTR.org Forms Instruction Manual](https://www.cibmtr.org/forms-instruction-manual).
- For more information, refer to the [2014 NIH Consensus Criteria](https://www.nhlbi.nih.gov/guidelines/hcv/hcv-index).
Q1-6: Survival

The date of actual contact with the recipient to determine medical status for this follow-up report is based on a medical evaluation conducted by a clinician with responsibility for the recipient’s care. Report the date of the medical evaluation performed closest to the designated time period of the form (e.g., Day+100, 6 months, or annual follow-up visit). Time windows are provided to guide selection of dates for reporting purposes. Recipients are not always seen within the time windows used for reporting follow-up dates, and some discretion is therefore required when determining which date to report. If the recipient is not seen within the time windows, report the date closest to the date of contact within reason.

If the Post-TED Form reports a subsequent transplant, report the date of latest follow-up as the day prior to the start of the preparative regimen. If no preparative regimen or conditioning was given, report the day prior to infusion as the date of contact.

Reporting Latest Follow-Up

When reporting the date of latest follow-up prior to a subsequent HCT, report the date specified above regardless whether there is actual patient contact on the date. This is an exception to standard date of follow-up reporting to ensure all dates are captured within the sequence of forms.

Question 1: Date of actual contact with the recipient to determine medical status for this follow-up report

Enter the date of actual contact with recipient to determine medical status for this follow-up report. Acceptable evaluations include those from the transplant center, referring physician, or other physician currently assuming responsibility for the recipient’s care. If an evaluation was not performed at Day+100, at 6 months, or on the HCT anniversary, choose the date of the visit closest to the actual time point.

If the recipient has not been seen by a clinician during the reporting period but the survival status is known, submit the Post-TED Form reporting only the survival status.

In general, the date of contact should be reported as close to the 100 day, 6 month, or annual anniversary to transplant as possible. Report the date of actual contact with the recipient to evaluate medical status for the reporting period. In the absence of contact with a clinician, other types of contact may include a documented phone call with the recipient, a laboratory evaluation, or any other documented recipient interaction on the date reported. If there was no contact on the exact time point, choose the date of contact closest to the actual time point. Below, the guidelines show an ideal approximate range for reporting each post-transplant time point:
<table>
<thead>
<tr>
<th>Time Point</th>
<th>Approximate Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 days</td>
<td>+/- 15 days (Day 85-115)</td>
</tr>
<tr>
<td>6 months</td>
<td>+/- 30 days (Day 150-210)</td>
</tr>
<tr>
<td>Annual</td>
<td>+/- 30 days (Months 11-13, 23-25, 35-37, etc)</td>
</tr>
</tbody>
</table>

Recipients are not always seen within the approximate ranges and some discretion is required when determining the date of contact to report. In that case, report the date closest to the date of contact within reason. The examples below assume that efforts were undertaken to retrieve outside medical records from the primary care provider, but no documentation was received.

**Example 1. The 100 day date of contact doesn’t fall within the ideal approximate range.**
The autologous recipient was transplanted on 1/1/13 and is seen regularly until 3/1/13. After that, the recipient was referred home and not seen again until 7/1/13 for a restaging exam and 7/5/13 for a meeting to discuss the results.

What to report:
- **100 Day Date of Contact:** 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)
- **6 Month Date of Contact:** 7/5/13 (note the latest disease assessment would likely be reported as 7/1/13)

**Example 2. The 100 day date of contact doesn’t fall within the ideal approximate range and the recipient wasn’t seen again until 1 year post-HCT.**
The autologous recipient was transplanted on 1/1/12 and is seen regularly until 3/1/12. After that, the recipient was referred home and not seen again until 1/1/13 for a restaging exam and 1/4/13 for a meeting to discuss the results.

What to report:
- **100 Day Date of Contact:** 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)
- **6 Month Form:** Indicate the recipient is lost to follow-up in FormsNet3
- **1 Year Date of Contact:** 1/4/13 (note the latest disease assessment would likely be reported as 1/1/13)

**Additional Information**

- A date of contact should never be used multiple times for the same recipient’s forms.
  - For example, 6/1/13 should not be reported for both the 6 month and 1 year form. Instead, determine the best possible date of contact for each reporting period; if there is not a suitable date of contact for a reporting period, this may indicate that the recipient was lost to follow-up.
• If the recipient has a disease evaluation just after the ideal date of contact, capturing that data on the form may be beneficial.
  ◦ For example, if the recipient’s 90 day restaging exam was delayed until day 115 and the physician had contact with the recipient on day 117, the restaging exams can be reported as the latest disease assessment and day 117 would be the ideal date of contact, even though it is just slightly after the ideal approximate range for the date of contact.

**Date of Contact & Death**

In the case of recipient death, the date of death should be reported as the date of contact regardless of the time until the ideal date of contact. The date of death should be reported no matter where the death took place (inpatient at the transplant facility, at an outside hospital, in a hospice setting, or within the recipient’s home).

If the death occurred at an outside location and records of death are not available, the dictated date of death within a physician note may be reported. If the progress notes detailing the circumstances of death are available, request these records. These records are useful for completing required follow-up data fields and the cause of death data fields on this form. If the exact date of death is not known, use the processed described for reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](http://CIBMTR.org).

**Example 3. The recipient has died before their six month anniversary.**

The recipient is transplanted on 1/1/13, was seen regularly through the first 100 days. They had restaging exams on 4/4/13 and was seen on 4/8/13, and then died on 5/13/13 in the hospital emergency room.

What to report:

100 Day Date of Contact: 4/8/13 (note the latest disease assessment would likely be reported as 4/4/13)
6 Month Date of Contact: 5/13/13 (though the death does not occur within the ideal approximate range for 6 months)

**Example 4. The recipient has died after their six month anniversary.**

The recipient is transplanted on 1/1/13, was seen regularly through the first 100 days. They had restaging exams on 4/22/13 and was seen on 4/23/13. Based on findings in the restaging exam, the recipient was admitted for additional treatment. The disease was found to be refractory on a 6/25/13 restaging exam, and the recipient was discharged to hospice on 7/8/13. The hospital was notified via telephone that the recipient died on 7/16/13.

What to report:

100 Day Date of Contact: 4/23/13 (note the latest disease assessment would likely be reported as 4/22/13)
6 Month Date of Contact: 7/16/13 (note the latest disease assessment would likely be reported as 6/25/13)

Date of Contact & Subsequent Transplant
If the recipient has a subsequent HCT, report the date of contact as the day before the preparative regimen begins for the subsequent HCT. If no preparative regimen is given, report the date of contact as the day before the subsequent HCT. In these cases, actual contact on that day is not required, and the day prior to the initiation of the preparative regimen (or infusion, if no preparative regimen) should be reported. This allows every day to be covered by a reporting period, but prevents overlap between transplant events.

Example 5. The recipient had a 2nd transplant with a preparative regimen.
The recipient has their first transplant on 1/1/13 and a planned second transplant on 2/1/13. The recipient was admitted on and received their first dose of chemotherapy for the preparative regimen for HCT #2 on 1/28/13.

What to report:
100 Day Date of Contact: 1/27/13 (regardless of actual contact on that date)

Example 6. The recipient had a subsequent transplant without a preparative regimen.
Following their first transplant on 1/1/13, a recipient with SCID required a subsequent allogeneic transplant due to poor graft function. The recipient has remained inpatient following the first transplant. The physician planned the second transplant for 5/31/13, and proceeded without a preparative regimen.

What to report:
100 Day Date of Contact: 4/11/13 (+/- 15 days)
6 Month Date of Contact: 5/30/13

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 2: Specify the recipient's survival status at the date of last contact:
Indicate the clinical status of the recipient on the date of actual contact for follow-up evaluation. If the recipient is alive continue with question 7. If the recipient has died, continue with question 3.

Question 3: Primary cause of death:
Report the underlying cause of death. Do not report the mode of death, such as cardiopulmonary arrest. According to the Centers for Disease Control and Prevention, National Center for Health Statistics, the underlying cause of death is "the disease or injury that initiated the chain of events that led directly or
inevitably to death.”

Report only one primary cause of death; see the Cause of Death Codes section of the Forms Instructions Manual for more details regarding cause of death. If the recipient has recurrent/persistent/progressive disease at the time of death, consider if the disease was the primary cause of death or a contributing cause of death. It should not be assumed that the presence of disease indicates that the disease was the primary cause of death.

If the primary cause of death is unclear, consult with a physician for their best medical opinion.

**Question 4: Specify**

Specify the details for primary cause of death requiring “other” specification. Options which require additional specification include “Other infection”, “Other pulmonary syndrome”, “Multiple organ failure”, “Other organ failure”, “Other hemorrhage”, “Other vascular”, and “Other cause”. Information reported in the specify field must pertain to the option selected (e.g., an infectious cause of death should be specified for “Other infection”).

**Question 5: Contributing cause of death:**

Report any additional causes of death. All contributing causes of death are important for analysis of transplant outcomes. Refer to the Cause of Death Codes section of the Forms Instructions Manual for more details regarding cause of death.

If there were multiple contributing causes of death, enable an additional instance to report additional causes.

**Question 6: Specify**

Specify the details for contributing cause of death requiring “other” specification. Options which require additional specification include “Other infection”, “Other pulmonary syndrome”, “Multiple organ failure”, “Other organ failure”, “Other hemorrhage”, “Other vascular”, and “Other cause”. Information reported in the specify field must pertain to the option selected (e.g., an infectious cause of death should be specified for “Other infection”).
Q7-13: Subsequent Transplant

Question 7: Did the recipient receive a subsequent HCT since the date of last report?

Indicate whether the recipient received a second (or third, etc.) hematopoietic stem cell infusion. Hematopoietic stem cells are defined as mobilized peripheral blood stem cells, bone marrow, or cord blood. The source of the hematopoietic stem cells may be allogeneic unrelated, allogeneic related, or autologous. For more information on how to distinguish infusion types (example: HCT versus DCI), see Appendix D.

If the recipient has received a subsequent HCT since the date of the last report, ensure the date of actual contact reported in question 1 is the date immediately prior to the start of the preparative regimen for the subsequent HCT. If no preparative regimen was given, report the date prior to infusion.

Question 8: Date of subsequent HCT

Report the planned or actual date of the subsequent HCT infusion. If the planned date is reported and changes, this field will need to be updated to reflect the actual date of subsequent HCT infusion. If multiple days of infusion are planned, report the first.

Question 9: What was the indication for subsequent HCT?

Indicate the reason for the subsequent HCT (check only one).

- **Graft failure / insufficient hematopoietic recovery.** Additional stem cells are required because the hematopoietic recovery indefinitely declined after the initial hematopoietic recovery or hematopoietic recovery was deemed insufficient or too slow for survival following previous high-dose therapy and HCT. If autologous cells are infused for this reason, this is considered autologous rescue; in this case, reporting will continue under the prior HCT date and a new Pre-TED form is not required.
- **Persistent primary disease.** Additional stem cells are required because of the persistent presence of disease pre and post-transplant (i.e., complete remission was never achieved following the previous transplant).
- **Recurrent primary disease.** Additional stem cells are required because of relapsed primary disease (i.e., complete remission was achieved pre or post-transplant, but the disease relapsed following the previous transplant).
- **Planned second HSCT, per protocol.** Additional stem cells are given as defined by the protocol for a subsequent transplant/infusion. This transplant is not based upon recovery, disease status, or any other assessment.
- **New malignancy (including PTLD and EBV lymphoma).** Additional stem cells are required because the recipient has developed a new malignancy. This does not include a transformation or progression of
the original malignancy for which the recipient was transplanted (refer to question 407 for more information). If “new malignancy” is selected, also complete questions 407-449.

- **Insufficient chimerism.** In the case of a stable, mixed donor chimerism, the infusion of additional cells (usually lymphocytes and not mobilized stem cells) is typically classified as a DCI. Verify with the transplant physician that the cells given should be reported as a subsequent transplant and that stable, mixed chimerism is the reason for the transplant. However, in the case of declining chimerism – when the percentage of donor cells is sequentially decreasing on several studies, indicating possible impending graft failure – additional stem cells are required. Usually the donor chimerism has fallen below 30-50%.

- **Other.** If additional stem cells are given for a reason other than the options listed, select “other” and complete question 10.

**Question 10: Specify other indication**

Specify the indication for subsequent HCT.

**Question 11: Source of HSCs**

Report the stem cell source of the recipient’s subsequent HCT. Allogeneic sources and autologous sources with indication other than “graft failure / insufficient hematopoietic recovery” will require another Pre-TED form to be completed for the subsequent HCT.

**Question 12: Has the recipient received a cellular therapy since the date of last report? (e.g. DCI)**

**Therapy Over Multiple Reporting Periods**

If course of cellular therapy carries over an HCT reporting period, and has already been reported on a prior form, do not re-report that course of cellular therapy. For example, if a course of cellular therapy includes three infusions, and the third infusion overlaps from the one year to two year HCT reporting period, do not report a cellular therapy since the date of the last report on the two year HCT follow up form.

Indicate whether the recipient received a cellular therapy for any reason within the reporting period. The most common type of post-HCT cellular therapy would be a donor cellular infusion (DCI) or donor lymphocyte infusion (DLI). These infusions are not intended to promote hematopoiesis. If the recipient received additional cells due to engraftment issues, or if they received an infusion of unmanipulated CD34+ cellular product (stimulated peripheral blood stem cells, bone marrow, or cord blood), report as a subsequent HCT rather than a cellular therapy. For more information on how to distinguish infusion types (example: HCT versus DCI), see “Appendix D.”

A DCI is a form of cellular therapy that uses cells from the original donor, and is commonly used to create a
graft-versus-leukemia / tumor (GVL / GVT) effect. The recipient does not receive a preparative regimen prior to receiving the donor cells because the purpose of a DCI is to activate the immune system rather than repopulate the marrow. The recipient may, however, be given therapy prior to the infusion for the purpose of disease control. The types of cells used in a DCI include, but are not limited to: lymphocytes, unstimulated peripheral blood mononuclear cells, dendritic cells, and / or mesenchymal cells.

Other forms of cellular therapy may include cytotoxic T-lymphocytes (CTLC) to treat infections or chimeric antigen receptor T-cells (CAR T-cells) to treat persistent, progressive or recurrent disease.

**Question 13: Date of cellular therapy**

Report the date of cellular therapy infusion. If multiple infusions were received in the reporting period, report the earliest. If infusions are continuing from a previous instance of DCI, only report in the period during which the first infusion was received.
ANC recovery is defined as an absolute neutrophil count (ANC) of $\geq 0.5 \times 10^9/L$ (500/mm$^3$) for three consecutive laboratory values obtained on different days. Date of ANC recovery is the date of the first of three consecutive laboratory values where the ANC is $\geq 0.5 \times 10^9/L$. At some institutions, the laboratory reports display the ANC value once there are sufficient white blood cells to perform a differential count. At other institutions, the laboratory reports do not display the ANC, and it must be calculated from the white blood cell count (WBC) and the percent of segmented and band neutrophils (if the differential was performed on a machine, the percent neutrophils will include both segmented and band neutrophils). If the laboratory report displays an automated ANC value of exactly 0.5, the actual ANC value should be calculated from the manual differential if available. The calculated value from the manual differential will determine ANC recovery. If your institution’s laboratory reports do not display the ANC value, use the following calculation to determine the ANC:

**Calculating Absolute Neutrophil Count (ANC)$^1$**
Traditionally, the definition of ANC recovery required selecting the first date of three consecutive days in which the recipient’s ANC was \( \geq 0.5 \times 10^9/L \) (500/mm\(^3\)). For various reasons it may not be possible to obtain daily laboratory values. Under those circumstances, report ANC recovery based upon three consecutive laboratory values (drawn more than a day apart) as long as the ANC remains \( \geq 0.5 \times 10^9/L \) (500/mm\(^3\)).

Tracking the date of ANC recovery may not always be straightforward. In some cases the ANC may fluctuate for a period of time before the recipient fully recovers. In other cases the ANC may remain above \( 0.5 \times 10^9/L \) for several days immediately post-HCT and then fall below \( 0.5 \times 10^9/L \). Do not begin counting ANC values of \( \geq 0.5 \times 10^9/L \) towards recovery until the ANC has dropped to the lowest level (nadir) post-HCT. If the recipient was transplanted using a non-myeloablative (NST) or reduced intensity (RIC) regimen, or was transplanted for an immunodeficiency (e.g., SCID, WAS), the recipient’s ANC may never drop below \( 0.5 \times 10^9/L \). If this is the case, an ANC recovery date will not be reported, and the “never below” option should be chosen. However, if the recipient’s ANC drops below \( 0.5 \times 10^9/L \) for even one day, this should be considered the nadir and “never below” should not be chosen. See the following example for more information regarding tracking the date of ANC recovery.

**Tracking ANC Recovery**

**Transplant Date = May 6**

<table>
<thead>
<tr>
<th>Date</th>
<th>WBC</th>
<th>%Neutrophils</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 7</td>
<td>900</td>
<td>0.6</td>
<td>540</td>
</tr>
<tr>
<td>May 8</td>
<td>850</td>
<td>0.59</td>
<td>502</td>
</tr>
<tr>
<td>May 9</td>
<td>720</td>
<td>0.7</td>
<td>504</td>
</tr>
<tr>
<td>Date</td>
<td>ANC</td>
<td>Differential</td>
<td>Date of first recovery: ANC ≥ 0.5×10^9/L</td>
</tr>
<tr>
<td>----------</td>
<td>------</td>
<td>--------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>May 10</td>
<td>300</td>
<td>0.45</td>
<td>135</td>
</tr>
<tr>
<td>May 11</td>
<td>15</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 12</td>
<td>30</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 13</td>
<td>50</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 14</td>
<td>250</td>
<td>0.4</td>
<td>100</td>
</tr>
<tr>
<td>May 15</td>
<td>800</td>
<td>0.7</td>
<td>560</td>
</tr>
<tr>
<td>May 16</td>
<td>1050</td>
<td>0.8</td>
<td>840</td>
</tr>
<tr>
<td>May 17</td>
<td>1000</td>
<td>0.7</td>
<td>700</td>
</tr>
<tr>
<td>May 18</td>
<td>1800</td>
<td>0.6</td>
<td>1080</td>
</tr>
<tr>
<td>May 19</td>
<td>2000</td>
<td>0.55</td>
<td>1100</td>
</tr>
<tr>
<td>May 20</td>
<td>2500</td>
<td>0.53</td>
<td>1325</td>
</tr>
<tr>
<td>May 21</td>
<td>2250</td>
<td>0.43</td>
<td>968</td>
</tr>
<tr>
<td>May 22</td>
<td>1500</td>
<td>0.45</td>
<td>675</td>
</tr>
</tbody>
</table>

**Question 14: Was there evidence of initial hematopoietic recovery?**

Indicate whether or not there was evidence of initial ANC recovery following this HCT.

Check only one response:

- If “yes, ANC ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L) achieved and sustained for 3 laboratory values,” continue with question 15.
- If “no, ANC ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L) was not achieved,” continue with question 16.
- Check “not applicable” if the recipient’s ANC never dropped below 0.5 × 10^9/L at any time post-HCT.
  This option is only applicable in the 100-day reporting period. Continue with question 16.
- Check “previously reported” if this is the 6 month or annual follow-up, and the initial ANC recovery has already been reported. Continue with question 16.

**Question 15: Date ANC ≥ 500/mm^3 (first of 3 labvalues):**

Enter the first date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L). For an example of tracking ANC recovery, see the Tracking ANC Recovery example above.

For more information regarding reporting partial or unknown dates, see General Instructions, General
Guidelines for Completing Forms.

Question 16: Did late graft failure occur?

Late (or secondary) graft failure is defined when the recipient meets criteria for initial engraftment but subsequently develops loss of a previously functioning graft by development of at least two lines of cytopenia. Late graft failure is more often associated with allogeneic HCT than with autologous HCT. Some possible causes for late graft failure include graft rejection related to residual host immunity, persistent or progressive disease, low donor cell yield, medication side-effect, infection or GvHD.²

If the recipient meets the criteria of graft failure, check “yes.”

Q17-18: Initial Platelet Recovery

Optional for Non-U.S. Centers

The following questions refer to initial platelet recovery following the HCT for which this form is being completed. All dates should reflect no platelet transfusions administered for seven consecutive days. Report the date of the first of three consecutive laboratory values ≥ 20 × 10^9/L obtained on different days, as shown in the Reporting Platelet Recovery example below. Note that platelet recovery may take place well after the recipient has returned to the referring physician for care. It is essential that information and laboratory values be obtained from the referring physician.

Transfusions temporarily increase blood cell counts. When the data is later used for analysis, it is important to be able to distinguish between a recipient whose own body was creating the cells and a recipient who required transfusions to support the counts.

The following example illustrates the procedure to follow for reporting platelet recovery.

Reporting Platelet Recovery

<table>
<thead>
<tr>
<th>Transfusion</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet Count</td>
<td>10,000</td>
<td>35,000</td>
<td>30,000</td>
<td>25,000</td>
<td>10,000</td>
<td>15,000</td>
<td>19,000</td>
<td>23,000</td>
<td>25,000</td>
<td>40,000</td>
<td>50,000</td>
</tr>
</tbody>
</table>

Report 1/8/08 as date platelet count ≥ 20 × 10^9/L
Question 17: Was an initial platelet count \( \geq 20 \times 10^9 / L \) achieved?

Indicate whether or not there was evidence of initial platelet recovery following this HCT.

Check only one response:

- If “yes,” continue with question 18.
- If “no,” continue with question 19.
- Check “not applicable,” if the recipient’s platelets never dropped below \( 20 \times 10^9 / L \) at any time post-HCT and a platelet transfusion was never required. If the recipient’s platelet count drops below \( 20 \times 10^9 / L \) and/or the recipient received a platelet transfusion even once, do not use this option. This option is only applicable in the 100-day reporting period. Continue with question 19.
- Check “previously reported” if this is the six-month or annual follow-up, and initial platelet recovery has already been reported on a previous form. Continue with question 19.

Question 18: Date platelet \( \geq 20 \times 10^9 / L \)

Enter the first date of three consecutive laboratory values obtained on different days where the platelet count was \( \geq 20 \times 10^9 / L \). Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in the Reporting Platelet Recovery example above, when determining the recovery date.

If three laboratory values were not obtained on consecutive days, but a sequential rise of \( \geq 20 \times 10^9 / L \) is demonstrated, follow the examples below when determining an estimated date.

Reporting Scenarios:

A. The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is \( 22 \times 10^9 / L \) on January 2, \( 24 \times 10^9 / L \) on January 3, and \( 28 \times 10^9 / L \) on January 4. The recipient does not come into the clinic for evaluation until one month later. The recipient has not received any more platelet transfusions and the platelet count is well above \( 20 \times 10^9 / L \). Report January 8 (day seven post-platelet transfusion) for the date of platelet recovery.

B. The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is \( \geq 20 \times 10^9 / L \) on January 2, January 3, and January 4. The recipient is then discharged back to their primary care physician. The transplant center receives a follow-up note from the primary care physician that states “recipient recovered their platelets in January of 2011.” Report an estimated date of recovery using the guidelines available in General Instructions.
Completing Forms.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.
Graft versus Host Disease (GVHD) is an immunological phenomenon resulting from the reaction of donor immune cells against major or minor histocompatibility antigens of the recipient. GVHD is primarily caused by donor-derived T-cells. Very rarely, GVHD may occur due to autologous reactivity (autologous GVHD), third party transfusions, or with identical twin transplantation.

Factors influencing the severity of GVHD are related to three main categories: 1) donor or graft, 2) recipient, and 3) treatment. The most influential donor/graft factor is the degree of genetic disparity between the donor and the recipient (HLA match), but other risk factors include female donor to male recipient, donor parity, older donors, and T-cell dose. The occurrence of acute GVHD becomes a risk factor for the development of chronic GVHD. Recipient age and prior infections are also factors.

In the past, GVHD was classified as acute or chronic based on its time to diagnosis following transplant, and other clinical and histological (biopsy or post-mortem) features. Today, there has been increased recognition that acute and chronic GVHD are not dependent upon time since HCT, so determination of acute or chronic should rest on clinical and histologic features. However, organ staging and overall grade should only be calculated from the clinical picture, not histology. Acute GVHD usually begins between 10 and 40 days after HCT but can appear earlier or later. The organs most commonly affected by acute GVHD are the skin, gut, or liver. Other sites, such as the lung, may be involved.

**Acute / Chronic GVHD**

If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 19-30). Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section.

Report any new or persistent acute GVHD symptoms occurring on or after the onset of chronic GVHD only in the chronic GVHD section. If chronic GVHD was diagnosed in a prior reporting period, report “no” for questions 19 and 21 in each subsequent reporting period.
Question 19: Did acute GVHD develop since the date of last report?

Questions 19 and 21 on the Post-TED Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 19 or question 21 must be answered “yes” unless there has been a prior / concurrent diagnosis of chronic GVHD (see note above question 19). There will not be a situation where “yes” is reported for both question 19 and question 21. If question 19 is answered yes and a diagnosis date has been reported in question 20, question 21 will be disabled in FormsNet3SM. Centers should report “yes” for question 19 to indicate the recipient developed acute GVHD in the following scenarios:

- Acute GVHD is diagnosed for the first time during the reporting period.
- An acute GVHD flare is diagnosed during the current reporting period and all of the following conditions are met:
  - The recipient’s prior acute GVHD symptoms did not persist from the prior reporting period into the beginning of the current reporting period.
  - The flare is diagnosed after at least 30 days without any active acute GVHD symptoms.
  - The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 19).

If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report “no” for question 19 and “yes” for question 21. Question 21 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer questions 19 and 21.

Report “no” for questions 19 and 21 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 19).

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

Acute GVHD Diagnosis Scenarios:
A. A recipient receives a HCT on 1/1/2015 and develops acute GVHD which is clinically diagnosed on 2/1/2015. At least one of their symptoms, attributed to acute GVHD, persists beyond the 100 day date of contact which is 4/5/2015. Treatment continues and symptoms completely resolve on 5/1/2015. Immunosuppression is tapered until a flare of acute GVHD is diagnosed on 5/25/2015. Immunosuppression is given and symptoms quickly resolve with no active acute GVHD beginning 6/10/2015. The six month date of contact is 6/20/2015. Another flare of acute GVHD is clinically diagnosed on 8/15/2015.

100 Day Post-TED Form:

Question 19: Report “yes” to indicate a new clinical diagnosis of acute GVHD.
Question 20: Report the initial date of diagnosis (2/1/2015).
Question 21: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 20.
Questions 22-28: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

Six Month Post-TED Form:

Question 19: Report “no” to indicate acute GVHD persists from a previous report. Notes, the flare of acute GVHD was < 30 days from symptoms resolution so it doesn’t count as a new reportable episode.
Question 20: Leave blank. This question will be skipped whenever question 19 is answered “no.”
Question 21: Report “yes” to indicate GVHD persists from a previous report.
Questions 22-28: Leave blank. Answering “yes” for question 21 prevents the center from re-reporting diagnosis information already captured on the 100 day form.

One Year Post-Infusion Data Form:

Question 19: Report “yes” to indicate a flare of acute GVHD occurred at least 30 days after resolving during a prior reporting period.
Question 20: Report the diagnosis date of the flare occurring during the reporting period (8/15/2015).
Question 21: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 20.
Questions 22-28: Answer these questions based on the assessments performed at the time of diagnosis of the flare of acute GVHD (8/15/2015).

B. A recipient receives a HCT on 1/1/2015 and develops acute skin GVHD on 2/1/2015 and then chronic eye GVHD on 3/1/2015. Both acute and chronic symptoms resolve by the 100 day date of contact (4/5/2015). While tapering their immunosuppression, the recipient has a flare of their acute skin GVHD on 5/30/2015. Treatment continues and symptoms completely resolve by the six month date of contact (6/20/
100 Day Post-Infusion Data Form:

Question 19: Report “yes” to indicate a new clinical diagnosis of acute GVHD.
Question 20: Report the initial date of diagnosis (2/1/2015).
Question 21: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 20.
Questions 22-28: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).
Questions 29-30: Answer these questions based on any symptoms and treatment documented from the onset of acute GVHD (2/1/2015) up to the diagnosis of chronic GVHD (3/1/2015). This instruction is provided in the note box above question 19.

Six Month Post-Infusion Data Form:

Question 19: Report “no” to indicate acute GVHD did not develop during the reporting period.
Question 20: Leave blank. This question will be skipped whenever question 19 is answered “no.”
Question 21: Report “no” to indicate acute GVHD did not persist from a previous report.

*If chronic GVHD has been diagnosed in a prior reporting period, report “no” for questions 19 and 21. Any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD must be reported in the chronic GVHD section of the form. Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section. This instruction has been provided in the note above question 19.*

**Question 20: Date of acute GVHD diagnosis**

Report the date of clinical diagnosis of acute GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed a rash one week prior to the physician clinically diagnosing acute skin GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of acute GVHD in the same reporting period, report the date of onset of the first episode of acute GVHD.

For more information regarding reporting partial or unknown dates, see General Instructions, *General Guidelines for Completing Forms.*
**Question 21: Did acute GVHD persist since the date of last report?**

Question 21 will only be enabled in FormsNet3SM if the center has reported “no” for question 19 and, therefore, has not reported a date of diagnosis in question 20. If prompted to answer question 21, report “yes” if acute GVHD was diagnosed in a prior reporting period and any of the following conditions are met:

- The recipient’s acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).
- The recipient’s acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred within 30 days of symptom resolution / quiescence.
- The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 19).

Report “no” for questions 19 and 21 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 19).

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

**Question 22: Overall grade of acute GVHD at diagnosis**

Indicate the overall grade of acute GVHD at the time of diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic). The acute GVHD grading scale is based on clinical evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on clinical severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, overall grading remains clinical and is based on the criteria published by Przepiorka et al., Bone Marrow Transplant 1995; 15(6):825-8, see the GVHD Grading and Staging table below.

If acute GVHD was present, but the grade at diagnosis was not documented and it cannot be determined from the grading and staging table, report “not applicable.”

Examples may include:

- Only elevated liver function tests without increased bilirubin
- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
• Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description below)

Upper GI GVHD
If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

GVHD Grading and Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Skin</th>
<th>Liver</th>
<th>Gut</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rash on &lt;25% of skin</td>
<td>Bilirubin 2-3 mg/dl</td>
<td>Diarrhea &gt; 500 ml/day or persistent nausea</td>
</tr>
<tr>
<td>2</td>
<td>Rash on 25-50% of skin</td>
<td>Bilirubin 3-6 mg/dl</td>
<td>Diarrhea &gt;1000 ml/day</td>
</tr>
<tr>
<td>3</td>
<td>Rash on &gt;50% of skin</td>
<td>Bilirubin 6-15 mg/dl</td>
<td>Diarrhea &gt;1500 ml/day</td>
</tr>
<tr>
<td>4</td>
<td>Generalized erythroderma with bullous formation</td>
<td>Bilirubin &gt;15 mg/dl</td>
<td>Severe abdominal pain, with or without ileus, and or grossly bloody stool</td>
</tr>
</tbody>
</table>

Grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>Stage 1-2</th>
<th>Stage 1</th>
<th>Stage 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>II</td>
<td>Stage 3</td>
<td>Stage 1</td>
<td>Stage 1</td>
</tr>
<tr>
<td>III</td>
<td>—</td>
<td>Stage 2-3</td>
<td>Stages 2-4</td>
</tr>
<tr>
<td>IV</td>
<td>Stage 4</td>
<td>Stage 4</td>
<td>—</td>
</tr>
</tbody>
</table>

1 Use “Rule of Nines” (Percent Body Surfaces table) or burn chart to determine extent of rash.

2 Range given as total bilirubin. Downgrade one stage if an additional cause of elevated bilirubin has been documented.

3 Volume of diarrhea applies to adults. For pediatric patients, the volume of diarrhea should be based on body surface area. Downgrade one stage if an additional cause of diarrhea has been documented.

4 Persistent nausea with or without histologic evidence of GVHD in the stomach or duodenum.

5 Criteria for grading given as minimum degree of organ involvement required to confer that grade.
Questions 23-28: List the stage for each organ at diagnosis of acute GVHD.

Report the stage of each organ at diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic).

**Skin:** Select the stage that reflects the body surface area involved with a maculopapular rash attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. See the Percent Body Surfaces table below to determine the percent of body surface area involved with a rash. Do not report ongoing rash not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

### Percent Body Surfaces

<table>
<thead>
<tr>
<th>Body Area</th>
<th>Percent</th>
<th>Total Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each Arm</td>
<td>9%</td>
<td>18%</td>
</tr>
<tr>
<td>Each Leg</td>
<td>18%</td>
<td>36%</td>
</tr>
<tr>
<td>Chest &amp; Abdomen</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Back</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Head</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Pubis</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Lower intestinal tract (use mL/day for adult recipients and mL/m^2/day for pediatric recipients):**

Select the stage that reflects the volume of diarrhea attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Use mL/day for adult recipients and mL/m^2/day for pediatric recipients. Input and output records may be useful in determining the volume of diarrhea. Do not report diarrhea ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, report “stage 0” for lower intestinal tract involvement. In this case, report “Not Applicable” for the overall grade unless stage 4 acute skin GVHD, stage 2-4 acute liver GVHD, or an extreme decrease in performance status was also documented at the time point being reported (at diagnosis or maximum grade during the reporting period). Report an overall grade of IV if stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status is documented at the time point being reported (see GVHD Staging and Grading Table). Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.
Upper intestinal tract: Select the stage that reflects the presence of persistent nausea or vomiting attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report nausea or vomiting ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

Liver: Select the stage that reflects the bilirubin level attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report hyperbilirubinemia ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

For recipients who have a normal bilirubin level with elevated transaminase levels attributed to acute GVHD, report this in “Other clinical organ involvement.”

Other site(s) involved with acute GVHD: Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 28. If reporting transaminitis under “other site,” write in “transaminitis” rather than “liver” when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under “other site.”

Question 29: Maximum Overall Grade of Acute GVHD

Indicate the overall maximum grade of acute GVHD since the date of the last report. Grading is based on clinical evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on clinical severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, overall grading remains clinical and is based on the criteria published by Przepiorka et al., Bone Marrow Transplant 1995; 15(6):825-8; see the GVHD Grading and Staging table above.

If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. See question 19 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.

Report the recipient’s maximum acute GVHD grade in the reporting period; this may differ from the grade at diagnosis or may be the same. If acute GVHD was present, but the maximum grade was not documented and it cannot be determined from the grading and staging table, report “not applicable.”

Examples may include:
• Only elevated liver function tests without increased bilirubin
• Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
• Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description above)

**Upper GI GVHD**
If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

**Acute GVHD Grading Scenarios:**

**A.** A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging / grading can be determined using the GVHD Grading and Staging table above.

**B.** A recipient developed acute liver GVHD with elevated LFTs (i.e., transaminases) with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in the GVHD Grading and Staging table above; “not applicable” would be the best option to report.

**C.** A recipient developed stage 2 skin involvement, which showed improvement in response to topical steroids. However, the recipient then developed hyperbilirubinemia attributed to stage 1 liver involvement; the skin involvement at that time was stage 1. In this case, grade II would be reported (assuming this was the extent of the recipient’s acute GVHD in the reporting period).

**D.** A recipient developed stage 2 skin involvement which resolved in response to topical steroids. Later in the reporting period, the recipient was diagnosed with mild chronic eye GVHD. Shortly thereafter, they were diagnosed with a stage 3 flare of acute skin GVHD. In this case, grade I would be reported. Do not consider any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD when completing the acute GVHD section of the form.

**Question 30: Date maximum overall grade of acute GVHD**

Report the date of maximum acute GVHD involvement, based on clinical grade. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date. If “not applicable” was reported for question 29, question 30 must be left blank.
Question 31: Did chronic GVHD develop since the date of last report?

Indicate whether a new clinical diagnosis of chronic GVHD was documented during the reporting period. If chronic GVHD was diagnosed during the reporting period, report “yes” and continue with question 32.

If the recipient had a flare of chronic GVHD occurring after at least a 30 day period of symptom quiescence, report “yes” and continue with question 32. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent chronic GVHD which is captured in question 33.

Report “no” if chronic GVHD was not clinically diagnosed – initially or as a flare – in the reporting period; this includes instances where chronic GVHD persists from a prior reporting period.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

Question 32: Date of chronic GVHD diagnosis:

Report the date of clinical diagnosis of chronic GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed shortness of breath one month prior to the clinical diagnosis of pulmonary chronic GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of chronic GVHD in the same reporting period, report the date of onset of the first episode of chronic GVHD.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 33: Did chronic GVHD persist since the date of last report?

Indicate whether chronic GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive chronic GVHD, or a prior history of GVHD. If “yes,” continue with question 34; questions concerning chronic GVHD at the time of diagnosis will be skipped. See question 31 for instructions on reporting a chronic GVHD flare.

If the recipient has no active symptoms during the reporting period, report “no” continue with question 37.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of
GVHD in the reporting period.

**Question 34: Maximum grade of Chronic GVHD (according to best clinical judgement)**

Report the maximum chronic GVHD involvement, based on clinical grade, since the date of the last report. The intent of this question is to capture the maximum grade based on the best clinical judgment. If the maximum clinical grade is not documented, request documentation from the recipient’s primary care provider.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period. Please note, questions 35 and 36 must still be answered if question 34 is reported as “unknown.”

**Organ Scoring of Chronic GVHD**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skin % BSA</strong></td>
<td>No BSA involved</td>
<td>1-18% BSA</td>
<td>19-50% BSA</td>
<td>&gt;50% BSA</td>
</tr>
<tr>
<td>Skin Features</td>
<td>No sclerotic features</td>
<td>N/A</td>
<td>Superficial sclerotic features, but not “hidebound”</td>
<td>Deep sclerotic features; “hidebound;” impaired mobility; ulceration</td>
</tr>
<tr>
<td>Mouth</td>
<td>No symptoms</td>
<td>Mild symptoms with disease signs but not limiting oral intake significantly</td>
<td>Moderate symptoms with disease signs with partial limitation of oral intake</td>
<td>Severe symptoms with disease signs with major limitation of oral intake</td>
</tr>
<tr>
<td>Eyes</td>
<td>No symptoms</td>
<td>Mild dry eye symptoms not affecting ADL (requirement of lubricant drops ≤ 3x/day)</td>
<td>Moderate dry eye symptoms partially affecting ADL (requiring lubricant drops &gt; 3x/day or punctal plugs) <strong>WITHOUT</strong> new vision impairment due to keratoconjunctivitis sicca (KCS)</td>
<td>Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) <strong>OR</strong> unable to work because of ocular symptoms <strong>OR</strong> loss of vision due to keratoconjunctivitis sicca (KCS)</td>
</tr>
<tr>
<td>GI Tract</td>
<td>No symptoms</td>
<td>Symptoms without significant weight loss (&lt; 5%)</td>
<td>Symptoms associated with mild to moderate weight loss (5-15%) within 3 months <strong>OR</strong> moderate diarrhea without significant interference with daily living</td>
<td>Symptoms associated with significant weight loss (&gt; 15%) within 3 months, requires nutritional supplement for most calorie needs <strong>OR</strong> esophageal dilation <strong>OR</strong> severe diarrhea with significant interference with daily living.</td>
</tr>
</tbody>
</table>
### Liver

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal total bilirubin and ALT or AP &lt; 3 x ULN</td>
<td>Normal total bilirubin with ALT ≥ 3 to 5 x ULN or AP ≥ 3 x ULN</td>
</tr>
</tbody>
</table>

### Lungs

#### Symptom Score:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>Mild symptoms (SOB after climbing one flight of steps)</td>
</tr>
</tbody>
</table>

#### Lung Score:

<table>
<thead>
<tr>
<th>FEV1</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 80%</td>
<td>FEV1 60-79%</td>
</tr>
</tbody>
</table>

### Joints and Fascia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>Mild tightness of arms or legs, normal or mild decreased range of motion AND not affecting ADL</td>
</tr>
</tbody>
</table>

### Genital Tract

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>No signs</td>
<td>Mild signs and females with or without discomfort on exam</td>
</tr>
</tbody>
</table>

### Other Features

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>No GVHD</td>
<td>Mild</td>
</tr>
</tbody>
</table>

---

**NIH Consensus Criteria, 2014**

1. Features to be scored by BSA: Maculopapular rash, lichen planus-like features, sclerotic features, papulosquamous lesions or ichthyosis, keratosis pilaris-like GVHD.

2. Scoring is based on severity of the signs instead of symptoms, based on limited available data and the opinions of experts. Female or male genital GVHD is not scored if a practitioner is unable to examine the patient.

3. May include ascites, pericardial effusion, pleural effusion(s), nephrotic syndrome, myasthenia gravis, peripheral neuropathy, polymyositis, weight loss without GI symptoms, eosinophilia > 500/μL, platelets < 100,000/μL, others.

**Question 35: Specify if chronic GVHD was limited or extensive:**

The grading system for chronic GVHD is divided into two categories: limited and extensive. Definitions are

Report “limited” if chronic GVHD includes only localized skin involvement and/or liver dysfunction. Report “extensive” if any of the following symptoms are attributed to chronic GVHD:

- Generalized skin involvement and/or liver dysfunction
- Liver histology showing chronic aggressive hepatitis, bridging necrosis, or cirrhosis
- Involvement of the eye: Schirmer’s test with <5 mm wetting, or
- Involvement of the salivary glands or oral mucosa, or
- Involvement of any other target organ

**Question 36: Date of maximum grade of chronic GVHD**

Report the date of maximum chronic GVHD involvement, based on clinical grade, during the current reporting period. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 37: Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, ≤10 mg/day for adults, <0.1 mg/kg/day for children)**

**Steroids and Non-Steroid Immunosuppression for GVHD**

Questions 37 and 38 will only be completed if the center has reported “Yes” for question 19, 21, 31, or 33. If each of these questions has been answered “No,” questions 37 and 38 will be left blank.

**Corticosteroids**

Corticosteroids are captured differently depending on whether they are used topically or systemically. Use the following guidelines when determining how to report corticosteroids used to treat acute GVHD:

- **Topical Creams for Skin:** Do not report topical ointments or creams used to treat skin GVHD including corticosteroid creams such as Triamcinolone or Hydrocortisone.
- **Other Topical Treatments:** Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. Do not consider these medications when answering question 37.
- **Systemic Treatments:** Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in question 37.
Indicate whether the recipient is still taking systemic steroids to treat or prevent GVHD on the date of contact. Refer to the guidelines included in the question text if the recipient is taking low dose steroids or steroids for adrenal insufficiency.

Indicate “not applicable” in any of the following scenarios:

- The recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD.
- This form is being completed for a subsequent HCT and the recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen is given).
- The recipient stopped taking systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD in a previous reporting period and did not restart systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) during the current reporting period.

Indicate “unknown” if there is no information to determine if the recipient is still taking systemic steroids. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD on the date of contact.

If the recipient has died prior to the discontinuation of systemic steroids used to treat or prevent acute and / or chronic GVHD, select “yes.”

**Question 38: Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for GVHD?**

Indicate whether the recipient is still taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent acute and / or chronic GVHD on the date of contact. Descriptions of many immunosuppressive agents are included below.

If the recipient did not receive non-steroidal immunosuppressive agents to treat or prevent acute and / or chronic GVHD during the reporting period, report “not applicable.”
Indicate “not applicable” in any of the following scenarios:

- The recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD.
- This form is being completed for a subsequent HCT and the recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen was given).
- The recipient stopped taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD in a previous reporting period and did not restart non-steroidal immunosuppressive agents (including PUVA) during the current reporting period.

Indicate “unknown” if there is no information to determine if the recipient is still taking non-steroidal immunosuppressive agents. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD in the reporting period.

**Immunosuppressive Agents:**

- **Aldesleukin (Proleukin):** Increases production of several white blood cells including regulatory T-cells. This drug is also known as interleukin-2.

- **ALG (Anti-Lymphocyte Globulin), ALS (Anti-Lymphocyte Serum), ATG (Anti-Thymocyte Globulin), ATS (Anti-Thymocyte Serum):** Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes. Also report the animal source. If “other” is selected, specify the source.

- **Azathioprine (Imuran):** Azathioprine inhibits purine synthesis. Usually it is used at low doses in combination with other treatments.

- **Bortezomib (Velcade):** A proteasome inhibitor.

- **Cyclosporine (CSA, Neoral, Sandimmune):** Calcineurin inhibitor which decreases cytokine production by T-cells. Usually given for ≥ 3 months.

- **Cyclophosphamide (Cytoxan):** Given in high doses near the date of infusion as single agent prophylaxis.

- **Extra-corporeal photopheresis (ECP):** The recipient’s blood is removed from the body, exposes to
psoralen and ultraviolet light, and re-infused.
FK 506 (Tacrolimus, Prograf): Inhibits the production of interleukin-2 by T-cells.

**Hydroxychloroquine (Plaquenil):** Hydroxychloroquine inhibits transcription of DNA to RNA and is commonly used as an anti-malarial drug.

**Interleukin Inhibitor:** Interleukin inhibitors suppress production of white blood cells and are grouped according to their target. Examples of IL-2 inhibitors include daclizumab (Zynbryta) and basiliximab (Simulect). Examples of IL-6 inhibitors include tocilizumab (Actemra) and siltuximab (Sylvant).

**In vivo monoclonal antibody:** Antibody preparations that are infused in the recipient following HSCT. Specify the antibody used as: anti CD25 (Zenapax, Daclizumab, AntiTAC), alemtuzumab (Campath), entanercept (Enbrel), infliximab (Remicade), and / or rituximab (Rituxan).

**In vivo immunotoxin:** Antibody preparations linked to a toxin that is infused in the recipient following HCT. Specify the immunotoxin.

**Janus Kinase 2 Inhibitors:** Suppress function of T-effector cells. Examples: ruxoloitinib (Jakafi, Jakavi) and tofacitinib (Xeljanz, Jakvinus).

**Methotrexate (MTX) (Amethopterin):** Inhibits the metabolism of folic acid. It is most often used with cyclosporine and is usually for a short duration of time.

**Mycophenolate mofetil (MMF) (CellCept, Myfortic):** Inhibits the de novo pathway used for lymphocyte proliferation and activation.

**Pentostatin (Nipent):** Inhibits adenosine deaminase, which blocks DNA (and some RNA) synthesis.

**Sirolimus (Rapamycin, Rapamune):** Inhibits the response to interleukin-2, blocking the activation of T-cells.

**Tyrosine Kinase Inhibitor (TKI):** Suppress function of tyrosine kinases thereby downregulating the function of many other cellular proteins / processes including fibrosis and inflammation. Examples: imatinib (Gleevec, Glivec), nilotinib (Tasigna), and dasatinib (Sprycel).

**UV Therapy:** UVA or UVB radiation administered to affected areas of the skin in order to suppress proliferation of cells responsible for GVHD.

**PUVA (Psoralen and UVA):** Psoralen is applied or taken orally to sensitize the skin, and then the skin is exposed to UVA radiation.
UVB: Broadband- or Narrowband-UVB radiation is applied to the affected areas of the skin.
Q39-45: Liver Toxicity Prophylaxis

Question 39: Was specific therapy used to prevent liver toxicity?

Liver toxicities in transplant patients may be related to drugs / treatments, infection, GVHD, iron overload, cirrhosis, or sinusoidal obstructive syndrome (SOS) / veno-occlusive disease (VOD). Agents such as ursodiol may be given as prophylaxis against one or more of these transplant-related liver injuries. Agents given to prevent liver toxicity will generally be started prior to or during the conditioning regimen, and may be continued well after transplant.

Indicate whether the recipient received any therapy intended to prevent liver toxicity during the reporting period, including therapy given during the conditioning regimen. Report only agents given to prevent liver toxicities, not those given to treat a diagnosed liver injury or toxicity. If liver toxicity prophylaxis was given, report “yes” and go to question 40. If liver toxicity prophylaxis was not given during the reporting period, report “no” and go to question 46.

Questions 40-45: Specify therapy (Defibrotide, N-acetylcysteine, tissue plasminogen activator (TPA), Ursodiol, Other)

Report all agents given during the reporting period to prevent liver toxicity, including therapy given during the conditioning regimen. Only report agents given to prevent liver toxicities, not those given to treat a diagnosed liver injury or toxicity. If “other” therapy is reported in question 44, specify agent(s) in question 45.
**Q46-47: Veno-occlusive disease (VOD) / Sinusoidal obstruction syndrome (SOS)**

Veno-occlusive disease (VOD) / Sinusoidal obstruction syndrome (SOS) occurs following injury to the hepatic venous endothelium, resulting in hepatic venous outflow obstruction due to occlusion of the hepatic venules and sinusoids. This typically results in a distinctive triad of clinical signs including hepatomegaly with right upper quadrant tenderness, third space fluid retention (e.g., ascites), and jaundice with a cholestatic picture. For more information on VOD / SOS including diagnostic criteria, refer to the **VOD / SOS section** of the Forms Instructions Manual.

**Question 46-47: Did veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS) develop since the date of last report?**

Indicate whether VOD / SOS was diagnosed during the reporting period. If “yes,” report the date of diagnosis in question 47. If VOD / SOS persisted from the prior reporting period, indicate “no” and go to question 47.

For more information regarding reporting partial or unknown dates, see General Instructions, **General Guidelines for Completing Forms**.
Q48-55: New Malignancy, Lymphoproliferative or Myeloproliferative Disorder

Question 48: Did a new malignancy, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the HCT or cellular therapy was performed? (include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders)

Indicate whether a new or secondary malignancy, lymphoproliferative disorder, or myeloproliferative disorder has developed. Do not report recurrence, progression, or transformation of the recipient's primary disease (disease for which the transplant was performed), or relapse of a prior malignancy.

New malignancies, lymphoproliferative disorders, or myeloproliferative disorders include but are not limited to:

- Skin cancers (basal, squamous, melanoma)
- New leukemia
- New myelodysplasia
- Solid tumors
- PTLD (post-transplant lymphoproliferative disorder) (report as lymphoma or lymphoproliferative disease)

The following should not be reported as new malignancy:

- Recurrence of primary disease (report as relapse or disease progression)
- Relapse of malignancy from recipient’s pre-HCT medical history
- Breast cancer found in other (i.e., opposite) breast (report as relapse)
- Post-HCT cytogenetic abnormalities associated with the pre-HCT diagnosis (report as relapse)
- Transformation of MDS to AML post-HCT (report as disease progression)

**Recurrence Skin Cancers**

For most malignancies, do not report recurrence, progression or transformation of the recipient’s primary disease (disease for which the transplant was performed) or relapse of a prior malignancy in the “New Malignancy” section. For example, a recipient had a basal cell skin cancer diagnosed on the neck four months post-HCT and six months later had another basal cell located on the nose. The lesion on the nose is not considered a metastasis from the neck, but a new discrete lesion. These
If a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was diagnosed during the reporting period, report “yes” and complete questions 49-55. If “no”, continue with question 56.

Copy and complete questions 49-55 to report each new malignancy diagnosed since the date of last report. The submission of a pathology report or other supportive documentation for each reported new malignancy is strongly recommended.

**Question 49-50: Specify new malignancy**

Copy and complete questions 49-55 to report each new malignancy diagnosed since the date of last report. The submission of a pathology report or other supportive documentation for each reported new malignancy is strongly recommended.

If the new malignancy or disorder does not fit into one of the categories specified in question 49, indicate “other new malignancy,” and specify the type in question 50.

**Question 51: Is the tumor EBV positive?**

If the disorder is lymphoma or lymphoproliferative disease, indicate if the tumor is EBV positive. This question only applies if lymphoma or lymphoproliferative disorder is selected in question 49.

**Question 52: Date of diagnosis**

Report the date of first pathological diagnosis (e.g., biopsy) of the new malignancy. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center, and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.

For malignancies or disorders without pathologic diagnosis, report the date of clinical diagnosis or date of specimen collection for laboratory assessment confirming diagnosis.

If exact date of diagnosis is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.
Question 53: Was documentation submitted to the CIBMTR? (e.g. pathology / autopsy report or other documentation)

Indicate whether documentation of the new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was submitted to CIBMTR (e.g., pathology report, autopsy report).

For further instructions on how to attach documents in FormsNet3, refer to the training guide.

Question 54-55: Was the new malignancy donor / cell product derived?

Indicate whether the new malignancy originated from the donor / cell product. If “yes,” indicate whether documentation was submitted to CIBMTR (e.g., cell origin evaluation (VNTR, cytogenetics, FISH)) in question 55.

For further instructions on how to attach documents in FormsNet3, refer to the training guide.
Chimerism studies are performed to determine the percent of blood or marrow cells post-transplant that are produced from donor hematopoietic stem cells and the percent that are produced from host (recipient) hematopoietic stem cells. Different types of blood cells and a variety of laboratory tests can be used to determine if a chimera (presence of both donor- and host-derived cells) exists. If cytogenetic testing was performed to look for disease markers, and the donor and recipient are different sexes, the test may also be used to determine if a chimera exists. If the donor and recipient are of the same sex, cytogenetic testing using the common staining technique, known as giesma banding (G-banding), cannot be used to determine if there is a chimera. However, quinicrine banding (Q-banding) can be used to identify if the cells are of donor origin or not in a same-sex transplant, as this staining technique highlights inherited chromosome polymorphisms on certain human chromosomes including 3, 4, 13, 15, 21, 22, and Y. This is not a commonly used staining technique and is only helpful when the polymorphism is documented pre-HCT.

**Chimerism Studies**
If chimerism studies were attempted, but no evaluable results were obtained, do not report the test.
When a multi-donor chimerism exists and includes a donor (or donors) from a previous HCT, report as a multi-donor chimerism though there may only be one donor for the current transplant.

**Question 56-57: Were chimerism studies performed since the date of last report?**

Indicate whether chimerism studies were performed within the reporting period. If “yes,” indicate whether documentation was submitted to CIBMTR (e.g., chimerism laboratory reports) in question 57.
If chimerism studies were not performed within the reporting period, select “no,” and continue with question 75.

**Question 58: Were chimerism studies assessed for more than one donor / multiple donors?**

Indicate whether this HCT included product(s) from multiple donors. When a multi-donor chimerism exists and includes a donor or donors from a previous HCT, report as a multi-donor chimerism even though there may only be one donor for the current transplant.

**Question 59-74: Provide date(s), method(s) and other information for all chimerism studies performed since the date of last report.**

Copy question 59-74 if needed for multiple chimerism studies. When reporting chimerism studies for multiple donors, there should be one instance for each donor for each chimerism test results.

Transplant centers may perform frequent chimerism studies. If there is a need to reduce the number of chimerism study results reported due to volume, ensure that the following are reported at a minimum:

- Studies performed on or at approximately Day+28
- Most recent studies performed prior to the date of contact, particularly for Day+100
- Most recent studies performed prior to and after an intervention (such as a donor cellular infusion)
- The first result to show complete / 100% donor chimerism

**Chimerism – Single Donor**

<table>
<thead>
<tr>
<th>Data Field</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>59. NMDP donor ID</td>
<td>If the donor or one of the donors was an NMDP PBSC or marrow donor, enter the 9 digit NMDP donor ID.</td>
</tr>
<tr>
<td>60. NMDP cord blood unit ID</td>
<td>If the donor or one of the donors was an NMDP cord blood unit, enter the 9 digit NMDP cord blood unit ID.</td>
</tr>
<tr>
<td>61. Non-NMDP unrelated donor ID</td>
<td>If the donor or one of the donors was a non-NMDP unrelated PBSC or marrow donor, enter the non-NMDP registry donor ID.</td>
</tr>
<tr>
<td>62. Non-NMDP cord blood unit ID</td>
<td>If the donor or one of the donors was a non-NMDP cord blood unit, enter the non-NMDP registry donor ID.</td>
</tr>
<tr>
<td>63. Date</td>
<td>If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry,</td>
</tr>
<tr>
<td>Column</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td><strong>birth or age</strong></td>
<td>provide the date of birth, if known; if date of birth is not known, provide the donor’s age at donation.</td>
</tr>
<tr>
<td><strong>64. Sex</strong></td>
<td>If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry, provide the biological sex.</td>
</tr>
<tr>
<td><strong>65. Date sample collected</strong></td>
<td>Enter the date the sample was collected for the chimerism test.</td>
</tr>
<tr>
<td><strong>66-67. Method</strong></td>
<td>Report the test method used for the reported chimerism study. Cytogenetic testing methods include karyotyping and fluorescent in situ hybridization (FISH). Cytogenetic methods are only valid for sex mismatched transplants with the exception of quinicrine banding. VNTR / STR is one of the most common molecular methods for assessing chimerism. See the Chimerism Methods table below for additional details on chimerism testing methods.</td>
</tr>
<tr>
<td><strong>68. Cell source</strong></td>
<td>Report whether the specimen taken for chimerism testing was from a marrow or peripheral blood source.</td>
</tr>
<tr>
<td><strong>69-70. Cell type</strong></td>
<td>Indicate the cell type tested. If the specimen was not sorted for a specific cell line, indicate “unsorted / whole.” See the Chimerism Cell Types table below for additional details on cell markers unique to certain cell lines.</td>
</tr>
<tr>
<td><strong>71. Total cells examined</strong></td>
<td>Cytogenetic testing methods include karyotyping and fluorescent in situ hybridization (FISH), each of which examines a specific and relatively low number of cells – generally 15 to 200, depending on specimen and test method. If a cytogenetic method was used, enter the total number of cells that were examined. If a non-cytogenetic test was used, leave these boxes blank.</td>
</tr>
<tr>
<td><strong>72. Number of donor cells</strong></td>
<td>Cytogenetic methods, karyotyping and FISH, examine a specific and relatively low number of cells – generally 15 to 200, depending on specimen and test method. If a cytogenetic method was used, enter the total number of cells that were examined and found to be of donor origin. If a non-cytogenetic test was used, leave these boxes blank.</td>
</tr>
<tr>
<td><strong>73. Were donor cells detected?</strong></td>
<td>Molecular testing methods include RFLP and VNTR / STR. If a molecular method was used, indicate whether donor cells were detected. Report “yes,” if the testing identified any percentage of cells as being of donor origin.</td>
</tr>
<tr>
<td><strong>74. Percent donor cells</strong></td>
<td>Molecular testing methods include VNTR / STR, RFLP, and AFLP. Report the percentage of donor cells identified by molecular testing. If the test result did not detect any recipient cell population within the sensitivity of the assay, report 100% donor cells. If the test detected recipient cells, but indicated donor cells “&gt; n%,” report “n + 1” percent donor cells. If the test detected donor cells but indicated donor cells “&lt; n%,” report “n – 1” percent donor cells.</td>
</tr>
</tbody>
</table>

**Chimerism Methods**

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karyotyping for XX / XY</td>
<td>Cells are grown in culture, stained, and examined under a microscope to identify the number of cells matching the sex of the donor. This method is only valid when donor and recipient are sex mismatched.</td>
</tr>
<tr>
<td>Fluorescent in situ</td>
<td>Cells are exposed to fluorescent DNA probes which attach to X and Y chromosomes. A microscope is used to identify the number of cells matching the sex of the donor. This</td>
</tr>
</tbody>
</table>
hybridization (FISH) for XX / XY | method is only valid when donor and recipient are sex mismatched. Do not report FISH testing for disease-specific abnormalities in the chimerism section of the Post-TED.

Restricted fragment length polymorphisms (RFLP) | A restriction fragment is a portion of DNA which has been cut out by an enzyme. RFLP testing begins by isolating DNA from the sample. Enzymes are used to cut the DNA at specific loci resulting in many unique restriction fragments. The fragments are separated according to size by electrophoresis. The unique pattern of separation is used to identify the percent donor DNA present in the sample.

Variable number tandem repeat (VNTR), micro- or minisatellite | VNTR refers to a portion of DNA containing a repeating sequence of base pairs (micro- or minisatellite). The number of times a micro- or minisatellite repeats within specific loci can differ between individuals. These differences are used to distinguish donor DNA from recipient DNA. VNTR testing involves obtaining samples from the recipient and donor prior to transplant. Specific loci are compared to determine which loci contain VNTRs unique to the donor. After transplant, DNA is isolated from recipient samples. Donor-specific VNTRs are amplified by PCR techniques. The sample is then analyzed to determine the percent donor DNA present.

Small tandem repeat (STR), micro- or minisatellite | STR also refers to a portion of DNA containing a repeating sequence of base pairs (micro- or minisatellite). The number of times a micro- or minisatellite repeats within specific loci can differ between individuals. These differences are used to distinguish donor DNA from recipient DNA. STR testing involves obtaining samples from the recipient and donor prior to transplant. Specific loci are compared to determine which loci contain STRs unique to the donor. After transplant, DNA is isolated from recipient samples. Donor-specific STRs are amplified by PCR techniques. The sample is then analyzed to determine the percent donor DNA present.

Amplified fragment length polymorphisms (AFLP) | A restriction fragment is a portion of DNA which has been cut out by an enzyme. AFLP testing begins by isolating DNA from the sample. Enzymes are used to cut the DNA at specific loci resulting in many unique restriction fragments. Many restrictions fragments are amplified using PCR techniques. The fragments are separated according to size by electrophoresis. The unique pattern of separation is used to identify the percent donor DNA present in the sample. Report AFLP testing using the VNTR/STR method option on the 2450 form.

Chimerism Cell Types

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unssorted / whole</td>
<td>The peripheral blood or bone marrow sample has not been sorted or selected for a certain cell line.</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>Also known as RBCs or erythrocytes; carry the CD235a cell marker</td>
</tr>
<tr>
<td>Hematopoietic progenitor cells</td>
<td>Includes CD34+ cells</td>
</tr>
<tr>
<td>Total mononuclear cells</td>
<td>Total mononuclear cells would be a specimen containing only and both lymphocytes and monocytes</td>
</tr>
<tr>
<td>T cells</td>
<td>Includes CD3+, CD4+, and / or CD8+ cells</td>
</tr>
<tr>
<td>B cells</td>
<td>Includes CD19+ or CD20+ cells</td>
</tr>
<tr>
<td>Cell Type</td>
<td>Description</td>
</tr>
<tr>
<td>-------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Granulocytes</td>
<td>Also known as polymorphonuclear leukocytes (PMNs, PMLs) and includes neutrophils, eosinophils, and basophils. Includes CD33+ cells</td>
</tr>
<tr>
<td>NK cells</td>
<td>Includes CD56+ cells</td>
</tr>
<tr>
<td>Other, specify</td>
<td>Use this option to report cell types that do not fit in a category above.</td>
</tr>
</tbody>
</table>
**Q75-97: Disease Assessment at the Time of Best Response to HCT**

This section collects the data known as “best response to transplant.” The purpose of this section is to report the recipient’s best response to the planned course of the HCT. This includes response to any therapy given for post-HCT maintenance or consolidation, but does not include response to treatment given for relapsed or persistent disease that was not planned before the HCT was executed. Best response is often achieved in the first 100 days. However, for some diseases such as multiple myeloma and CLL, the best response to HCT may take longer.

If the recipient relapses/progresses and receives therapy for the disease relapse/progression, the response to that additional therapy should not be reported in this section. The best response prior to the relapse/progression should be reported. Reporting periods subsequent to that in which best response prior to the start of unplanned was reported will indicate that best response was previously reported.

**Malignant Diseases Only**

Only complete questions 75-97 if the HCT being reported was given to treat a malignant disease. If the HCT being reported was given to treat a non-malignant disease, leave questions 75-97 blank. FormsNet should enable/disable this section based on the primary disease reported on the Pre-TED Disease Classification Form (Form 2402). Contact your CRC if you believe FormsNet is incorrectly enabling/disabling these fields.

**Reporting Complete Remission (CR) Post-HCT**

Complete remission (CR) criteria vary by disease and are outlined in the CIBMTR Forms Instructions Manual. Please refer to the appropriate disease response criteria section of the Forms Instructions Manual and review the criteria to report CR.

**Amyloidosis**

Centers were previously instructed to report “Not applicable” for pre-HCT disease status on the Pre-TED Form (Form 2400) or Disease Classification Form (Form 2402) for all amyloidosis cases regardless of response. However, instruction has now been modified so that if a patient was in complete remission prior to HCT by meeting all applicable CR criteria, CR is selected as pre-HCT disease status instead of “Not applicable.” “Continued complete remission” should then be selected for the post-HCT response status. If a validation error has occurred for question 75 on the Post-TED Form due to the scenario described above, do not override the error. Instead, change the pre-HCT response reported.
Question 75: Compared to the disease status prior to the preparative regimen, what was the best response to HCT since the date of the last report? (Include response to any therapy given for post-HCT maintenance or consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease):

If the recipient was already in CR at the start of the preparative regimen, check “Continued complete remission (CCR)” and continue with question 98.

If the recipient achieved CR post-HCT (excluding unplanned therapy), check “complete remission (CR)” and continue with question 77.

If the recipient has not achieved a post-HCT CR to date, check “not in complete remission” and continue with question 76.

If the recipient’s disease status was not evaluated post-HCT, check “not evaluated” and continue with question 98. This option is not commonly used, as this would indicate that no tests (radiological, laboratory, or a clinical assessment) were performed to assess the CR status at any time during the reporting period.

If the recipient never achieved a post-transplant complete response and started unplanned therapy, given for relapsed, persistent, or progressive disease, in a previous reporting period, indicate “not evaluated.”

Question 76: Specify disease status if not in complete remission:

For recipients “not in complete remission,” indicate whether clinical evidence of disease persisted on disease-specific assessments within the reporting period. If all assessments have shown resolution of disease, but not all assessments required to report complete remission have been completed, indicate “no disease detected but incomplete evaluation to establish CR.” This option is also appropriate for scenarios in which the recipient has not previously achieved a post-HCT CR but does not have any disease assessments performed within the reporting period. Indicate “disease detected” if disease persists by any method of radiological or clinical assessment; persistence of abnormalities by molecular, cytogenetic, or flow cytometry assessments does not constitute “disease detected.”

Example 1: A recipient with multiple myeloma goes to transplant in VGPR, without a bone marrow
showing < 5% plasma cells completed prior to transplant. Post-transplant serum and urine electrophoreses and immunofixations are negative. However, no bone marrow biopsy is performed within the 100-day reporting period. In this case, “not in complete remission” should be selected for question 75, and “no disease detected by incomplete evaluation to establish CR” for question 76.

**Example 2:** A recipient with AML goes to transplant in primary induction failure. Post-transplant, they recover their counts, but had circulating blasts noted on differential. They expire due to persistent disease with their last CBC performed on their date of death showing circulating blasts. In this case, “not in complete remission” should be selected for question 75, and “disease detected” in question 76.

**Example 3:** Similar to example 2, a recipient with AML goes to transplant in primary induction failure. They expire on D+11 due to infection, and had not engrafted as of that date. Their last CBC showed a WBC of 0.5 × 10⁹/L with no blasts detected on their differential. A bone marrow biopsy was not performed between transplant and the date of death. In this case, “not in complete remission” should be selected for question 75, and “no disease detected by incomplete evaluation to establish CR” in question 76.

**Question 77: Was the date of best response previously reported?**

Indicate whether complete remission was reported in a previously reporting period; if “yes,” continue with question 98 and if “no,” continue with question 78. This question does not apply for “not in complete remission” responses to question 75.

**Question 78: Date assessed:**

Report the date complete remission was achieved. This date should fall after transplant but before or on the date of contact for the current reporting period. This should reflect the date of specimen collection or imaging for the latest assessment required to fulfill complete remission criteria for the recipient’s transplant disease.

**Disease Assessment at Time of Best Response**

Questions 79-97 refer to disease assessments performed at the time of best response (question 78). The following guidelines should be used to determine whether testing was performed at the time of best response:

If the recipient’s best response is **“Not in Complete Remission,”** report the latest assessment performed during the reporting period. If the recipient has started treatment for relapsed, progressive, or persistent disease (excluding treatment for minimal residual disease), report the latest assessment prior to the initiation of therapy.
If the recipient’s best response is “Complete Remission,” report testing performed closest to the date of best response (questions 78) and within the time windows in the Disease Assessment Time Windows table.

**Disease Assessment Time Windows**

<table>
<thead>
<tr>
<th>Follow-Up Form</th>
<th>Approximate Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 Day</td>
<td>+/- 15 days of date of best response (question 78)</td>
</tr>
<tr>
<td>6 Month</td>
<td>+/- 15 days of date of best response (question 78)</td>
</tr>
<tr>
<td>Annual</td>
<td>+/- 30 days of date of best response (question 78)</td>
</tr>
</tbody>
</table>

**Disease Assessment Reporting Scenarios:**

**A.** A recipient receives a transplant on 1/1/2015 for multiple myeloma in partial remission. Prior to HCT, FISH testing detects an IGH rearrangement associated with the recipient’s primary disease. During the 100 day reporting period, the recipient achieves a very good partial remission. FISH testing is only performed on 2/1/2015 is positive for the previously detected IGH rearrangement. The 100 day date of contact is 4/15/2015. In this case, the center would report the recipient was “Not in Complete Remission” on the 100 Day Post-TED Form. The center would report FISH testing was performed on 2/1/2015. When the best response is “Not in Complete Remission” report the most recent testing performed during the reporting period (assuming treatment was not started for relapsed, progressive, or persistent disease during the reporting period – see Scenario B).

**B.** A recipient receives a transplant on 1/1/2015 for multiple myeloma in partial remission. Prior to HCT, FISH testing detects an IGH rearrangement associated with the recipient’s primary disease. During the 100 day reporting period, the recipient has disease progression and starts treatment on 3/1/2015. FISH testing is performed on 2/1/2015 and 3/15/2015. Both tests are positive for the previously detected IGH rearrangement. The 100 day date of contact is 4/15/2015. In this case, the center would report the recipient was “Not in Complete Remission” on the 100 Day Post-TED Form. The center would report FISH testing was performed on 2/1/2015. When the best response is “Not in Complete Remission” report the most recent testing performed during the reporting period and prior to treatment for relapsed, progressive or persistent disease.

**Note:** For all subsequent reporting periods, the center would report “Not Evaluated” for question 75 and skip questions 76-97. If treatment was started in a prior reporting period, the center is not able to report and assessments performed during the reporting period and prior to treatment.

**C.** A recipient receives a transplant on 1/1/2015 for AML in primary induction failure. Prior to HCT, molecular testing confirms the recipient’s disease is FLT3 positive. On 2/1/2015, the recipient achieves a
hematologic remission, but FLT3 is not tested at that time. Later, on 2/10/2015, molecular testing is performed and confirms the recipient is FLT3 negative. In this case, the center would report the recipient achieved a CR on 2/1/2015 on the 100 Day Post-TED Form. The center would report molecular testing was performed at the time of best response as testing was done within 15 days of 2/1/2015.

**D.** A recipient receives a transplant on 1/1/2015 for AML in primary induction failure. Prior to HCT, molecular testing confirms the recipient’s disease is FLT3 positive. On 2/1/2015, the recipient achieves a hematologic remission, but FLT3 is not tested at that time. Later, on 3/1/2015, molecular testing is performed and confirms the recipient is FLT3 negative. In this case, the center would report the recipient achieved a CR on 2/1/2015 on the 100 Day Post-TED Form. The center would report no molecular testing was performed at the time of best response as testing was not done within 15 days of 2/1/2015.

**Molecular**

**Question 79: Was the disease status assessed by molecular testing (e.g. PCR)?**

Molecular assessment involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection and can indicate known genetic abnormalities associated with the disease for which the HCT was performed. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include chromosomal microarray / chromosomal genomic array, Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

Report “not applicable” if molecular studies were never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary transplant disease.

Report “no” if molecular studies were not performed during the reporting period.

If the recipient’s best response is “Not in Complete Remission,” report the latest assessment performed during the reporting period and prior to treatment for relapsed, progressive, or persistent disease (excluding treatment for minimal residual disease). If testing was not performed prior to the initiation of treatment, report “no” and go to question 82.

If the recipient’s best response is “Complete Remission,” report testing performed closest to the date of best response (questions 78) and within the time windows in the Disease Assessment Time Windows table. If testing was not performed within the applicable time window, report “no” and go to question 82.
**Question 80: Date assessed:**

If the best response is “complete remission,” report the date of testing performed nearest the date of best response and prior to relapse or progression, if applicable.

If the best response is “not in complete remission,” report the date of the most recent testing performed during the reporting period and prior to treatment for relapsed, progressive, or persistent disease, if applicable. If no treatment for relapsed, progressive, or persistent disease was given, report the date of the most disease-specific testing performed within approximately 30 days of the follow-up date.

Report the date of specimen collection for molecular disease assessment. If exact date is not known, refer to [General Instructions, General Guidelines for Completing Forms](#) for information about reporting partial or unknown dates.

**Question 81: Was disease detected?**

Report whether the recipient’s primary disease was detected by molecular testing on the date reported in question 80. In order to be considered positive for disease, the assay must detect a number of copies of the molecular marker exceeding the threshold for sensitivity of the assay, for a quantitative study. However, do note that presence of only a single marker amongst numerous tested is sufficient to indicate disease detected.

**Flow Cytometry**

**Question 82: Was the disease status assessed via flow cytometry?**

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. This allows for the detection of abnormal cell populations for some diseases.

Report “not applicable” if flow cytometry was never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary transplant disease.

Report “no” if flow cytometry was not performed during the reporting period.

If the recipient’s best response is “Not in Complete Remission,” report the latest assessment performed during the reporting period **and** prior to any treatment for relapsed, progressive, or persistent disease (excluding treatment for minimal residual disease). If testing was not performed prior to the initiation of treatment, report “no” and go to question 85.

If the recipient’ best response is “Complete Remission,” report testing performed closest to the date of best
response (questions 78) and within the time windows in the Disease Assessment Time Windows table. If testing was not performed within the applicable time window, report “no” and go to question 85.

**Question 83: Date assessed**

If the best response is “complete remission,” report the date of testing performed nearest the date of best response and prior to relapse or progression, if applicable.

If the best response is “not in complete remission,” report the date of the most recent testing performed during the reporting period and prior to treatment for relapsed, progressive, or persistent disease, if applicable. If no treatment for relapsed, progressive, or persistent disease was given, report the date of the most disease-specific testing performed within approximately 30 days of the follow-up date.

Report the date of specimen collection for flow cytometry assessment. If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

**Question 84: Was disease detected?**

Report whether the recipient’s primary disease was detected by flow cytometry on the date reported in question 83. Report “disease detected” if an abnormal cell population associated with the recipient’s primary transplant disease was detected regardless of the sensitivity of the flow cytometry panel performed; this means an abnormal cell population detected by MRD flow cytometry would be reported in the same way as an abnormal cell population detected by a standard flow cytometry assay.

**Cytogenetic Testing (Karyotyping or FISH)**

**Question 85: Was the disease status assessed by cytogenetic testing (karyotyping or FISH)?**

Cytogenetic studies involve the study of chromosomes, typically through one of two methods: karyotyping or fluorescence in situ hybridization (FISH). Blood, bone marrow, or tissue preparations may be tested by either of these two methods. Karyotyping is both less sensitive and less specific than FISH testing; FISH studies identify only abnormalities detectable by the employed probe set, and cannot provide information about the presence or absence of chromosomal abnormalities or markers outside the specific probe set utilized.

Report “**not applicable**” if cytogenetic studies were never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary transplant disease.

Report “**no**” if cytogenetic studies were not performed during the reporting period.
If the recipient’s best response is “Not in Complete Remission,” report the latest assessment performed during the reporting period and prior to any treatment for relapsed, progressive, or persistent disease (excluding treatment for minimal residual disease). If testing was not performed prior to the initiation of treatment, report “no” and go to question 92.

If the recipient’s best response is “Complete Remission,” report testing performed closest to the date of best response (questions 78) and within the time windows in the Disease Assessment Time Windows table. If testing was not performed within the applicable time window, report “no” and go to question 92.

Question 86: Was the disease status assessed via FISH?

FISH XX/XY probe sets are not considered relevant to disease assessment, and should not be reported in the disease assessment section.

Report “not applicable” if FISH studies were never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary transplant disease.

Report “no” if FISH studies were not performed during the reporting period.

If the recipient’s best response is “Not in Complete Remission,” report the latest assessment performed during the reporting period and prior to any treatment for relapsed, progressive, or persistent disease (excluding treatment for minimal residual disease). If testing was not performed prior to the initiation of treatment, report “no” and go to question 89.

If the recipient’s best response is “Complete Remission,” report testing performed closest to the date of best response (questions 78) and within the time windows in the Disease Assessment Time Windows table. If testing was not performed within the applicable time window, report “no” and go to question 89.

Question 87: Date assessed

If the best response is “complete remission,” report the date of testing performed nearest the date of best response and prior to relapse or progression, if applicable.

If the best response is “not in complete remission,” report the date of the most recent testing performed during the reporting period and prior to treatment for relapsed, progressive, or persistent disease, if applicable. If no treatment for relapsed, progressive, or persistent disease was given, report the date of the most disease-specific testing performed within approximately 30 days of the follow-up date.

Report the date of specimen collection for FISH assessment. If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.
Question 88: Was disease detected?

Report whether the recipient’s primary disease was detected by FISH testing on the date reported in question 87.

Question 89: Was the disease status assessed via karyotyping?

Report “not applicable” if karyotyping was never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary transplant disease.

Report “no” if karyotyping was not performed during the reporting period.

If the recipient’s best response is “Not in Complete Remission,” report the latest assessment performed during the reporting period and prior to any treatment for relapsed, progressive, or persistent disease (excluding treatment for minimal residual disease). If testing was not performed prior to the initiation of treatment, report “no” and go to question 92.

If the recipient’s best response is “Complete Remission,” report testing performed closest to the date of best response (questions 78) and within the time windows in the Disease Assessment Time Windows table. If testing was not performed within the applicable time window, report “no” and go to question 92.

Question 90: Date assessed

If the best response is “complete remission,” report the date of testing performed nearest the date of best response and prior to relapse or progression, if applicable.

If the best response is “not in complete remission,” report the date of the most recent testing performed during the reporting period and prior to treatment for relapsed, progressive, or persistent disease, if applicable. If no treatment for relapsed, progressive, or persistent disease was given, report the date of the most disease-specific testing performed within approximately 30 days of the follow-up date.

Report the date of specimen collection for karyotyping. If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

Question 91: Was disease detected?

Report whether the recipient’s primary disease was detected by karyotyping on the date reported in question 90. Do not include clinically insignificant polymorphism, or chromosomal abnormalities of no known significance, as disease detected; this includes anomalies such as age-dependent loss of the chromosome Y.
Radiologic

Question 92: Was the disease status assessed by radiological assessment (e.g. PET, MRI, CT)

Radiologic assessments are imaging techniques used to assess disease response to transplant, typically for lymphomas or solid tumors, though valuable in some less common presentations of disease, such as leukemia cutis. Imaging techniques used to evaluate disease response typically include PET, CT, or MIBG, but may include x-ray, skeletal survey, or ultrasound in some cases.

Report “not applicable” if radiological assessments were never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary transplant disease.

Report “no” if radiological assessments were not performed during the reporting period.

If the recipient’s best response is “Not in Complete Remission,” report the latest assessment performed during the reporting period and prior to any treatment for relapsed, progressive, or persistent disease (excluding treatment for minimal residual disease). If testing was not performed prior to the initiation of treatment, report “no” and go to question 95.

If the recipient’s best response is “Complete Remission,” report testing performed closest to the date of best response (questions 78) and within the time windows in the Disease Assessment Time Windows table. If testing was not performed within the applicable time window, report “no” and go to question 95.

Question 93: Date assessed

If the best response is “complete remission,” report the date of the assessment performed nearest the date of best response and prior to relapse or progression, if applicable.

If the best response is “not in complete remission,” report the date of the most recent testing performed during the reporting period and prior to treatment for relapsed, progressive, or persistent disease, if applicable. If no treatment for relapsed, progressive, or persistent disease was given, report the date of the most disease-specific testing performed within approximately 30 days of the follow-up date.

Report the date of radiological assessment. For recipients with “complete remission” reported in question 76, this may match the date CR was achieved reported in question 79 for recipients with lymphomas, solid tumors, or other diseases with imaging criteria for reporting CR. If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.
Question 94: Was disease detected?

Report whether the recipient’s primary disease was detected by radiologic assessment on the date reported in question 93.

Clinical/Hematologic

Question 95: Was the disease status assessed by clinical/hematologic assessment?

Clinical/hematologic assessment is the least sensitive method of disease detection. Examples include circulating blasts in the bloodstream for AML, and enlargement of a malignant mass for lymphoma or a solid tumor on physical examination. Every recipient who has an evaluation by a physician has a “clinical” assessment. Do not include radiologic or imaging assessments when reporting for question 95.

If the recipient’s best response is “Not in Complete Remission,” report the latest assessment performed during the reporting period and prior to any treatment for relapsed, progressive, or persistent disease (excluding treatment for minimal residual disease). If testing was not performed prior to the initiation of treatment, report “no” and go to question 98.

If the recipient’s best response is “Complete Remission,” report testing performed closest to the date of best response (questions 78) and within the time windows in the Disease Assessment Time Windows table. If testing was not performed within the applicable time window, report “no” and go to question 98.

Question 96: Date assessed

If the best response is “complete remission,” report the date of the assessment performed nearest the date of best response and prior to relapse or progression, if applicable. This will likely match the date CR was achieved reported in question 78, since complete remission criteria generally require clinical or hematologic assessment to confirm.

If the best response is “not in complete remission,” report the date of the most recent testing performed during the reporting period and prior to treatment for relapsed, progressive, or persistent disease, if applicable. If no treatment for relapsed, progressive, or persistent disease was given, report the date of the most disease-specific testing performed within approximately 30 days of the follow-up date.

If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

Question 97: Was disease detected?

Report whether clinical / hematologic abnormalities associated with the primary disease were detected. In
general, if the clinical/hematologic assessment date is that same as that reported in question 78, for recipients achieving complete remission in the reporting period, the answer to question 97 should be “no.”
Q98-160: Post-HCT Therapy

Malignant Diseases Only

Only complete questions 98-160 if the HCT being reported was given to treat a malignant disease. If the HCT being reported was given to treat a non-malignant disease, leave questions 98-160 blank. FormsNet should enable / disable this section based on the primary disease reported on the Pre-TED Disease Classification Form (Form 2402). Contact your CRC if you believe FormsNet is incorrectly enabling / disabling these fields.

Report therapy given since the date of last report for reasons other than relapse, persistent, or progressive disease. This may include maintenance and consolidation therapy as well as treatment for minimal residual disease. Do not report any therapy given for relapse, persistent, or progressive disease.

Question 98: Was therapy given since the date of the last report for reasons other than relapse, persistent, or progressive disease? (Include maintenance and consolidation therapy)

Indicate whether therapy was given during the reporting period for maintenance or consolidation; this therapy may have been specifically planned as part of the original transplant protocol or determined after transplant. Do not include therapy given for relapse, persistent, or progressive disease. Any post-transplant therapy included as part of the initial transplant protocol should be reported in this area of the form.

Question 99: Systemic therapy

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body. Indicate whether systemic therapy was given. Indicate “yes” if the recipient received systemic therapy during the reporting period for reasons other than relapse, persistent, or progressive disease.

Questions 100-155: Specify systemic therapy

Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Treatment may consist of one or multiple drugs, and may be given in an inpatient or outpatient setting; additionally, drugs may be administered on a single day, over consecutive days, or continuously.

Form options are arranged by drug class, which is determined by the chemical structure and action against cancer cells. Review each option within the drug classes to determine whether any agents from that class were given. Report “yes” or “no” for each drug class with an agent administered during the current reporting period for reasons other than relapse, persistent, or progressive disease. For each drug class where “yes” indicated, report “yes” or “no” for each agent listed below. If the recipient received a therapeutic agent that
is not listed within the class, select “other” and specify; if the recipient received a therapeutic agent that does not fall into any of the drug class options available on the form, select “yes” for question 154 and specify in question 155.

**Drug Classes**

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoclonal antibody (mAb)</td>
<td>Monoclonal antibodies are developed to bind to a specific cell surface marker or protein. These antibodies either prompt the recipient’s immune system to attack the target or they deliver treatments directly to sites of disease (e.g., radioimmunotherapy). <em>Do not report PD1 or tyrosine kinase inhibitors under this class. These drugs are captured separately.</em></td>
</tr>
<tr>
<td>Tyrosine kinase inhibitors (TKI)</td>
<td>Tyrosine kinases (TKs) are proteins responsible for many cell functions and can be found in the cell membrane, cytoplasm, and nucleus. This large category of proteins is involved in many different cellular processes. Overactive TKs can result in significant disruption of normal cellular processes including uncontrolled growth and proliferation. TKI’s disrupt the function of these overactive proteins allowing other normal cell processes such as adhesion and apoptosis to resume. <em>Do not report FLT3 or BTK inhibitors under this class. These drugs are captured separately.</em></td>
</tr>
<tr>
<td>FLT3 inhibitor</td>
<td>The FLT3 gene produces a specific receptor type tyrosine kinase which acts as a cell surface receptor for cytokines. This protein has been shown to be overactive in certain malignancies such as AML. Treatments have been developed to target and disrupt FLT3 protein function and restore normal cellular processes. Report all FLT3 targeted therapies under this class.</td>
</tr>
<tr>
<td>Hypomethylating agent</td>
<td>Methylation of specific nucleotides impacts whether specific portions of DNA are available for transcription. Some cancers experience significant cell growth and proliferation due to excessive methylation of DNA which can turn off tumor suppressor genes. Hypomethylating agents counter this process by reducing the amount of DNA methylation and restoring function to tumor suppressor genes. Report all hypomethylating agents under this class.</td>
</tr>
<tr>
<td>Proteasome inhibitor</td>
<td>Certain intracellular proteins, such as P53, are necessary for the activation of apoptosis in cancer cells. Proteasomes break down many intracellular proteins including P53. Proteasome inhibitors disrupt the function of proteasomes and are believed to slow or prevent the excessive degradation of the proteins which activate apoptosis. Report all proteasome inhibitors under this class.</td>
</tr>
<tr>
<td>Immune modulating agent</td>
<td>Immune modulating agents have varied targets and mechanisms of action, but are all similarly intended to prompt an anti-tumor response from the recipient’s own immune system. <em>Do not report mAb therapy or PD1 inhibitors under this class. These drugs are captured separately.</em></td>
</tr>
<tr>
<td>PD1 inhibitor</td>
<td>PD1 is a cell surface receptor protein present on T-cells. It detects the presence of normal cell surface molecules on healthy cells and prevents T-cells from destroying them. Some cancer cells also produce similar cell surface molecules which prevent T-cells from recognizing and attacking them. PD1 inhibitors block this interaction allowing T-cells to attack cancer cells. Report all PD1 inhibitors under this class.</td>
</tr>
<tr>
<td>BTK inhibitor</td>
<td>Bruton’s tyrosine kinase is a protein involved in B-cell maturation. This protein has been shown to be overactive in certain malignancies such as CLL. Treatments have been captured separately.</td>
</tr>
</tbody>
</table>
developed to target and disrupt BTK function and restore normal cellular processes. Report all BTK inhibitors under this class.

Chemotherapy  Any systemic cytotoxic agents not already reported under a drug class above. *Do not report intrathecal therapy under this class. These treatments should be reported under “other therapy” in questions 160-161.*

Other systemic therapy  Any therapeutic agents that the recipient received that do not fall into any of the drug class options available above (e.g., dexamethasone) should be reported under this class.

**Question 156: Radiation**

Radiation therapy uses high-energy radiation to kill cancer cells. External beam radiation is one of the more frequently used types of radiation. In this method, a beam of radiation is delivered to a specific part of the body, such as the mediastinum. Radiation may be planned if bulky disease was present just prior to transplant for a recipient with lymphoma or a solid tumor. Indicate “yes” if the recipient received radiation therapy during the reporting period for reasons other than relapse, persistent, or progressive disease.

**Question 157: Cellular therapy**

Cellular therapy refers to the infusion of human or animal derived cells, which may or may not be modified or processed to achieve a specific composition. Examples include T-cell, NK cell, and mesenchymal cell infusions as well as donor cellular infusions. Indicate “yes” if the recipient received any form of cellular therapy for reasons other than relapse, persistent, or progressive disease or decreasing / loss of donor chimerism; hematopoietic cell transplantation should not be reported as cellular therapy, as this is captured in questions 7-13 of the Post-TED form.

**Question 158: Blinded randomized trial**

A blinded, randomized trial refers to a research treatment protocol in which the participant is assigned to the control arm or investigational group, and the researcher or clinician is not informed whether the subject is receiving the placebo or standard of care versus the investigational therapy. This makes it impossible to report agents or therapies the recipient is receiving. Indicate “yes” if the recipient is receiving therapy on a randomized, blinded clinical trial during the reporting period for reasons other than relapsed, persistent, or progressive disease or decreasing / loss of donor chimerism.

**Questions 159-160: Other therapy**

Report whether the recipient received additional therapy for reasons other than relapsed, persistent, or progressive disease or declining / loss of donor chimerism which does not fit into the previous form categories. Examples may include intrathecal therapy or surgery. Specify the other therapy given in question 160.
Q161-234: Relapse or Progression Post-HCT

Report if the recipient has experienced a clinical/hematologic relapse or progression post-HCT. If the relapse or progression was detected in a previous reporting period indicate that and continue on. If the first clinical/hematologic relapse occurred since the date of the last report, indicate the date it was first detected in this reporting period.

**Question 161: Did the recipient experience a clinical/hematologic relapse or progression post-HCT?**

Clinical/hematologic assessment is the least sensitive method of disease detection. Examples include circulating blasts in the bloodstream for AML, or enlargement of a malignant mass for lymphoma or a solid tumor. Every recipient who has an evaluation by a physician has a “clinical” assessment. Include radiographic evidence of relapse or progression as clinical/hematologic relapse or progression. Disease specific criteria for establishing relapse or progression are published as part of the CIBMTR Forms Instructions Manual. If the recipient dies, and the relapse or progression of disease is discovered by autopsy, the date of assessment should be reported as the date of death, not the autopsy date.

If clinical/hematologic evidence of relapse/progressive disease was found at any time post-transplant, check “yes” and continue with question 162.

If clinical/hematologic evidence of relapse/progressive disease was not found at any time post-transplant, check “no” and continue with question 164.

**Question 162: Was the date of clinical/hematologic relapse or progression previously reported?**

Only the date of first clinical/hematologic relapse or progression post-transplant needs to be reported. Therefore, if the recipient experienced clinical/hematologic relapse or progression in a prior reporting period, report “yes” and continue with question 164. If this is the report of first instance of clinical/hematologic relapse or progression, indicate “no” and continue with question 163.

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**Malignant Diseases Only**

Only complete questions 161-163 if the HCT being reported was given to treat a malignant disease. If the HCT being reported was given to treat a non-malignant disease, leave questions 161-163 blank. Questions 164-234 must be completed regardless of disease type. FormsNet should enable / disable this section based on the primary disease reported on the Pre-TED Disease Classification Form (Form 2402). Contact your CRC if you believe FormsNet is incorrectly enabling / disabling these fields.
**Question 163: Date first seen:**

Indicate the date relapse/progressive disease was determined by clinical/hematological evaluation. If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

**Question 164: Was intervention given for relapsed, persistent or progressive disease, or decreased/loss of chimerism since the date of last report?**

Indicate whether therapy was given during the reporting period for persistent disease, relapsed / progressive disease, or for decreased / loss of donor chimerism. Do not include therapy given for maintenance or planned post-transplant consolidation. Any post-transplant therapy included as part of the initial transplant protocol should not be reported in this area of the form. See the intervention reporting scenarios provided below for further clarification.

**Interventions for Decreased / Loss of Chimerism**

The Post-TED Form (Form 2450) captures interventions given for decreased or loss of chimerism in the relapse / progression section of the form. If the recipient receives an intervention for decreased or loss of chimerism during the reporting period, report the therapy in questions 164-234. This instruction may differ from prior guidelines regarding how to report interventions for decreased / loss of chimerism on past revisions (1-3) of the Post-TED Form.

**Question 165: Specify reason for which intervention was given**

Indicate whether therapy was given for persistent disease, relapsed / progressive disease, or for decreased / loss of donor chimerism. In some instances, therapy may be given to treat disease and decrease / loss of chimerism. In these cases, report the indication pertaining to the recipient's disease status (i.e., “persistent disease” or “relapsed / progressive disease”). If therapy continued from a prior reporting period and a new therapy was started for a different reason during the current reporting period, report the reason the new therapy was started. See the intervention reporting scenarios provided below for further clarification.

**Question 166-171: Specify the method(s) of detection for which intervention was given**

Indicate the methods detecting the reason for which therapy for persistent disease, relapsed / progressive disease, or for decreased / loss of donor chimerism was given (as reported in question 165). For each option, select “yes” if the last assessment by that method was performed prior to the start of the intervention(s) and was consistent with the rationale reported in question 165. There may be some cases for which an assessment by a particular method was last performed in the prior reporting period, but was still consistent with the justification reported in question 165; in this case, the response should still indicate “yes.” For example, in the 100-day reporting period, the last cytogenetic assessment detected a new
abnormality associated with the recipient’s primary transplant disease. In this case, monosomy 7 was identified on a peripheral blood sample for a recipient transplanted for AML in CR1 with normal cytogenetics prior to transplant. In the 6-month reporting period, relapse was detected in the bone marrow morphology (clinical assessment) and concurrent flow cytometry (flow cytometry) and therapy was initiated for relapsed / progressive disease. In this case, each of questions 166, 168, and 169 would be answered “yes” on the Post-TED form in the 6-month reporting period.

If multiple therapies were given during the reporting period for different reasons (e.g., the recipient initially receives treatment for decreased chimerism and subsequently receives different treatment for relapse during the same reporting period), report “yes” for any methods of detection confirming the reason in question 165. See the intervention reporting scenarios provided below for further clarification.

If assessment by that method was not performed or was performed and not consistent with the reason for which intervention was given reported in question 165, report “no.”

See below for definitions and examples of each method of detection:

- **Clinical / hematologic**: Clinical / hematologic assessment is the least sensitive method of disease detection. Examples include circulating blasts in the bloodstream for AML, or enlargement of a malignant mass for lymphoma or a solid tumor. Every recipient who has an evaluation by a physician has a “clinical” assessment. Examples of clinical/hematologic assessments include: bone marrow biopsy / morphologic evaluation, complete blood count, serum protein electrophoresis, etc.

- **Radiologic (e.g., PET, MRI, CT)**: Radiologic assessments are imaging techniques used to assess disease response. Imaging techniques used to evaluate disease response typically include PET, CT, or MIBG, but may include x-ray, skeletal survey, or ultrasound in some cases.

- **Cytogenetic**: Cytogenetic studies involve the study of chromosomes, typically through one of two methods: karyotyping or fluorescence in situ hybridization (FISH). Blood, bone marrow, or tissue preparations may be tested by either of these two methods. Karyotyping is both less sensitive and less specific than FISH testing; FISH studies identify only abnormalities detectable by the employed probe set, and cannot provide information about the presence or absence of chromosomal abnormalities or markers outside the specific probe set utilized.

- **Flow cytometry**: Flow cytometry is a technique that can be performed on blood, marrow, or tissue preparations where the cell surface markers can be quantified on cellular material. This allows for the detection of abnormal cell populations for some diseases. Flow cytometry may also be referred to as immunophenotyping.

- **Disease specific molecular marker**: Molecular assessment involves determining whether a
molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection, and can indicate known genetic abnormalities associated with the disease for which the HCT was performed.

- **Chimerism testing**: Chimerism testing refers to cytogenetic or molecular evaluation used to detect presence of donor- and recipient-specific cells. Examples include VNTR / STR for recipient specific markers or FISH testing using an XX / XY probe set after sex mismatched transplant.

**Question 172: Date intervention started**

Report the date therapy was started for the reason specified in question 165; if multiple instances, cycles, or lines of therapy are administered, report the date of the first treatment. If treatment was started in a prior reporting period and continues into the current reporting period, report the original therapy start date (prior to the start of the current reporting period) and override the validation error in FormsNet3SM using the code “verified correct.” If therapy was stopped in a prior reporting period and restarted (or a new therapy was started) during the current reporting period, report the earliest date treatment was administered during the current reporting period. See the [intervention reporting scenarios](#) provided below for further clarification.

**Intervention Reporting Scenarios**

A. A recipient with NHL in complete remission at the time of HCT has a relapse during the 100 day reporting period. Relapse was detected by a PET scan and a lymph node biopsy. Following these assessments, rituximab was started on 5/1/2016. The disease did not respond to this therapy prompting a switch to brentuximab on 6/1/2016. The 100 Day date of contact is 6/15/2016.

100 Day Post-TED Form:

Q164: Report “Yes” to indicate therapy was given for relapsed disease during this reporting period.
Q165: Report “Relapsed / progressive disease.”
Q166-171: Report “Yes” for clinical/hematologic (lymph node biopsy) and radiological (PET Scan). All other methods of detection must be reported “no.”
Q172: Report “5/1/2016” to reflect the date of the first treatment given for relapsed disease.
Q173-234: Report both rituximab and brentuximab as treatments for relapsed disease given during the reporting period.

B. A recipient with multiple myeloma in VGPR at the time of HCT was started on maintenance lenalidomide during the six month reporting period. Later in the reporting period, progression was detected by serum protein electrophoresis on 9/15/2014 and so the recipient stopped lenalidomide and started bortezomib as well as dexamethasone on 9/20/2014 The recipient continued bortezomib and dexamethasone treatment into the one year reporting period.
Six Month Post-TED Form:

Q164: Report “Yes” to indicate therapy was given for relapsed disease during this reporting period.
Q165: Report “Relapsed / progressive disease.”
Q166-171: Report “Yes” for clinical/hematologic (serum protein electrophoresis). All other methods of detection must be reported “no.”
Q172: Report “9/20/2014” to reflect the date of the first treatment given for progressive disease.
Q173-234: Report both bortezomib and dexamethasone as treatments for progressive disease given during the reporting period. The lenalidomide therapy should not be reported in this section of the form. This medication was given as maintenance therapy and will therefore be reported under Post-HCT Therapy.

One Year Post-TED Form:

Q164: Report “Yes” to indicate therapy was given for relapsed disease during this reporting period.
Q165: Report “Relapsed / progressive disease.”
Q166-171: Report “Yes” for clinical/hematologic (serum protein electrophoresis). Centers are instructed to report “yes” for all methods of assessment performed prior to the start of treatment which confirmed the reason therapy was given (question 165). This includes assessments which may have been performed during a prior reporting period.
Q172: Report “9/20/2014” to reflect the date of the first treatment given for relapsed disease. Reporting a date outside the current reporting period will cause a FormsNet3 error. Centers are instructed to override this error using the code “Verified Correct.”
Q173-234: Report both bortezomib and dexamethasone as treatments for progressive disease given during the reporting period.

C. A recipient with Ph+ ALL in CR at the time of HCT has decreasing donor chimerism during the six month reporting period. To improve donor chimerism, two DLI s were given during the six month reporting period with the first infusion administered on 1/1/2015. One additional DLI was given at the beginning of the one year reporting period on 2/1/2015. Relapse was detected on 2/15/2015 by cytogenetic and molecular assays performed on peripheral blood samples. Relapse was confirmed by a bone marrow biopsy performed on 2/20/2015 and treatment with dasatinib was commenced that same day. Dasatinib therapy was continued into the two year reporting period.

Six Month Post-TED Form:

Q164: Report “Yes” to indicate therapy was given for decreased chimerism during this reporting period.
Q165: Report “Decrease / loss of chimerism.”
Q166-171: Report “Yes” for chimerism testing. All other methods of detection must be reported “no.”
Q172: Report “1/1/2015” to reflect the date of the first DLI given for decreased chimerism.
Q173-234: Report the DLI’s given during the reporting period as “Cellular Therapy.”

One Year Post-TED Form:

Q164: Report “Yes” to indicate therapy was given for decreased chimerism and relapsed disease during this reporting period.
Q165: Report “Relapsed / progressive disease.” When interventions are given to treat disease and decrease / loss of chimerism, report the indication pertaining to the recipient’s disease status (i.e., “persistent disease” or “relapsed / progressive disease”).
Q166-171: Report “Yes” for clinical / hematologic, cytogenetic, and disease specific molecular marker. All other methods of detection must be reported “no.” This question must be answered based on the reason for the intervention as specified in question 165.
Q172: Report “2/20/15” to reflect the first new treatment administered during the reporting period.
Q173-234: Report the DLI and dasatinib as treatments received during the reporting period. Any treatments received during the reporting period for persistent disease, relapsed / progressive disease, or decrease / loss of chimerism must be reported in question 173-234.

Two Year Post-TED Form:

Q164: Report “Yes” to indicate therapy was given for relapsed disease during this reporting period.
Q165: Report “Relapsed / progressive disease.”
Q166-171: Report “Yes” for clinical / hematologic (bone marrow biopsy), cytogenetic, and disease specific molecular marker. All other methods of detection must be reported “no.” The first treatment administered during the reporting period was dasatinib (continued from prior reporting period). Questions 166-171 must be answered based on the methods of detection confirming the reason the first treatment during the reporting period was administered.
Q172: Report “2/20/2015” to reflect the date dasatinib was started. Reporting a date outside of the current reporting period will cause a FormsNet3 error. Centers are instructed to override this error using the code “Verified Correct.”
Q173-234: Report dasatinib given for relapsed disease. No other treatment was given during the reporting period.

D. A recipient with multiple myeloma in PR at the time of HCT was started on lenalidomide during 100 day reporting period (started 3/15/2012) due to persistent disease (detected by serum electrophoresis testing). This treatment was not planned and was given due to an unsatisfactory disease response to HCT. Thirty days after lenalidomide was started, a karyotype assessment confirmed persistent cytogenetic abnormalities present in a bone marrow sample. Lenalidomide was continued into the six month reporting period, during which, there was disease progression (detected by serum electrophoresis). Lenalidomide
was stopped and carfilzomib was started on 5/30/2012. By the end of the six month reporting period, the recipient achieved a complete remission in response to carfilzomib and was switched to a lower maintenance dose of carfilzomib which was continued into the one year reporting period.

100 Day Post-TED Form:

Q164: Report “Yes” to indicate therapy was given for persistent disease during this reporting period.
Q165: Report “Persistent disease.”
Q166-171: Report “Yes” for clinical / hematologic (serum protein electrophoresis). All other methods of detection must be reported “no.” The karyotype test would not be reported as a method of detection since it was performed after treatment was started and, therefore, did not inform the decision to start lenalidomide.
Q172: Report “3/15/2012” to reflect the date of the first treatment for persistent disease.
Q173-234: Report lenalidomide as the only treatment given during the reporting period.

Six Month Post-TED Form:

Q164: Report “Yes” to indicate therapy was given for persistent and progressive disease during this reporting period.
Q165: Report “relapsed / progressive disease.” If therapy continued from a prior reporting period and a new therapy was started for a different reason during the current reporting period, report the reason the new therapy was started.
Q166-171: Report “Yes” for clinical / hematologic (serum protein electrophoresis). All other methods of detection must be reported “no.”
Q172: Report “5/30/2012” to reflect the date of the first treatment for progressive disease.
Q173-234: Report the lenalidomide and carfilzomib as treatments received during the reporting period. Any treatments received during the reporting period for decrease / loss of chimerism, relapsed disease, or progressive disease must be reported in question 173-234.

One Year Post-TED Form:

Q164: Report “No” to indicate therapy was not given for decrease / loss of chimerism, relapsed disease, or progressive disease during this reporting period. The lower dose carfilzomib given as maintenance (to keep the recipient in CR) must be reported in the Post-HCT Therapy Section of the Post-TED Form. Reporting “No” for question 164 will disable questions 165-234.

Question 173: Systemic therapy

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body. Indicate whether systemic
therapy was given. Indicate “yes” if the recipient received systemic therapy during the reporting period for relapsed, persistent, or progressive disease, or decreased / loss of donor chimerism. If therapy has continued from a previous reporting period, report the original start date and override the validation error in FormsNet3SM using the code “verified correct.”

**Questions 174-229: Specify systemic therapy**

Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Treatment may consist of one or multiple drugs, and may be given in an inpatient or outpatient setting; additionally, drugs may be administered on a single day, over consecutive days, or continuously.

Form options are arranged by drug class, which is determined by the chemical structure and action against cancer cells. See the Drug Classes table for additional information regarding drug classes. Review each option within the drug classes to determine whether any agents from that class were given. Report “yes” or “no” for each drug class with an agent administered during the current reporting period for relapsed, persistent, or progressive disease or for decreased / loss of donor chimerism. For each drug class where “yes” indicated, report “yes” or “no” for each agent listed below. If the recipient received a therapeutic agent that is not listed within the class, select “other” and specify; if the recipient received a therapeutic agent that does not fall into any of the drug class options available on the form, select “yes” for question 228 and specify in question 229.

**Question 230: Radiation**

Radiation therapy uses high-energy radiation to kill cancer cells. External beam radiation is one of the more frequently used types of radiation. In this method, a beam of radiation is delivered to a specific part of the body, such as the mediastinum. Radiation may be planned if bulky disease was present just prior to transplant for a recipient with lymphoma or a solid tumor. Indicate “yes” if the recipient received radiation therapy during the reporting period for relapsed, persistent, or progressive disease.

**Question 231: Cellular therapy**

Cellular therapy refers to the infusion of human or animal derived cells, which may or may not be modified or processed to achieve a specific composition. Examples include T-cell, NK cell, and mesenchymal cell infusions as well as donor cellular infusions. Indicate “yes” if the recipient received any form of cellular therapy for relapse, persistent, or progressive disease or decreasing / loss of donor chimerism; hematopoietic cell transplantation should not be reported as cellular therapy, as this is captured in questions 7-13 of the Post-TED form.

**Question 232: Blinded randomized trial**

A blinded, randomized trial refers to a research treatment protocol in which the participant is assigned to the
control arm or investigational group, and the researcher or clinician is not informed whether the subject is receiving the placebo or standard of care versus the investigational therapy. This makes it impossible to report agents or therapies the recipient is receiving. Indicate “yes” if the recipient is receiving therapy on a randomized, blinded clinical trial during the reporting period for relapsed, persistent, or progressive disease or decreasing / loss of donor chimerism.

Questions 233-234: Other therapy

Report whether the recipient received additional therapy for relapsed, persistent, or progressive disease or declining / loss of donor chimerism which does not fit into the previous form categories. Examples may include dexamethasone, intrathecal therapy or surgery. Specify the other therapy given in question 234.
Q235-238: Current Disease Status

Malignant Diseases Only

Only complete questions 235-238 if the HCT being reported was given to treat a malignant disease. If the HCT being reported was given to treat a non-malignant disease, leave questions 235-238 blank. FormsNet should enable / disable this section based on the primary disease reported on the Pre-TED Disease Classification Form (Form 2402). Contact your CRC if you believe FormsNet is incorrectly enabling / disabling these fields.

Question 235: What is the current disease status?

Indicate the disease status of the primary transplant disease as of the last evaluation in the reporting period. Complete remission (CR) criteria vary by disease, and are outlined in the CIBMTR Forms Instructions Manual. If the recipient achieves CR or continues in CR at the time of last evaluation in the reporting period, indicate “complete remission (CR).” If the recipient is not in CR due to presence of disease on last evaluation in the reporting period or an incomplete evaluation that does not allow for reporting CR, indicate “not in complete remission.” If the recipient’s disease status was not evaluated post-HCT, check “not evaluated” and continue with question 98. This option is not commonly used, as this would indicate that no tests (radiological, laboratory, or a clinical assessment) were performed to assess the CR status at any time during the reporting period.

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

Question 236: Specify disease status if not in complete remission

Disease status criteria are generally based upon clinical assessment confirming ongoing presence or absence of disease. However, there are also situations in which an evaluation may have been performed but be incomplete and not have all testing required in order to meet the criteria for reporting complete remission (CR).

For recipients “not in complete remission,” indicate whether clinical evidence of disease persisted on disease-specific assessments within the reporting period. If all assessments have shown resolution of disease, but not all assessments required to report complete remission have been completed, indicate “no disease detected but incomplete evaluation to establish CR.” This option is also appropriate for scenarios in which the recipient has not previously achieved a post-HCT CR but does not have any disease assessments...
performed within the reporting period. Indicate “disease detected” if disease persists by any method of radiological or clinical assessment; persistence of abnormalities by molecular, cytogenetic, or flow cytometry assessments does not constitute “disease detected.”

**Example 1:** A recipient with multiple myeloma goes to transplant in VGPR, without a bone marrow showing < 5% blasts completed prior to transplant. Post-transplant serum and urine electrophoreses and immunofixations are negative. However, no bone marrow biopsy is performed within the 100-day reporting period. In this case, “not in complete remission” should be selected for question 235, and “no disease detected by incomplete evaluation to establish CR” for question 236.

**Example 2:** A recipient with AML goes to transplant in primary induction failure. Post-transplant, they recover their counts, but had circulating blasts noted on differential. They expire due to persistent disease with their last CBC performed on their date of death showing circulating blasts. In this case, “not in complete remission” should be selected for question 235, and “disease detected” in question 236.

**Example 3:** Similar to example 2, a recipient with AML goes to transplant in primary induction failure. They expire on D+11 due to infection, and had not engrafted as of that date. Their last CBC showed a WBC of 0.5 × 10⁹/L with no blasts detected on their differential. A bone marrow biopsy was not performed between transplant and the date of death. In this case, “not in complete remission” should be selected for question 235, and “no disease detected by incomplete evaluation to establish CR” in question 236.

**Question 237-238: Date of most recent disease assessment**

Indicate whether the date of most recent disease assessment is known or unknown. Use known even if only approximate date is known, then refer to General Instructions, [General Guidelines for Completing Forms](#), for information about reporting partial or unknown dates. “Unknown” should only be used when there is no record – exact or approximate – of disease assessment within the reporting period.

Report the date of latest clinical / hematologic assessment consistent with disease status reported in questions 235-236.

- If there are multiple disease assessments within the reporting period, report the date of the most recent disease-specific evaluation consistent with the disease status reported in questions 235-236.
- If there are no disease-specific assessments within the reporting period, report the latest assessment in which the recipient was clinically assessed by a physician or midlevel clinician. In this scenario, this date does not need to be consistent with the disease status reported in question 235-236.
Comprehensive Baseline & Follow-up Manuals

This section provides explanatory text for each question on the Baseline, Follow-up, IDMs, HLA, and Infusion forms.

2000: Recipient Baseline
2004: Infectious Disease Markers
2005: Confirmation of HLA Typing
2006: Hematopoietic Stem Cell Transplant (HCT) Infusion
2100: Post-HCT Follow-Up
2900: Recipient Death
2000: Recipient Baseline

A transplant center designated as a Comprehensive Report Form center will submit data on the Pre-TED Form, followed by either the Post-TED Form or the Comprehensive Report Forms. The type of follow-up form used for a specific recipient is determined by the CIBMTR’s form selection algorithm (see General Instructions, Center Type and Data Collection Forms).

The Baseline Form is one of the Comprehensive Report Forms. This form captures pre-HCT data such as: recipient demographics, organ function and hematologic status, preparative regimen, and socioeconomic information. The Baseline Form is due within 60 days after HCT.

For recipients receiving a subsequent HCT, the recipient will remain on the original follow-up form track (TED or Comprehensive Report Forms) assigned by the form selection algorithm, except for situations where the recipient has enrolled into a study requiring comprehensive report forms. For recipients assigned to Comprehensive Report Forms by the form selection algorithm, centers will submit an additional Pre-TED form.

Q1-5: Recipient Demographics
Q6-14: Clinical Status of Recipient Prior to the Preparative Regimen
Q15-38: Organ Function Prior to the Preparative Regimen
Q39-54: Hematologic Findings Prior to the Preparative Regimen
Q55-75: Infection
Q76-247: Pre-HCT Preparative Regimen
Q248-264: Socioeconomic Information

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/20/2018</td>
<td>2000: Recipient Baseline</td>
<td>Modify</td>
<td>Removed If the specific organism is not listed, use the “other, specify” code 209 — candida, 219 — aspergillus, or 259 — fungus and report the name of the organism in the space provided for question 59. Modified language to complete a Fungal</td>
</tr>
<tr>
<td>Date</td>
<td>Version</td>
<td>Action</td>
<td>Notes</td>
</tr>
<tr>
<td>------------</td>
<td>---------</td>
<td>--------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>4/16/18</td>
<td>2000</td>
<td>Add</td>
<td>Infection Form for all organisms. Removed the list of fungal organisms. Added Fungal Infection Diagnosis Reporting Scenario to the instructions for question 57.</td>
</tr>
<tr>
<td>3/1/18</td>
<td>2000</td>
<td>Add</td>
<td>Added Infusion Without a Preparative Regimen note box at the beginning of Q6-14: Clinical Status of Recipient Prior to the Preparative Regimen (Conditioning), Q15-38: Organ Function Prior to the Preparative Regimen (Conditioning), and Q39-54: Hematologic Findings Prior to the Preparative Regimen (Conditioning).</td>
</tr>
<tr>
<td>2/7/18</td>
<td>2000</td>
<td>Modify</td>
<td>Updated the list of fungal species that require Form 2046 to be completed. Items added are in red. Items removed are struck out. This list is provided in the instructions for questions 58-59. Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Other Aspergillus specify, Aspergillus NOS, Aspergillus terreus, Aspergillus ustus, Blastomyces (dermatitidis), Candida albicans, Candida non-albicans, Cryptococcus gattii, Cryptococcus neoformans, Fusarium (all species), Histoplasma (capsulatum), Mucorales (all species), Mucormycosis, Rhizopus (all species), Scedosporium (all species), Zygomycetes NOS, Suspected fungal infection</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2000</td>
<td>Modify</td>
<td>Added table explaining how to report IgG versus IgM CMV results to question 65. [see table in text]</td>
</tr>
<tr>
<td>6/26/15</td>
<td>2000</td>
<td>Add</td>
<td>Added the following explanatory text to questions 256-263: Report the recipient’s source of health insurance as of the date of HCT. If the recipient carries more than one source, select “yes” for all that apply. For each option, select “yes” or “no” and do not leave any options blank. U.S.-based, government-sponsored health insurance should be reported in question(s) 256 and/or 257. Non-U.S.-based, government-sponsored health insurance (such as the National Health Service in the United Kingdom) should be reported in question 258. Insurance purchased through an U.S. Affordable Care Act Government Exchange should report this in questions 262-263. If the recipient has a health insurance that is not listed, select “yes” for “other” and specify the health insurance in question 263.</td>
</tr>
<tr>
<td>6/12/15</td>
<td>2000</td>
<td>Modify</td>
<td>Modified the informational text in question 105: ATG or alemtuzumab (Campath) given for GVHD prophylaxis prior to Day 0 should be reported in the preparative regimen section of the Baseline Form. If ATG, alemtuzumab, or cyclophosphamide is given after Day 0 for GVHD prophylaxis, it should be reported in the acute GVHD prophylaxis section on the 100 Day Post-HCT Data form. For ATG, Campath, and Cyclophosphamide: If these agents are given for GVHD prophylaxis both prior to and after Day 0, they must be reported in separate sections of the Comprehensive Report Forms. Report doses given prior to Day 0 in the preparative regimen section of the Baseline Form (questions 107-242). If given after Day 0 as GVHD prophylaxis, report in the GVHD prophylaxis section of the 100 Day Post-HCT Data (questions 111-139).</td>
</tr>
</tbody>
</table>
| 5/29/15    | 2000    | Modify | Added the following instruction to question 4: If the recipient is White, Southeast Asian, or Pacific Islander, but a more specific
Race Detail is not available, report the patient is “Other [White, Southeast Asian, or Pacific Islander respectively].

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/16/15</td>
<td>2000: Recipient Baseline</td>
</tr>
<tr>
<td>Modify</td>
<td>Modify</td>
</tr>
</tbody>
</table>

Removed the following text from Q78: Enter the date the preparative regimen began. Use the earliest date from questions 82, (radiation), or 109-176 and 193-241 (systemic therapy). All dates reported in the preparative regimen section must be equal to or after the date reported for this question.

and added information about autologous reporting: “Use the earliest date from questions 82 (radiation), or 109-176 and 193-241 (systemic therapy). Additional radiation and/or intrathecal chemotherapy start dates may be prior to the date the preparative regimen began.”
Q1-5: Recipient Demographics

Questions 1-2: Country of primary residence: (check only one)

Select the recipient’s country of residence. If “other” is chosen, continue with question 2 and specify the country. If the recipient’s country of primary residence is the United States of America, continue with question 3. If the recipient’s country of primary residence is not the United States, continue with question 4.

Question 3: State of residence of recipient (for residents of USA)

If the United States was selected as the recipient’s primary country of residence, enter the recipient’s state of permanent residence at the time of transplant.

Question 4: Race

Indicate the race of the recipient. If this recipient has reported that they are more than one race, you may indicate each race by adding an additional instance in the FormsNet application. The race groups provided are specific to the United States. If the recipient declines to provide this information, select “not reported.”

If the recipient is White, Southeast Asian, or Pacific Islander, but a more specific Race Detail is not available, report the patient is “Other [White, Southeast Asian, or Pacific Islander respectively].

For non-U.S. centers, select “not reported” if the rules/regulations of your country prohibit the collection or reporting of race data (or due to lack of documentation). If race data is reported, it may be necessary to consult with the recipient to select the race group(s) with which they most closely identify.

For more information regarding race, see Appendix I.

Question 5: Race Detail

Indicate the detailed race of the recipient. If this recipient has reported that they are more than one detailed race, you may indicate each detailed race by adding an additional instance in the FormsNet application.

For more information regarding race, see Appendix I.
Q6-14: Clinical Status of Recipient Prior to the Preparative Regimen (Conditioning)

Infusion Without a Preparative Regimen
Questions 6-14 must be answered even if no preparative regimen was given.

Question 6: Specify blood type: (for allogeneic HCTs only)
Indicate the recipient’s blood type as “A,” “B,” “AB,” or “O.” Blood type is an important characteristic in allogeneic transplant because products may require manipulation to minimize the risk of immune reaction due to incompatibility.

Question 7: Specify Rh factor: (for allogeneic HCTs only)
Indicate the recipient’s Rh (rhesus) factor. The Rh factor is an important characteristic in allogeneic transplant because products may require manipulation to minimize the risk of immune reaction due to incompatibility.

Question 8: Does the recipient have a history of smoking cigarettes?
The intent of this question is to determine the recipient’s history of smoking cigarettes only. Do not report the use of cigars, pipe tobacco, chewing tobacco, or other drugs. The recipient’s smoking history is usually documented on the transplant admission summary.

Indicate whether the recipient has a history of smoking cigarettes. If “yes,” continue with question 9. If “no” or “unknown” continue with question 15.

Question 9: Has the recipient smoked cigarettes within the past year?
Indicate if the recipient has a history of smoking cigarettes within the year prior to HCT.

Question 10: Has the recipient smoked cigarettes prior to but not during the past year?
Indicate if the recipient smoked cigarettes prior to, but not during, the year prior to HCT. The intention of this question is to ascertain if the recipient has smoked cigarettes in the past, but not within the year prior to transplant. Indicate “yes” if the recipient has smoked cigarettes, but not during the past year leading up to transplant. Indicate “no” if the recipient has a history of smoking that continued into the year prior to transplant. Select “unknown” if it is not known if the recipient smoked cigarettes prior to, but not during, the
Questions 11-12: Number of years:

Indicate if the number of years the recipient smoked cigarettes is “known” or “unknown.” If “known,” report the total number of years the recipient smoked cigarettes, rounded to the nearest year, in question 12. If “unknown,” continue to question 13.

Questions 13-14: Average number of packs per day:

Indicate if the number of packs per day is “known” or “unknown.” If known, report the average number of packs per day the recipient smoked/smokes in question 14. See Table 1 below to calculate the number of packs per day from a reported cigarette(s) per day history.

If the progress notes state the recipient’s smoking history in pack-years, use this definition: Pack-year history = (number of packs per day) X (number of years). See the examples below to calculate packs per day from a reported pack-year history.

If this information is not documented, select “unknown” and continue with question 15.

Table 1. Conversion Into Packs per Day

<table>
<thead>
<tr>
<th>Cigarettes/Day</th>
<th>Packs/Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>0.1</td>
</tr>
<tr>
<td>3-4</td>
<td>0.2</td>
</tr>
<tr>
<td>5-6</td>
<td>0.3</td>
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<td>7-8</td>
<td>0.4</td>
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<td>9-10</td>
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<tr>
<td>11-12</td>
<td>0.6</td>
</tr>
<tr>
<td>13-14</td>
<td>0.7</td>
</tr>
<tr>
<td>15-16</td>
<td>0.8</td>
</tr>
<tr>
<td>17-19</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Pack-Year History Examples

- 1 pack per day for 20 years = 20 pack-year history
- ½ packs per day for 20 years = 10 pack-year history
- Progress Note states: Recipient has smoked for 20 years and has a 40 pack-year history.
- $40 \text{ (pack-year history)} / 20 \text{ (years)} = 2 \text{ packs per day}$
- Report "average number of packs per day" as 2
Questions 15-38: Provide last laboratory values recorded for recipient’s organ function (testing done within 30 days prior to the start of the preparative regimen).

These questions are intended to determine the clinical status of the recipient prior to the start of the preparative regimen for stem cell transplantation. Testing may be performed multiple times within the pre-transplant work-up period; report the most recent laboratory value obtained for each specific test. Laboratory values obtained on the first day of the preparative regimen may be reported as long as the blood was drawn before any radiation or systemic therapy was administered.

For each organ function test below, indicate if the value is “known” or “unknown” prior to the start of the preparative regimen. Indicate the values for each test. If necessary, convert values so they can be reported in the units of measurement available on the form.

**AST (SGOT):** Aspartate aminotransferase, or serum glutamic oxalate transaminase, is an enzyme measured in serum or plasma that reflects liver function and liver cell integrity. Elevated levels of AST may indicate liver damage.

**Total serum bilirubin:** Bilirubin is a pigment that is formed from the breakdown of hemoglobin in red blood cells. Serum bilirubin is a test of liver function that reflects the ability of the liver to take up, process, and secrete bilirubin. Total bilirubin includes the direct (conjugated) and indirect (unconjugated) bilirubin values. If your laboratory reports direct and indirect separately, add the two together to report the total serum bilirubin.

**LDH:** Lactate dehydrogenase is an enzyme found in the cytoplasm of almost all tissues, which converts L-lactate into pyruvate, or pyruvate into L-lactate depending on the oxygen level. For some diseases, high levels indicate active disease (e.g., lymphoma and multiple myeloma).

**Serum creatinine:** Creatinine is a normal metabolic waste that is primarily filtered from the blood by the kidneys and then excreted in the urine. Since it is generally produced at a constant rate, the clearance rate and the serum level are widely used as indicators of kidney function.
**Total serum ferritin:** Ferritin is a protein that stores, transports, and releases iron. Iron is toxic to cells, so it is stored within the ferritin protein for use. Ferritin that is too low might be indicative of iron deficiency related anemia. Ferritin that is too high might be indicative of iron overload. It is tracked for some diseases, such as hemophagocytic lymphohistiocytosis.

**Serum albumin:** Serum albumin is a protein found in the blood. Levels are most often reported on a chemistry panel, but may occasionally be found in a separate liver function test report.

**Date Sample Collected:**
Report the date the sample was collected. This date should be before the date of the start of the preparative regimen; however, laboratory values obtained on the first day of the preparative regimen may be reported as long as the blood was drawn before any radiation or systemic therapy was administered.

**Upper Limit of Normal for your Institution:**
Report the upper limit of normal for each assessment result. Normal values may vary by laboratory, so it is important to report the upper limit of normal for each assessment.
Q39-54: Hematologic Findings Prior to the Preparative Regimen (Conditioning)

Question 39: Date CBC tested: (testing within 30 days of start of preparative regimen)

These questions are intended to determine the clinical status of the recipient prior to the preparative regimen for stem cell transplantation. Testing may be performed multiple times within the pre-transplant work-up time period; report the most recent laboratory value obtained for each specific test. Laboratory values obtained on the first day of the preparative regimen may be reported as long as the blood was drawn before any radiation or systemic therapy was administered.

Questions 40-54: Provide last laboratory values recorded just prior to preparative regimen:

For each value below, indicate if the result was “known” or “unknown” prior to the start of the preparative regimen. Indicate the units for each test, taking care to convert them to a unit available on the form, if necessary.

**WBC:** The white blood cell count is a value that represents all of the white blood cells in the blood. If the count is too high or too low, the ability to fight infection may be impaired.

**Neutrophils:** Neutrophils are a subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage or an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. Neutrophils are also known as polymorphonuclear leukocytes (PMNs).

**Lymphocytes:** Lymphocytes are another subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage of an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage.

**Hemoglobin:** Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered “anemia” and blood transfusions or growth factors may be required to increase the hemoglobin level. Also indicate if the recipient received a red blood cell transfusion within 30 days prior to testing.
**Hematocrit**: The hematocrit is the percentage (sometimes displayed as a proportion) of red blood cells relative to the total blood volume. A low hematocrit may require red blood cell transfusions or growth factors. Indicate if the recipient received a red blood cell transfusion within 30 days prior to testing.

**Platelets**: Platelets are formed elements within the blood that help with coagulation. A low platelet count, called thrombocytopenia, may lead to easy bleeding or bruising. Thrombocytopenia may require platelet transfusions. Indicate if the recipient received a platelet transfusion within 7 days prior to testing.
Q55-75: Infection

Question 55: Did the recipient have a history of clinically significant fungal infection (documented or suspected) at any time prior to the preparative regimen?

Fungal infections play a major role in the clinical outcome of a transplant recipient. The intent of this question is to identify serious fungal infection(s) that might have an effect on the outcome of the HCT. For the purposes of this manual, the term “clinically significant” refers to conditions that are treated at the time of pre-HCT evaluation, or that have affected the recipient's medical history, that might cause complications post-HCT.

Examples of fungal infections include, but are not limited to the following: invasive aspergillosis (infection codes 210-213, 219), zygomycosis (infection code 240) and other molds (infection codes 230, 240, 242, 261), invasive candidiasis (infection codes 200-209), cryptococcosis (infection code 220), endemic mycosis (infection code 241), other yeasts (infection code 250), and pneumocystis (PCP/PJP) (infection code 260). Include any fungal abscesses of the lungs, sinuses, liver, or spleen.

Non-invasive fungal infections such as thrush and nail fungus should not be reported.

If the recipient has a history of clinically significant fungal infection at any time prior to this HCT event, check “yes” and continue with question 56. For a subsequent HCT, report any documented significant fungal infections in the recipient's medical history, between the start of the preparative regimen of the previous HCT to just prior to the preparative regimen for the current HCT.

If the recipient does not have a history of clinically significant fungal infection at any time prior to this HCT event, check “no” and continue with question 64. For assistance with reporting fungal infections, consult with a transplant physician.

Question 56: Did the recipient have more than one fungal infection (documented or suspected) at any time prior to the preparative regimen?

Indicate if the recipient had more than one fungal infection at any time prior to the preparative regimen.

If the infection was due to yeast, and recurred in ≤ 14 days, it is considered a single incident and should not be reported multiple times.

If the infection was due to mold, and recurred in ≤ 90 days, it is considered a single incident and should not be reported multiple times.
**Question 57: Date of onset:**

Enter the date of onset of the fungal infection. For suspected fungal infections, enter the date of a radiology test or date treatment was started as the date of onset.

**Fungal Infection Diagnosis Reporting Scenario:**

A recipient has a CT scan on 4/1/2015 due to a persistent cough. The CT scan documents multiple nodules. An *Aspergillus* galactomannan was drawn in the blood on 4/2/2015 and the patient underwent a bronchoscopy on 4/3/2015. Fluid from the bronchoaveolar lavage was stained for fungal elements and submitted for culture. The stain was positive for fungal elements and the culture grew *Aspergillus*. The blood galactomannan was also positive.

- The date of diagnosis of infection will be 4/2/2015. This is the date the galactomannan was obtained and positive.
- If galactomannan was negative and the BAL negative, the date of infection would be 4/1/2015 (the date of the CT scan).

**Question 58-59: Select organism from list below:**

From the list of “Codes for Commonly Reported Fungal Organisms,” select the code corresponding to the identified or suspected fungus. Report the code in the boxes provided.

A Fungal Infection Form (F2046) must be completed for all organisms.

**Question 60-62: Select site(s) from list below:**

From the list of “Codes for Common Sites of Infection,” select the code corresponding to the site of the infection. If more than one site was involved, report the codes for up to three affected sites.

If three or more sites were infected with the same fungal organism, enter code 2 (Disseminated – generalized, isolated at 3 or more distinct sites).

**Disseminated Infections**

The CIBMTR acknowledges that a discrepancy exists between the CIBMTR definition (3 or more sites) and the BMT CTN definition (2 or more sites) for disseminated infections.

**Question 63: Was this fungal infection active within 2 weeks prior to the preparative regimen?**

Indicate if the fungal infection was active within the two weeks prior to the start of the preparative regimen.
For suspected fungal infections, select “yes” if the recipient received fungal treatment (not prophylaxis) and/or had a finding on an x-ray or CT scan consistent with a suspected fungal infection within 2 weeks prior to the preparative regimen.

**Questions 64-75: Testing for evidence of prior viral exposure/infection:**

For each of the tests below, indicate if the results of the test were “reactive” or “not reactive.” If the test was performed but the results were not clearly reactive or non-reactive, report the results as “inconclusive.” “Not done” indicates that the test was not performed.

**Serologic Tests**

Serologic tests should be completed during the pre-HCT work-up phase, or approximately one month prior to the start of the preparative regimen. **Exception:** If a recipient has a documented history of a reactive CMV test at any time prior to transplant, the CMV test might not be repeated during the pre-HCT work-up phase. In this case, it is acceptable to report a CMV test from greater than one month prior to the start of the preparative regimen.

If a recipient tests positive for Hepatitis B core antibody (Anti HBc), Hepatitis B surface antigen (HBsAg), Hepatitis B DNA, Hepatitis C antibody (Anti HCV), and/or Hepatitis C NAT serologic tests, also complete the HEP Form (2047).

If a recipient tests positive for HIV antibody or HIV NAT serologic tests, also complete the HIV Form (2048).

**HTLV1 antibody:** Human T-Lymphotropic virus I/II (HTLV I/II) is a retrovirus in the same class as HIV. HTLV I/II is associated with certain leukemias and lymphomas, as well as demyelinating diseases such as multiple sclerosis.

Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” “inconclusive,” or “not done.”

**Cytomegalovirus antibody:** CMV is a common virus that infects 50-80% of adults worldwide and is transmitted from person to person through bodily fluids. The virus that causes CMV is part of the herpes virus family and, like other herpes viruses, CMV may be dormant for a period of time before the virus is activated in the host. CMV infections are usually harmless in a healthy immune system and typically cause only mild symptoms, if any. However, if a person’s immune system is seriously weakened (as in an immunosuppressed stem cell recipient) the virus can have serious consequences such as
pneumonia, liver failure, and even death. Determining a recipient’s past exposure to CMV is important for transplant outcomes research.

Most laboratory reports indicate a positive result as *reactive*, and a negative result as *non-reactive*. Occasionally, laboratory reports show a specific antibody titer. In this case, the laboratory result must be compared to the reported standards to determine the reactive or non-reactive result.

<table>
<thead>
<tr>
<th>CMV antibody tested</th>
<th>Results</th>
<th>What to report on F2400 or F2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>Positive/reactive</td>
<td>Reactive</td>
</tr>
<tr>
<td></td>
<td>Negative/non-reactive</td>
<td>Non-reactive</td>
</tr>
<tr>
<td></td>
<td>Inconclusive</td>
<td>Inconclusive (or not done on F2400)</td>
</tr>
<tr>
<td>IgM</td>
<td>Positive/reactive</td>
<td>Reactive</td>
</tr>
<tr>
<td></td>
<td>Negative/non-reactive</td>
<td>Not Done</td>
</tr>
<tr>
<td></td>
<td>Inconclusive</td>
<td>Inconclusive (or not done on F2400)</td>
</tr>
<tr>
<td>Total IgG + IgM</td>
<td>Positive/reactive</td>
<td>Reactive</td>
</tr>
<tr>
<td></td>
<td>Negative/non-reactive</td>
<td>Non-reactive</td>
</tr>
<tr>
<td></td>
<td>Inconclusive</td>
<td>Inconclusive (or not done on F2400)</td>
</tr>
</tbody>
</table>

- **Recipients < 6 months:** If the recipient is less than 6 months old, report any positive CMV antibody results as “inconclusive” due to the presence of maternal antibodies. However, in infants less than 6 months old, positive CMV PCR results indicate a CMV infection and the results may be reported as “reactive.”

- **Exposure to IVIG:** Exposure to IVIG may result in a false positive CMV antibody result. If the recipient has been exposed to IVIG leading up to HCT (within 3-6 months), indicate the CMV antibody results using the following guidelines:
  - If the recipient had a non-reactive CMV antibody result prior to IVIG therapy and then routine CMV PCR results showed no copies of CMV, the CMV antibody may be reported as “non-reactive,” even if the CMV antibody became reactive *during* IVIG treatment.
  - If CMV PCR results quantified copies of CMV DNA (e.g., was positive) during IVIG treatment, the results may be reported as “reactive.”
  - If the recipient did not have a CMV antibody test prior to the initiation of IVIG, but had a positive antibody test during the IVIG therapy, report “inconclusive.”
  - “Not done” should be reported if no CMV antibody tests were done prior to the initiation of IVIG therapy, even if CMV PCR testing was negative during IVIG treatment (because CMV PCR only detects active infection, not prior exposure).
For other situations, if the laboratory reports CMV testing by PCR (DNA detection) but no CMV antibody testing is done during the pre-transplant work-up or within one month prior to transplant, report the result as "not done." CMV testing by PCR is used to detect the presence of the CMV virus and does not test for prior exposure.

Indicate the test result documented on the laboratory report as either "reactive," "non-reactive," "inconclusive," or "not done."

**Anti-EBV (Epstein-Barr virus antibody):** Epstein-Barr Virus (EBV) is a common virus of the herpes family. It can cause infectious mononucleosis, but in most cases is asymptomatic. EBV establishes a lifelong dormant infection in some cells of the body’s immune system. Serious post-transplant complications related to EBV include EBV viremia (reactivation) and post-transplant lymphoproliferative disease (PTLD).

Indicate the test result documented on the laboratory report as either “positive,” “negative,” “inconclusive,” or “not done.”

**Hepatitis B surface antibody:** Hepatitis B is caused by the hepatitis B virus (HBV). Infection with this virus can cause scarring of the liver, liver failure, liver cancer, and even death. Hepatitis B is spread through infected blood and other body fluids. Acute hepatitis B infection does not usually require treatment because most adults clear the infection. Treatment of chronic infection may be necessary to reduce the risk of cirrhosis and liver cancer.

The hepatitis B surface antibody test reveals the presence of hepatitis B antibodies, indicating previous exposure to HBV (or successful vaccination), but the virus is no longer present and the person cannot pass on the virus.

Indicate the test result documented on the laboratory report as either "reactive," "non-reactive," "inconclusive," or "not done."

A Hepatitis insert (Form 2047) is **not** required for a positive result.

**Anti-HBc (hepatitis B core antibody):** The enzyme-linked immunosorbent assay (ELISA) technique tests for the antibody directed against the hepatitis B virus core proteins. The hepatitis B core antibody test can indicate previous HBV infection. Currently there is no licensed confirmatory test for Anti-HBc. If the screening test is reactive, a second Anti-HBc test is performed using a different manufacturer’s test kit.

Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” or “not done.”
If the result is “positive,” a Hepatitis insert (Form 2047) is also required.

**HBsAg (hepatitis B surface antigen):** The ELISA or enzyme immunoassay (EIA) techniques test for the presence of proteins produced by the hepatitis B virus. Confirmatory testing is done using a neutralization test. The first marker appears approximately three weeks following infection, and disappears approximately six months later.

Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” or “not done.”

If the result is “positive,” a Hepatitis insert (Form 2047) is also required.

**Hepatitis B – DNA:** The HBV DNA test is more sensitive than regular serologic tests, and is often used in conjunction with those tests to monitor patients with chronic HBV infections. If Hepatitis B – NAT testing was done, report the results in this section.

Indicate the test result documented on the laboratory report as either “positive,” “negative,” “inconclusive,” or “not done.”

If the result is “positive,” a Hepatitis insert (Form 2047) is also required.

**Anti-HCV (hepatitis C antibody):** Hepatitis C is a serious infection caused by the hepatitis C virus (HCV), which attacks the liver and may cause life-long infection. HCV is considered the most serious hepatitis infection because of its significant long-term health consequences. The infection is often asymptomatic, but once established, chronic infection can cause inflammation of the liver. This condition can progress to fibrosis and cirrhosis. In some cases, those with cirrhosis will go on to develop liver failure or liver cancer. Presence of the antibody in the blood represents exposure to HCV, which is most often spread by blood-to-blood contact. No vaccine against HCV is available.

The ELISA technique tests for antibodies to the HCV. Confirmatory testing is done using the recombinant immunoblot assay (RIBA) test. These tests can determine past exposure to HCV, but not current viral load.

Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” “inconclusive,” or “not done.”

If the result is “positive,” a Hepatitis insert (Form 2047) is also required.

**Hepatitis C – NAT:** Nucleic acid testing (NAT) is a combination PCR test that detects the presence of viral genes (HCV RNA) rather than antigens or antibodies. This test allows earlier detection and
provides more sensitivity than previously used tests.

Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” “inconclusive,” or “not done.”

If the result is “positive,” a Hepatitis insert (Form 2047) is also required.

**Hepatitis A Antibody:** Hepatitis A is an acute infectious disease of the liver caused by the hepatitis A virus (HAV). HAV is often transmitted via contaminated food and drinking water, and is prevalent in developing countries and areas with poor hygiene standards. Hepatitis A may cause influenza-like symptoms, but is often asymptomatic. There is a highly effective HAV vaccine available that can provide protection for up to 20 years.

A total antibody test (which detects both IgM and IgG antibodies) detects both current and previous infection with HAV and will also be positive after receiving the hepatitis A vaccine.

If the laboratory reports a HAV IgM antibody only, not total IgG/IgM or HAV IgG antibody alone; report the result as “not done.”
Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” “inconclusive,” or “not done.”

A Hepatitis insert (Form 2047) is not required for a positive result.

**HIV antibody:** HIV infection is caused by exposure to one of two viruses: HIV-1 or HIV-2. HIV-2 is less virulent and has a longer incubation period than HIV-1. Both types of HIV progressively destroy lymphocytes, which are an important part of the body’s immune defense. HIV can lead to acquired immunodeficiency syndrome (AIDS), a condition in which the immune system begins to fail, leading to life-threatening opportunistic infections. Infection with HIV occurs by the transfer of bodily fluids and is present as both free virus particles and virus within infected immune cells.

HIV antibody testing is done using combination ELISA which detects antibodies to the HIV-1 and HIV-2 viruses. HIV-1 is confirmed by Western Blot, which detects specific proteins using gel electrophoresis. There is currently no licensed confirmatory test for HIV-2. If the screening test is reactive, HIV-2 is confirmed by specific ELISA.

The results of HIV assessments are often kept in confidence and may not be reportable to anyone other than the patient and their physician. If HIV testing was done, but the results are not available, select “not reported.”

Indicate the test result documented on the laboratory report as either “positive,” “negative,”
“inconclusive,” “not done,” or “not reported.”

If the result is “positive,” an HIV insert (Form 2048) is also required.

**HIV – NAT:** Nucleic acid testing (NAT) is a PCR test that detects the presence of viral genes rather than antigens or antibodies. This test allows earlier detection and provides more sensitivity than previously used tests.

The results of HIV assessments are often kept in confidence and may not be reportable to anyone other than the patient and their physician. If HIV testing was done, but the results are not available, select “not reported.”

Indicate the test result documented on the laboratory report as either “positive,” “negative,” “inconclusive,” “not done,” or “not reported.”

If the result is “positive,” an HIV insert (Form 2048) is also required.
Q76-247: Pre-HCT Preparative Regimen (Conditioning)

Question 76: Was a pre-HCT preparative regimen given?

Recipients are generally transplanted using a specific protocol that defines the radiation and/or systemic therapy the recipient is intended to receive in preparation for transplant. This protocol, which may be either a research protocol or standard of care protocol, should be referred to when completing this section.

However, there are instances when a preparative regimen may not be given. Examples may include, but are not limited to:

- Primary diagnosis of an immune deficiency.
- Subsequent allogeneic HCT due to loss of, or poor, neutrophil engraftment.

If a preparative regimen was given, select “yes” and continue with question 77. If a preparative regimen was not given, select “no” and continue with question 248.

Question 77: Specify protocol intent: (check only one)

Indicate whether “all agents given as outpatient,” “some, but not all, agents given as inpatient,” or “all agents given as inpatient.” Agents are defined as systemic therapy drugs or radiation therapy.

Question 78: Date pre-HCT preparative regimen (irradiation or drugs) began:

Use the earliest date from questions 82 (radiation), or 109-176 and 193-241 (systemic therapy). Additional radiation and/or intrathecal chemotherapy start dates may be prior to the date the preparative regimen began. Report additional radiation in questions 87-104 and additional intrathecal chemotherapy in questions 177-190.

Example:
Radiation Order: TBI, 200 cGy/day April 15-17, 2009 & CNS Radiation, 200 cGy/day April 1-3, 2009
Report “Additional Radiation date started”: April 1, 2009
Report “Date pre-HCT preparative regimen began” as: April 15, 2009
began.

**Question 79: Was irradiation performed as part of the pre-HCT preparative regimen?**

If irradiation was performed as part of the preparative regimen, check “yes” and continue with question 80. If irradiation was not performed, check “no” and continue with question 87. Irradiation performed as previous treatment should not be reported in this section, but as previous treatment on the appropriate Disease Specific Form or in question 87, if applicable (radiation given within 14 days of the pre-HCT preparative regimen).

**Question 80: What was the radiation field?**

Indicate if the recipient received irradiation to “total body,” “total body by tomotherapy,” “total lymphoid or nodal regions,” or “thoraco-abdominal region.” This information is often available on the radiation oncology summary.

**Question 81: Total dose: (dose per fraction X total number of fractions)**

Enter the total dose of radiation given. If radiation was given as a single dose, the amount of radiation delivered in the single dose constitutes the total dose. If the radiation was given in fractionated doses, multiply the total number of fractions by the dose per fraction to determine the total dose. Enter the total dose of radiation in either grays (Gy) or centigrays (cGy).

**Example:**
- **Radiation Order:** TBI, 200 cGy/day for three days (3 doses)
- **Total dose:** 200 cGy x 3 doses = 600 cGy
- **Report “Total Dose” as:** 600 cGy

**Question 82: Date started:**

Enter the date the single dose or first fraction of radiation was administered.

**Question 83: Was the radiation fractionated?**

Radiation is either delivered as a single dose or in several treatments (fractions). Radiation is fractionated to increase the destruction of diseased cells as they do not recover as quickly as disease-free cells.

If the radiation was fractionated, check “yes” and continue with question 84. If the radiation was not fractionated, check “no” and continue with question 87.
**Question 84: Dose per fraction:**

Enter the dose per fraction in either grays (Gy) or centigrays (cGy).

The dose per fraction multiplied by the total number of fractions (question 86) must be equal to the total dose reported in question 81.

**Question 85: Number of days: (include “rest” days)**

Enter the total number of days radiation therapy was delivered including any days of rest between days when therapy was administered. The number of days radiation was administered can be greater than the number of fractions.

**Example:**

Radiation Order: TBI, 200 cGy/day every other day (Mon-Wed-Fri) \(\times\) 3 doses

Total dose: 200 cGy \(\times\) 3 doses = 600 cGy

Report “Number of days” as: 5

**Question 86: Total number of fractions:**

Enter the total number of fractions (treatments) of radiation that were administered. The recipient may receive more than one fraction per day (hyperfractionation).

The total number of fractions multiplied by the dose per fraction (question 84) must be equal to the total dose reported in question 81.

**Question 87: Was additional radiation given to other sites within 14 days of the pre-HCT preparative regimen?**

In this section, report any sites that received a “radiation boost.” Boosts are often given to smaller sites that may have residual malignant cells or to areas that were shielded (ex. chest wall or lung). Include any radiation boosts that were administered **within 14 days** prior to the preparative regimen start date up to the

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**Additional Radiation**

Additional radiation start dates may be prior to the date the preparative regimen began. If additional radiation began more than 14 days prior to the start of preparative regimen, but at least one dose was received within 14 days prior to the preparative regimen, report the actual start date of the additional radiation in this section, even if the start date is more than 14 days prior to the start of the preparative regimen. Radiation treatments completed more than 14 days prior to the start of the preparative regimen should be reported on the appropriate Disease Specific Form in the treatment section.

In this section, report any sites that received a “radiation boost.” Boosts are often given to smaller sites that may have residual malignant cells or to areas that were shielded (ex. chest wall or lung). Include any radiation boosts that were administered **within 14 days** prior to the preparative regimen start date up to the
date of infusion.

**Questions 88-104: Specify radiation field:**

Indicate if the recipient received radiation to each site listed. For each site that received additional radiation, indicate the dose, units, and start date.

**Question 105: Were drugs given for pre-HCT preparative regimen?**

- **Preparative Regimen: Drugs**
  The following questions refer to the drug therapy that was actually given as part of the preparative regimen versus the prescribed drug therapy that was reported on the Pre-TED. In this section, include any intrathecal drugs the recipient received for prophylaxis or treatment of CNS disease within 14 days prior to the start date of the preparative regimen. Do not include drugs that are intended to offset the side effects of the systemic therapy (e.g., corticosteroids for nausea, MESNA for hemorrhagic cystitis, etc.).

  - Occasionally, protocols list drugs that may be given before and after day 0. If the drugs are given before and after day 0, only the doses given before day 0 should be quantified in the preparative regimen section. The doses given after day 0 should be reported on the Post-HCT Disease Specific form (if applicable on that form) or GVHD Prophylaxis section of the 100 Day Post-HCT Data Form (Form 2100). For example, if bortezomib or rituximab is given on Days -2, +1, +4, and +7, report the day -2 dose in the preparative regimen section, and the post-transplant doses as planned post-HCT therapy on the disease insert.

  - For ATG, Campath, and Cyclophosphamide: If these agents are given for GVHD prophylaxis both prior to and after Day 0, they must be reported in separate sections of the Comprehensive Report Forms. Report doses given prior to Day 0 in the preparative regimen section of the Baseline Form (questions 107-242). If given after Day 0 as GVHD prophylaxis, report in the GVHD prophylaxis section of the 100 Day Post-HCT Data (questions 111-139).

  - The form lists each drug by the generic name. The form also lists some drugs by broad categories, with specific drugs listed individually. For example, anthracycline is listed as the broad drug category, followed by the specific drugs of daunorubicin, doxorubicin, and idarubicin.

If the recipient received drugs as part of the preparative regimen, select “yes” and continue with question
106. If the recipient did not receive drugs as part of the preparative regimen, check “no” and continue with question 248. Ensure that the drugs being given correspond appropriately with the Pre-TED (Form 2400).

**Question 106: Dosing body weight used for pre-HCT preparative regimen (adjusted body weight):**

Report the recipient’s dosing (adjusted) body weight calculated by the pharmacy/physician to determine the total dose of the drugs given as part of the preparative regimen. The dosing body weight is usually documented on the transplant preparative regimen chemotherapy orders.

If different dosing body weights were used for the calculation of drug doses (for example, the dose for cyclophosphamide was calculated with the recipient’s adjusted body weight and the fludarabine was calculated using the recipient’s actual weight), leave this field blank, override the error, and attach documentation directly to the form showing the different weights and drug calculations.

**Questions 107-242: Specify preparative regimen drugs:**

For each drug listed, indicate whether or not it was given as part of the preparative regimen. Report the total dose of each drug that was actually given. **Do not report the prescribed dose or the daily dose.** The pharmacy record or Medication Administration Record (MAR) should be used for determining the exact total does given.

Some drugs used as part of the preparative regimen are administered with guidance of serum pharmacokinetic testing to determine the recipient’s metabolism of the drug. This allows for individual “customization” of the drug dosing to optimize the desired effect and minimize the toxicity. Depending upon when the drug used to monitor drug levels is administered, it can be reported in one of two different ways on the CIBMTR Pre-TED (2400) and Baseline (2000) forms.

A common example of this situation occurs in the use of busulfan. In some cases, a “test dose” of the drug is given before the actual preparative regimen is started, and this dose is used for acquiring drug levels that are used to adjust the dose that will be used in the preparative regimen. In other situations, the first dose of the drug is given in the usual fashion as part of the preparative regimen. After this first dose, serum drug levels are drawn and sent to a reference lab. The drug is continued at the starting dose until the lab results are reported and adjustment is made to later doses.

When a drug is used for the preparative regimen where pharmacokinetics will be tested, it is important to distinguish whether the testing will be done with a “test dose” before beginning the preparative regimen or using the first dose of the preparative regimen. The reporting of the dosing for the CIBMTR forms depends upon this distinction. This helps distinguish whether the dose is part of the therapeutic regimen, or not.

**A test dose was given > 24 hours prior to the intended therapeutic dosing.**
**Example:** A patient with AML underwent allogeneic HCT from a sibling; busulfan and cyclophosphamide were used as the preparative regimen. The patient presented to clinic 9 days before the HCT, where a dose of busulfan at 0.5 mg/kg was given intravenously. Blood samples were drawn for the next 6 hours, after which the patient left the clinic. His samples were sent to a lab, results were returned the next day, and an adjusted dose of busulfan was calculated. He returned to the hospital 6 days before HCT, and began to receive busulfan at the adjusted dose intravenously for 4 days, followed by cyclophosphamide, and proceeded to receive his cells. Since he received 0.5 mg/kg as a “test dose,” this would not be reported in his total preparative regimen dose.

If a test dose was given, where the dose was distinct from the therapeutic dosing preparative regimen (often 1-2 or more days prior to the initiation of regular dosing), the following should be reported:

- On the Pre-TED (2400) form, the total prescribed dose per protocol would NOT include the test dose.
- On the Baseline (2000) form, the start date of the chemotherapy agent should be reported as the date the first therapeutic dose was administered. The actual dose received would NOT include the test dose.

**The first dose of therapeutic dosing is used for monitoring.**

**Example:** A patient with MDS received an allogeneic HCT from an unrelated donor; busulfan and fludarabine were used as the preparative regimen. She was admitted to the hospital 7 days before her HCT, and received a dose of busulfan at 0.8 mg/kg IV at 6:00 AM. Serum samples were drawn every 30 minutes until the next dose of Busulfan at 0.8 mg/kg IV was given at 12:00 noon. Her blood was sent to a reference lab, and she continued to receive busulfan every 6 hours. On day -6, the lab called with her drug levels, and it was determined that the current dose was correct. No adjustment was made, and she completed all 16 doses of busulfan. Since the dose of busulfan (0.8 mg/kg) that was used for drug testing was ALSO her first dose of the preparative regimen, it should be included in the amount of drug that was given for preparative regimen.

If the first dose of the preparative regimen was used to determine pharmacokinetics, the following should be reported:

- On the Pre-TED (2400) form, the total prescribed dose per protocol would include the dose used for monitoring.
- On the Baseline (2000) form, the start date of the chemotherapy agent should be reported as the date the first dose was administered. The actual dose received would include the dose used for monitoring.

Test doses must be reported consistently at your center. Since most centers follow a consistent approach to pharmacokinetic testing, it should be straightforward for the center to adopt a consistent approach to the reporting of test doses.
Drug doses must be reported in whole numbers. If the total dose includes a decimal, round to the nearest whole number (round up if 0.5 or greater). For paper submission, do not modify the number of boxes or include decimal values.

The “other, specify” category should only be used if the drug is not one of the listed options. If more than one “other” drug is prescribed, list the generic name of the drugs in the space provided and attach a copy of the source document using the Log of Appended Documents (Form 2800).

Drugs given for prophylaxis of infection, GVHD, or organ toxicity should not be reported in this section. Report these drugs on the 100 Day Follow-up Form (2100).

If the Baseline is completed for a subsequent HCT, do not report therapy that was given to treat the recipient’s disease (between the previous and current planned HCTs) in the preparative regimen section. Report this therapy on the appropriate Disease Specific Form.

**Question 243: Were pharmacokinetics performed to determine preparative drug dosing?**

Pharmacokinetic testing can be used to determine whether the drug concentration in the bloodstream is appropriate to the dose given. This reflects the speed of absorption and elimination of the drug. These tests are usually performed with a test dose prior to the preparative regimen, or performed after the first dose of systemic therapy, where multiple samples are drawn at specific time points following the first dose. The samples are sent to a laboratory that performs the testing to determine the drug concentration. Pharmacokinetic evaluation of busulfan dosing, as in the examples shown above, is common. If it is not known whether or not this testing was performed, consult with a transplant physician.

Indicate if pharmacokinetics were performed to determine preparative regimen drug dosing. If “yes,” continue with question 244. If “no,” continue with question 248.

**Questions 244-247: Specify drugs:**

Indicate which drug(s) were pharmacokinetically tested. If “other” is chosen, specify the drug in question 247.
Q248-264: Socioeconomic Information

Question 248: Is the recipient an adult (18 years of age or older) or emancipated minor?

Indicate if the recipient is 18 years of age or older, or if under 18, has been declared an emancipated minor by law. An emancipated minor is a child who has been granted the status of adulthood by a court order or other formal arrangement.

If “yes,” continue with question 249. If “no,” continue with question 250.

Question 249: Specify the recipient’s marital status:

Report the recipient’s marital status as of the date of HCT. If the recipient is in a same-sex partnership, but they are not legally married in their state, report “married or living with a partner.”

Questions 250-251: Specify the category which best describes the recipient’s current occupation: (if the recipient is not currently employed, check the box which best describes his/her last job.)

Report the recipient’s occupation category prior to illness.

If the recipient is unemployed, select the option that best describes his/her most recent job.

If the recipient is “under school age,” select this option, and continue with question 253.

The “other, specify” category should only be used if the recipient’s occupation does not fit into one of the broad occupation categories listed. Please review the text associated with each answer to ensure that the occupation is being reported within the correct category. One common oversight is the reporting of “other” when the recipient’s occupation actually fits best in the “Professional, technical, or related occupation” category.

Question 252: What is the recipient’s current or most recent work status prior to illness?

The question on the form currently refers to the recipient’s current or most recent work status prior to the illness; however, the intent of the question is to capture the recipient’s most recent work status prior to the start of the preparative regimen.

Report the recipient’s most recent work status prior to the preparative regimen. This refers to the employment status at the time in which they were no longer able to work due to the illness or due to preparation for their transplant. If the recipient is on medical leave other than medical disability (such as...
short-term or long-term medical leave), report their employment status prior to the start of their leave. If they are on medical disability, select “medical disability.”

**Example 1.**
Patient was diagnosed with AML and had been working a full-time job. The patient was on a medical leave as the AML treatment prevented them from returning to work prior to the HCT. The correct option to choose would be “Full time.”

**Example 2.**
Patient was diagnosed with Multiple Myeloma and had been working a full-time job. Due to treatment related side effects, the patient had to reduce their hours and only work part-time. The correct option to choose would be “Part time, due to illness” & not “Full time”. Full time would not be chosen because the most recent status of their employment was part time. Full time would have been chosen had the recipient stopped working and was on a medical leave from their employer due to their illness.

**Example 3.**
Patient was diagnosed with Non-Hodgkin’s Lymphoma and worked part time during her treatment. Following initial therapy, the recipient began working full time. After the recipient’s retirement, her annual scan showed relapse, treatment began again and the recipient proceeded to transplant. “Retired” would be reported on the form.

If the recipient’s occupation was reported as “student” in question 250, specify “full time,” “part time,” or “unknown” in question 252.

**Question 253: What is the highest educational grade the recipient completed?**
Report the recipient’s highest completed educational level as of the date of HCT. If the recipient is a student who is currently in the middle of a school year, indicate the previous education level completed.

**Question 254: Is the recipient currently in school, or was enrolled prior to illness?**
Indicate if the recipient is a current student, or was a student prior to illness.

**Question 255: Is the recipient covered by health insurance?**
Indicate if the recipient has health insurance.

If “yes,” continue with question 256. If “no,” continue with question 264.
Questions 256-263: Specify type of health insurance:

Report the recipient’s source of health insurance as of the date of HCT. If the recipient carries more than one source, select “yes” for all that apply. For each option, select “yes” or “no” and do not leave any options blank. U.S.-based, government-sponsored health insurance should be reported in question(s) 256 and/or 257. Non-U.S.-based, government-sponsored health insurance (such as the National Health Service in the United Kingdom) should be reported in question 258. Insurance purchased through an U.S. Affordable Care Act Government Exchange should report this in questions 262-263. If the recipient has a health insurance that is not listed, select “yes” for “other” and specify the health insurance in question 263.

Question 264: Specify the recipient’s combined household gross annual income: (include earnings by all family members living in the household, before taxes.) (For U.S. residents only)

Indicate the sum of the before-tax annual incomes for all family members living in the recipient’s household. If the recipient decides not to provide this information, select “recipient declines to provide this information.” If annual income is only known for some of the income earners in the house or if it is not known what the household’s gross annual income is, select “unknown.”
2004: Infectious Disease Markers

Form 2004 will come due in the following instances:

- Non-NMDP unrelated donor (TED or CRF track)
- Non-NMDP unrelated cord blood (TED or CRF track)
- Related cord blood (TED or CRF track)
- HLA-identical sibling (CRF track or when consented for “Research Sample Repository” on TED track)
- HLA-matched other relative or HLA-mismatched relative (CRF track or when consented for “Research Sample Repository” on TED track)

If the donor or cord blood unit was secured through the NMDP, IDM test results will be reported by the donor center on NMDP Forms 24 and 50, or will be submitted by the cord blood bank through CORD Link®.

Infectious diseases result from pathogens that enter the human body and multiply. Examples of pathogens include viruses, bacteria, fungi, and parasites. Infectious diseases may be transmitted through liquids, food, body fluids, contaminated objects, or airborne particles.

An Infectious Disease Marker (IDM) indicates if an individual currently has, or previously has had, an infectious disease that could be transferred to another person.

- Antibody testing assesses whether an individual’s immune system recognizes an antigen presentation, which indicates previous exposure to the pathogen.
- Antigen testing, such as testing for the presence of the Hepatitis B surface antigen, assesses whether the individual has an active infection, where the pathogen is present in the blood. Antigen testing is done because the individual may not yet have developed antibodies against the pathogen at the time of infection.

The purpose of IDM testing is to assess the donor’s exposure to infectious diseases and the likelihood of their transmitting a disease to the recipient.

For a glossary of terms used in this section of the manual, see Appendix B.

Q1-9: Donor/Cord Blood Unit Identification
Q10-46: Infectious Disease Markers

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual
can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please [click here](#) or reference the retired manual section on the [Retired Forms Manuals](#) webpage.

<table>
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<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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<td>2004: Infectious Disease Markers</td>
<td>Add</td>
<td>Added the following text to Q10-46: Infectious Disease Markers section: If testing is only performed on the harvested product and not on the peripheral blood sample, report those samples accordingly.</td>
</tr>
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<td>05/16/2015</td>
<td>2004: Infectious Disease Markers</td>
<td>Add</td>
<td>Added the following text to question 20: “Non-U.S. centers should answer this question, regardless of FDA licensure.”</td>
</tr>
</tbody>
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Q1-9: Donor/Cord Blood Unit Identification

**Question 1: Specify non-NMDP donor**

Indicate whether the reported IDMs are for a related donor (peripheral blood stem cells or bone marrow), an unrelated donor with product procured from a source other than the NMDP (peripheral blood stem cells or bone marrow), or a non-NMDP cord blood unit (report related or autologous cord blood units as non-NMDP cord blood units).

If the donor is related to the recipient, continue with question 4. If the donor is not related to the recipient and the donation is not an NMDP product, continue with question 2. If the product is a cord blood unit obtained from a non-NMDP bank, including related and autologous cord blood products, continue with question 3.

**Question 2: Non-NMDP unrelated donor ID**

Specify the unrelated donor identification number used by the donor registry to identify and track the [peripheral blood stem cell or bone marrow] donor. Continue with question 4.

**Question 3: Non-NMDP cord blood unit ID**

Specify the cord blood unit identification number used by the cord blood bank to identify and track the unit. Continue with question 4.

**Questions 4-5: Date of birth (donor/infant)**

Indicate whether the donor’s or infant cord donor’s date of birth is “known” or “unknown.” If “known,” report the donor’s or infant cord donor’s date of birth in question 5; if the date of birth is known, it is not necessary to complete questions 6-7 specifying the donor or infant cord donor age. If “unknown,” continue with question 6.

**Questions 6-7: Age**

Indicate whether the donor’s or infant cord donor’s age at the time of product collection is “known” or “unknown.” If “known,” report the donor or infant cord donor’s age at the time of product collection in question 7. If donor is less than one year old, report age in months rounded to the nearest whole month. If the product was collected at birth, report “0” months. If “unknown,” continue with question 8.
Question 8: Sex (donor/infant)

Indicate the biological sex of the product donor or infant cord donor.

Question 9: Who is being tested for IDMs?

Indicate whether the donor (for peripheral blood stem cells and/or bone marrow products), mother of an infant cord donor, or cord blood unit itself is being tested for IDMs. Maternal IDMs and cord blood unit IDMs apply only to cord blood products; if both maternal and cord blood IDMs are available, report the results from cord blood unit testing. Cord blood banks send documentation accompanying the cord that will specify IDM results and the source of the specimen sent for IDM testing; most cord blood banks perform IDM testing on maternal serum due to the limited volume and cell count of cord blood units.
Q10-46: Infectious Disease Markers

Report the final test results. Final test results could refer to either the initial screening test or the confirmatory test. If a screening test is negative, a confirmatory test might not be done. In this case, use the screening test as the final test result. However, if a screening test is positive, a confirmatory test may be done. In this case, use the confirmatory test as the final test result. If testing is only performed on the harvested product and not on the peripheral blood sample, report those samples accordingly.

When reporting inconclusive or indeterminate test results, leave the results data field blank in the FormsNet application and override the error as “unknown.”

Hepatitis B Virus (HBV)

Hepatitis B infection is caused by the hepatitis B virus (HBV). Hepatitis B is spread through infected blood and other body fluids. Signs and symptoms of infection generally occur 60-150 days after exposure and include fever, fatigue, nausea, vomiting, and jaundice (secondary to liver inflammation). Patients with an acute hepatitis B infection generally do not require treatment; approximately 95% of adults who get acute hepatitis B will recover without developing chronic hepatitis B infection. Chronic hepatitis B infection is generally monitored for progression or evidence of liver damage, at which point patients may be treated with antiviral drugs. Chronic hepatitis B infection can lead to liver scarring (cirrhosis) and liver cancer (hepatocellular carcinoma). In the United States, the hepatitis B vaccine is now part of the routine childhood vaccination schedule.

Question 10: Hepatitis B surface antigen (HBsAg)

The hepatitis B surface antigen is a protein expressed on the surface of the hepatitis B virus. Its presence in the blood serum indicates acute or active chronic infection. In acutely infected patients, blood will test HBsAg positive within one to nine weeks of exposure to the virus. Patients who do not go on to develop chronic infection will be surface antigen negative by 15 weeks after the onset of symptoms. Chemiluminescent immunoassay (CIA), electrochemiluminescent immunoassay (ECLIA), or enzyme-linked immunosorbent assay (ELISA) are used to test for the presence of hepatitis B surface antigens; research indicates CIA and ECLIA may be more sensitive for detecting low levels of HBsAg. Positive HBsAg results require confirmation with specific antigen neutralization.

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 11.

If HBsAg testing was not done, indicate “not done” and continue with question 12.
Question 11: Date sample collected

Indicate the date the sample was collected for infectious disease marker testing.

Question 12: Hepatitis B core antibody (Anti-HBc)

The total hepatitis B core antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of the core antigen by liver cells. Since core antigen is present only in infected liver cells and cannot be detected in the blood of an infected individual, only core antibody is tested, since it circulates in the peripheral blood. After infection, total core antibodies will persist for life. Presence of core antibodies can indicate active and/or prior infection, but hepatitis core antibodies will not be present in individuals with no history of natural infection with HBV. This means that vaccinated individuals will not be anti-HBc positive because vaccination results in the body developing antibodies to the hepatitis B surface antigen. Chemiluminescent immunoassay (CIA), enzyme-linked immunosorbent assay (ELISA), or Elecsys anti-HBc is used to test for the presence of hepatitis B core antibodies. Currently, there is no licensed confirmatory test for anti-HBc in the United States; confirmation of antibody presence is done by performing a second anti-HBc test using a different manufacturer’s test kit.

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 13.

If anti-HBc testing was not done, indicate “not done” and continue with question 14.

Question 13: Date sample collected

Indicate the date the sample was collected for infectious disease marker testing.

Hepatitis C Virus (HCV)

Hepatitis C infection is caused by the hepatitis C virus (HCV). Hepatitis C is generally spread through infected blood. Newly infected individuals are generally asymptomatic, though signs and symptoms of infection, similar to those seen in other viral hepatitis infections, can develop. Since acute hepatitis C infection is generally asymptomatic, it is rarely identified or treated during the acute infection stage. Approximately 15-25% of infected individuals will clear the virus without treatment, and will not develop chronic hepatitis C infection. Chronic hepatitis C infection can lead to chronic liver disease and/or scarring.
of the liver (cirrhosis); chronic HCV is the leading indication for liver transplant in the United States. Currently no approved vaccination for hepatitis C exists.

**Question 14: Hepatitis C antibody (Anti-HCV)**

The total hepatitis C antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of antigens by the hepatitis C virus. Antibodies can generally be detected as soon as four weeks after exposure and will persist for life. Enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA) is used to screen for hepatitis C antibodies; confirmatory testing is done by recombinant immunoblot assay (RIBA). A positive ELISA or CIA result without confirmation by RIBA is considered an indeterminate result, unless HCV RNA is detected in the blood by PCR.

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 15.

If anti-HCV testing was not done, indicate “not done” and continue with question 16.

**Question 15: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Human T-Lymphotrophic Virus (Anti-HTLV I/II)**

Human T-lymphotropic viruses include two distinct and separate retroviruses, HTLV-1 and HTLV-2. In 2005 two additional HTLV virus types (HTLV-3 and HTLV-4) were discovered and found to be closely related to the two originally known lymphotropic viruses. The mechanism of transmission of HTLV-1 and HTLV-2 is somewhat uncertain, but believed to be through exposure to blood or other body fluids, or through vertical transmission (maternal-fetal transmission). Patients infected with HTLV-1 or HTLV-2 are generally asymptomatic, and there is currently no treatment or vaccine. Infection with HTLV-1 is associated with an increased risk of T-cell leukemia/lymphoma. Patients with HTLV-1 or HTLV-2 are also at risk for HTLV-associated myelopathy, also known as tropical spastic paraparesis, a progressive and permanent disease of the central nervous system.

**Question 16: Human T-Lymphotrophic Virus antibody (Anti-HTLV I/II)**

Testing for antibodies to HTLV is typically done by enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). The immunoassays are typically combined and will detect antibodies to HTLV-1 and HTLV-2. There is no way to determine if a positive result is due to antibodies to HTLV-1, HTLV-2, or both. Currently, there is no licensed confirmatory test for anti-HTLV I/II in the United States; confirmation of antibody presence is done by performing a second anti-HTLV I/II test using a different manufacturer’s test kit.
Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 17.

If anti-HTLV I/II testing was not done, indicate “not done” and continue with question 18.

**Question 17: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Human Immunodeficiency Virus (HIV)**

HIV infection is caused by exposure to one of two viruses, either HIV-1 or HIV-2. HIV-2 is less virulent and has a longer incubation period than HIV-1. Both types of HIV progressively destroy CD4+ cells, which include T-helper cells, monocytes, and their derivatives (macrophages and dendritic cells), and are an important part of the body's immune defense. HIV can lead to acquired immunodeficiency syndrome (AIDS), a condition in which the immune system begins to fail, leading to life-threatening opportunistic infections. Mechanism of HIV transmission is through exposure to blood or other body fluids, or through vertical transmission (maternal-fetal transmission).

**Question 18: Human Immunodeficiency Virus p24 antigen (HIV-1 p24 antigen)**

The HIV p24 antigen is a viral core protein that is detectable in the blood during acute infection; it is detectable earlier than HIV antibody. The p24 antigen appears approximately two weeks after exposure and will be present in the blood for three to five months. Once antibodies to HIV are detectable in the blood, p24 antigen is usually no longer detectable by immunoaassay due to antigen-antibody binding. Enzyme-linked immunosorbent assay (ELISA) is used to test for the presence of p24 antigen; it may be done in conjunction with antibody testing in order to detect the virus in all stages of infection. Positive p24 antigen results require confirmation with specific antigen neutralization.³

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 19.

If HIV-1 p24 antigen testing was not done, indicate “not done” and continue with question 20.

If HIV-1 p24 testing was performed but results are not being reported to CIBMTR (for example, donor declines to release results), indicate “not reported” and continue with question 20.

**Question 19: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Question 20: Was FDA licensed NAT testing for HIV-1/HCV performed?**

Nucleic acid testing (NAT) is a combination PCR test that detects the presence of viral genes rather than antigens or antibodies. This test allows earlier detection and provides more sensitivity than previously used tests.

If the test results include HBV NAT testing or if a non-FDA licensed NAT test was used, report these results under question 43, *Other Infectious Disease Marker*.

If FDA-licensed NAT testing was used to assess the patient for presence of HIV-1 and/or HCV RNA, check “yes” and continue with question 21. If no FDA-licensed NAT testing was used to assess the patient for presence of HIV-1 or HCV RNA, check “no” and continue with question 25.

Non-U.S. centers should answer this question, regardless of FDA licensure.

**Question 21: Human Immunodeficiency Virus-1 (HIV-1) NAT**

Report the laboratory result as “positive” or “negative,” and continue with question 22.

If HIV-1 NAT testing was performed but results are not being reported to CIBMTR (for example, donor declines to release results), indicate “not reported” and continue with question 23.

**Question 22: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Question 23: Hepatitis C (HCV) NAT**

Report the laboratory result as “positive” or “negative,” and continue with question 24.

**Question 24: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Question 25: Anti-HIV 1 and anti-HIV 2**

The HIV-1 and HIV-2 antibodies are produced by the body in response to the antigens presented by the HIV-1 and HIV-2 viruses, such as p24 (HIV-1) core antigen and p26 (HIV-2) core antigen. Antibodies are not detectable as early during the course of infection as the viral antigens, but will persist for the patient’s
lifetime once developed. Enzyme-linked immunosorbent assay (ELISA) is used to test for the presence of HIV-1 and HIV-2 antibodies. Most laboratories will utilize a combined assay that detects both viral antibodies, but in some cases they will be done as separate tests. Positive HIV-1 antibody results require confirmation by western blot, which uses gel electrophoresis to detect specific proteins. Currently, there is no licensed confirmatory test for anti HIV-2 in the United States; confirmation of antibody presence is done by performing a second anti HIV-2 test using a different manufacturer’s test kit.

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative) only if the patient was evaluated for antibodies to both HIV-1 and HIV-2. Continue with question 26.

If the patient was only assessed for antibodies to one virus, report “not done” and continue with question 27.

If no anti HIV-1 and anti HIV-2 testing was done, indicate “not done” and continue with question 27.

If anti HIV-1 and anti HIV-2 testing was performed but results are not being reported to CIBMTR (for example, donor declines to release results), indicate “not reported,” and continue with question 27.

Question 26: Date sample collected

Indicate the date the sample was collected for infectious disease marker testing.

Syphilis

Syphilis is a bacterial disease that spreads by contact with open syphilis sores that generally occur on the external genitalia and anus. It can also be spread through transmission from mother to fetus, also known as “vertical transmission.” It is caused by Treponema pallidum bacterium and can be treated with antibiotics; in the early stages of disease, syphilis is generally curable. Late stage syphilis—generally untreated or resistant disease—can cause permanent damage to internal organs or lead to neurosyphilis, where the bacterium invades the central nervous system.

Question 27: Serologic test for syphilis (STS)

Serologic testing for syphilis includes several testing methods which are either nontreponemal or treponemal. Examples of nontreponemal testing are Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) testing. Nontreponemal testing includes any evaluation done to detect antiphospholipid antibodies that are created by the body in response to syphilis infection; however, these antibodies are not specific for Treponema pallidum, and may also be created as response to HIV, malaria, pneumonia, or Lyme disease. Confirmatory testing must be done with treponemal methods for any positive result. Treponemal testing utilizes Treponema pallidum or its components to test for antibodies specific to syphilis infection. Treponemal testing includes fluorescent treponemal antibody absorption (FTA-ABS),
microhemagglutination assay for antibodies to *Treponema pallidum* (MHA-TP), and *Treponema pallidum* hemagglutination assay (TPHA).

Report the laboratory result as "reactive" (positive) or "non-reactive" (negative), and continue with question 28.

If STS testing was not done, indicate “not done” and continue with question 29.

**Question 28: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Cytomegalovirus (CMV)**

Cytomegalovirus (CMV), also known as human herpes virus 5 (HHV5), is one of the *Herpesviridae* family and is very common. It is estimated that 50-80% of people in the United States are infected by age 40. In healthy individuals, infection with CMV may not lead to any symptoms; however, the virus will lay dormant in the body after initial infection and can reoccur. In immunocompromised patients, such as immunosuppressed transplant recipients or HIV/AIDS patients, the virus can have serious consequences such as pneumonia, liver failure, and death.

**Question 29: Cytomegalovirus antibody (Anti-CMV) (IgG or Total)**

Testing for antibodies to CMV is typically done by enzyme-linked immunosorbent assay (ELISA) or latex agglutination testing. These test methods can be used to detect IgM and/or IgG, which are both antibodies to CMV. The presence of IgM antibodies indicates a recent or current infection, usually within the past six months. The presence of IgG antibodies indicates a previous infection and confers a long-term immune response to the virus. All other factors being equal, CMV-negative products are generally preferred for CMV-naïve recipients. Results may be expressed as quantified antibody titer. In this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative.4

Report the laboratory result as "reactive" (positive) or "non-reactive" (negative), and continue with question 30. A positive IgM or IgG assay is considered a "positive" or "reactive" result. Any previous history of positive antibody assay can be reported as a "positive" or "reactive" test result, even if the donor was not retested. All CMV testing on cord blood units should be reported as "non-reactive." If IDM testing for a cord blood unit was done on maternal serum, report the documented testing result.

If anti-CMV testing was not done, indicate “not done” and continue with question 31.
Question 30: Date sample collected

Indicate the date the sample was collected for infectious disease marker testing.

**West Nile Virus (WNV)**

West Nile Virus (WNV) is part of the *Flaviviridae* family and can infect birds, humans, and other mammals. It is spread by exposure to infected blood, most commonly through a mosquito vector. It can also be spread through transmission from mother to fetus (also known as “vertical transmission”), blood transfusions, organ transplant, or needlesticks. Mild or moderate symptoms of WNV may include fever, tiredness, headache and body aches, skin rash, and swollen lymph nodes. Severe symptoms of WNV include encephalitis, myelitis, and meningitis.

**Question 31: West Nile Virus NAT (WNV-NAT)**

Nucleic acid testing (NAT) is a PCR test that detects the presence of viral genes (WNV RNA) rather than antigens or antibodies. This test allows earlier detection and is more sensitive than antibody testing.

Report the laboratory result as “positive” or “negative,” and continue with question 32. Do not report WNV enzyme-linked immunosorbent assay (ELISA) testing results; report this or any other WNV or anti-WNV testing under “Other Infectious Disease Marker” in questions 43-46.

If WNV-NAT testing was not done, indicate “not done” and continue with question 33. Do not use the “not applicable” option; “not done” is the most appropriate response for all situations in which WNV-NAT testing was not done.

**Question 32: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Chagas (T. cruzi)**

Chagas disease is caused by the parasitic protozoan *Trypanosoma cruzi* (T. cruzi), which is endemic in South America, Central America, and the Caribbean. Chagas is spread through exposure to infected blood, most commonly through an insect vector such as triatomine bugs. It can also be spread through transmission from mother to fetus (also known as “vertical transmission”), blood transfusions, organ transplant, or needlesticks. In acute infection, there are rarely severe symptoms; most cases are asymptomatic or will exhibit generalized, non-specific symptoms. Treatment with anti-parasitic drugs during
the acute phase is often curative. Of the individuals who are untreated and enter the chronic phase of infection, only 20-40% will ever have signs and symptoms related to Chagas disease. Symptomatic Chagas disease can affect the nervous, digestive, and cardiac systems and can be very severe, even resulting in death.

**Question 33: Chagas**

Testing for antibodies to *T. cruzi* is generally done by enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). If active infection is suspected, another evaluation, such as PCR, may be done to confirm and identify the strain of infection. In 2011, the FDA approved a more specific immunoassay that evaluates the donor for antibodies to specific excreted-secreted antigens presented by the *T. cruzi* pathogen. This assessment is intended to be a supplemental test for individuals who have been repeatedly reactive to the previously approved immunoassays.

Report the laboratory result as “positive” or “negative,” and continue with question 34.

If Chagas testing was not done, indicate “not done” and continue with question 35.

**Question 34: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Herpes Simplex Virus (HSV)**

Herpes Simplex Virus includes two viruses, HSV-1 and HSV-2, which are two of the human herpes viruses (*Herpesviridae* family). Other human herpes viruses include cytomegalovirus (CMV), Epstein-Barr virus (EBV), and varicella zoster virus (VZV). HSV-1 is typically manifested as skin lesions or lesions of the oral mucous membranes; it may also infect the genitalia, but this is less common. HSV-2 is typically manifested as lesions of the external genitalia. Both HSV-1 and HSV-2 are spread through contact with lesions during active infection; HSV-1 can be spread through saliva. After initial infection, the virus will lay dormant in the body and can reoccur. Stress, fatigue, and infection can all cause the virus to be reactivated. According to data from 1999-2004, the seroprevalence of HSV-1 in individuals in the United States between ages 14-49 is estimated at 57.7%, while the seroprevalence of HSV-2 for the same population is estimated at 17.2%.


**Question 35: Herpes simplex virus antibody (Anti-HSV)**

Testing for antibodies to HSV is typically done by enzyme-linked immunosorbent assay (ELISA), glycoprotein G-specific immunoblot assay, or Western Blot. These immunoassays detect antibodies to both
HSV-1 and HSV-2, though the results will specify whether detected antibodies are specific to HSV-1 or HSV-2 (or both). Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative.

Report the laboratory result as “positive” or “negative,” and continue with question 36. If either HSV-1 or HSV-2 antibodies are detected, report “positive.”

If anti-HSV testing was not done, indicate “not done” and continue with question 37.

**Question 36: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Epstein-Barr Virus (EBV)**

Epstein-Barr Virus (EBV) is one of the human herpes viruses (*Herpesviridae* family). EBV infection may cause infectious mononucleosis, particularly in young adults. Infectious mononucleosis symptoms include fever, sore throat, lymphadenopathy, and fatigue. After initial infection, the virus will lay dormant in the body and can reoccur; recurrence of EBV is often subclinical. Late events associated with prior EBV infection include Burkitt’s lymphoma, post-transplant lymphoproliferative disorder (PTLD), and nasopharyngeal carcinoma.

**Question 37: Epstein-Barr virus antibody (Anti-EBV)**

Testing for antibodies to EBV is typically done by enzyme-linked immunosorbent assay (ELISA). This immunoassay can be used to detect IgM and/or IgG antibodies to EBV. The presence of IgM antibodies indicates a recent or current infection, usually within the past four to six months. Presence of IgG antibodies indicates a previous infection and confers long-term immune response to the virus. Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative.

Report the laboratory result as “positive,” “negative,” or “inconclusive,” and continue with question 38.

If anti-EBV testing was not done, indicate “not done” and continue with question 39.

**Question 38: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.
Varicella Zoster Virus (VZV)

Varicella zoster virus (VZV) is one of the human herpes viruses (Herpesviridae family). VZV, known as chickenpox with its initial presentation, manifests as pruritic skin blisters and typically first presents in childhood. After the initial infection, the virus will lay dormant in the body and can reoccur. Recurrence results in herpes zoster, more commonly known as shingles, which manifests as a painful, blistering skin rash.

Question 39: Varicella zoster virus antibody (Anti-VZV)

Testing for antibodies to VZV is generally done by fluorescent-antibody-to-membrane-antigen (FAMA), enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). These immunoassays can be used to detect IgM and/or IgG antibodies to VZV. Presence of IgM antibodies indicates a recent or current infection, usually within the past four to six months. Presence of IgG antibodies indicates a previous infection and confers a long-term immune response to the virus. Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative.

Report the laboratory result as “positive” or “negative,” and continue with question 40.

If anti-VZV testing was not done, indicate “not done” and continue with question 41.

Question 40: Date sample collected

Indicate the date the sample was collected for infectious disease marker testing.

Toxoplasmosis

Toxoplasmosis is caused by the parasitic protozoan Toxoplasma gondii, or T. gondii. Toxoplasmosis is spread through ingestion of contaminated food or water, or contact with infected cat feces. T. gondii infection is usually subclinical in healthy individuals, but infection can cause serious symptoms in pregnant women and immunocompromised individuals. Chronic, dormant T. gondii infection may follow initial exposure, and can then reoccur. Severe toxoplasmosis can affect the brain, eyes, and other organs and can cause permanent organ damage.

Question 41: Toxoplasmosis

Testing for antibodies to T. gondii is generally done by enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). These immunoassays can be used to detect IgM and/or IgG antibodies to T. gondii. The presence of IgM antibodies indicates a recent or current infection, usually within the past four to six months. The presence of IgG antibodies indicates a previous infection and confers a
long-term immune response to the virus. Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative. Confirmatory testing is available to verify a positive serological result; this is done by Toxoplasma Serological Profile (TSP), which is a panel of multiple antibody ELISAs and agglutination testing.

Report the laboratory result as “positive” or “negative,” and continue with question 42.

If Toxoplasmosis testing was not done, indicate “not done” and continue with question 43.

**Question 42: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Other Infectious Disease Marker**

Testing may be done for antibodies to pathogens other than those already listed on this form. If the donor was tested for any other infectious disease markers, report in questions 43-46. Questions 44-46 can be duplicated to report multiple additional IDM results.

Examples of other testing that may be reported as an “other infectious disease marker” include:

- Anti-HBs
- Anti-HBe
- WNV by ELISA
- Lyme disease

**Question 43: Other infectious disease marker**

Indicate if the donor was tested for an IDM other than those already listed on this form; do not report PCR results. If the donor was tested for other IDMs, check “yes” and continue with question 44. If the donor was not tested for any other IDMs, check “no” and continue with signature section.

**Question 44: Date sample collected**

Indicate the date the sample was collected for infectious disease marker testing.

**Question 45: Specify test and method**

Specify the pathogen(s) evaluated, the immunoassay or other test used, and the immunoglobulins measured.
Question 46: Specify test results

Report the qualitative laboratory results of the IDM (ex: reactive/non-reactive); do not report quantified titer levels.
2005: Confirmation of HLA Typing

For transplants using an NMDP donor or cord blood unit, the donor’s HLA typing is reported on NMDP Form 22 (Confirmation of Donor HLA Typing) and the recipient’s HLA typing is reported on NMDP Form 117 (Final Recipient HLA Typing).

In all other situations, the Confirmation of HLA Typing form (Form 2005) is used to report HLA typing for both the donor and recipient on the Transplant Essential Data (TED) and comprehensive report form (CRF) tracks. This includes:

- Non-NMDP unrelated donor
- Non-NMDP unrelated cord blood unit
- Related cord blood unit
- HLA matched relative donor
- HLA mismatched relative donor
- Recipient of any of the donor types listed above
- Match siblings/syngeneic recipients and donors participating in the Related HCT Specimen Repository

A separate Form 2005 should be completed for each non-NMDP donor, recipient, or cord blood unit; however, only the recipient form is required for syngeneic transplants and HLA identical siblings. Both maternal and paternal typing should be submitted, if available, for all mismatched related donor transplants on the CRF track. Additionally, cord blood maternal typing should be submitted, if available, for all unrelated cord blood transplants on the CRF track. Maternal typing is requested in addition to, and not in place of, typing performed on the donor / CBU. Typing on the donor / CBU must be reported when meeting any of the descriptions above.

If the recipient is receiving a subsequent HCT from the same donor and HLA Typing Forms have already been completed for the first HCT, the center does not need to complete a second set of HLA Typing Forms for the subsequent infusion. However, if a recipient is receiving a subsequent HCT from a different donor fitting one of the descriptions above, the HLA Typing Form must be completed for the new donor.

The human immune system recognizes and defends against threats from outside the body. An important component of the immune system is the human leukocyte antigen (HLA) genes. These genes produce proteins, some of which are expressed on the surface of cells. These surface proteins allow cells to recognize self from non-self. Cells with matching proteins are recognized as self and passed over. However, when the proteins do not match between cells, one cell is identified as non-self, and an immune reaction is triggered to destroy it.
If the HLA of a donor and a recipient do not match closely, the immune response could result in the recipient’s body attacking the transplanted cells (resulting in graft failure), or the transplanted cells attacking the recipient’s body (graft-versus-host disease).

HLA genes are divided into three classes. The two classes that are important in matching donors and recipients are class I (HLA-A, B, C) and class II (includes HLA-DR, DQ). All HLA genes are encoded on an area of chromosome six known as the Major Histocompatibility Complex (MHC).

Finding a good donor-recipient HLA match can be difficult because HLA is highly polymorphic, or variable. It can be completely unique to an individual. Since DNA is inherited from parents, the likelihood of a complete match is greater between full biological siblings than two unrelated individuals. Each individual has two copies of chromosome six (one from each parent). This means that each parent will be a haploidentical (half) match. A full sibling will have a 25% chance of being an identical HLA match, a 25% chance of being completely non-identical, and a 50% chance of being a haploidentical match.

**Figure 1. Example of Single HLA-A Locus Inheritance**

<table>
<thead>
<tr>
<th>HLA-A Heredity</th>
<th>Biological Mother</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biological Father</strong></td>
<td>HLA-A*01</td>
</tr>
<tr>
<td>HLA-A*02</td>
<td>01, 02</td>
</tr>
<tr>
<td>HLA-A*24</td>
<td>01, 24</td>
</tr>
</tbody>
</table>

The nomenclature (naming system) of HLA is an ever-evolving field, with an international committee dedicated to maintaining standards for identifying the genes and their allele sequences. Allele names consist of 3 to 5 parts, depending on what is known about that individual allele.
Figure 2. HLA Nomenclature

The HLA prefix will precede the specific HLA locus (gene), which will be separated from allele-specific information by an asterisk. The first field will refer to a broad group of alleles (otherwise known as the “allele family”); this designation will be separated from the next field by a colon. The second field will refer to the specific allele, which yields a specific HLA protein. Third and fourth fields may be specified, but are considered less important since they represent differences at a DNA level, rather than at a level of protein expression, due to a synonymous coding region (exon) or substitution in the non-coding region of the gene (intron). The name may be followed by a letter, which can alter the meaning of the preceding nomenclature. For example, the letter “N” signifies a null allele that does not test serologically.

DNA testing is done at low, intermediate, or high resolution.

Low-resolution testing is equivalent to serologic testing that identifies the allele group as represented by the first field of an HLA name (e.g., HLA-A*02).

Intermediate-resolution testing is molecular testing that may have remaining ambiguities. It reports allele groups that may contain 2 to 100 or more alleles. The nomenclature for these ambiguities is not internationally standardized; it is defined by the reporting lab or organization. NMDP reports frequently include letter sets that refer to possible genotypes within an allele group. Other laboratories may list all possible genotypes (e.g., DRB1*01:01 or 01:02, DRB1*01:01/01:02), where each specified allele is possible at a single locus.
High-resolution testing, or testing at the molecular level, provides further information about the gene itself, including what specific proteins will be expressed by the cells and even differences in sequence that do not impact protein expression. For cellular transplant, matching at the high resolution level is critically important.

**Complete this form specifying the recipient or donor HLA at the level it was typed.**

For a glossary of terms used in this section of the manual, see Appendix B.

**Links to Sections of the Form:**
- Q1-12: Donor/Cord Blood Unit Identification
- Q13-35: HLA Typing by DNA Technology
- Q36-41: Antigens Defined by Serologic Typing
- Q42-58: Optional Antigen Reporting

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
</table>
Q1-12: Donor/Cord Blood Unit Identification

Question 1: Specify the person for whom this typing is being done

Indicate whether the reported HLA typing is the final recipient typing, from a related donor (biological mother, biological father, or other biological relative), an unrelated donor with product procured from a source other than the NMDP, a non-NMDP cord blood unit, or maternal HLA typing for a cord blood unit with product procured from a source other than the NMDP. The HLA typing must be reported for a non-NMDP cord blood unit; maternal typing is optional. Report related or autologous cord blood units as non-NMDP cord blood units.

If the reported HLA typing is for:

- The recipient, go to question 13.
- The recipient's biological relative, go to question 5.
- PBSC or bone marrow donor not related to the recipient, go to question 2.
- Cord blood unit with typing sample taken from the cord blood unit or infant, go to question 3.
- Maternal HLA typing, go to question 3.

Question 2: Non-NMDP unrelated donor ID

Specify the unrelated donor identification number used by the donor registry to identify and track the peripheral blood stem cell or bone marrow donor. Continue with question 7.

Question 3: Non-NMDP cord blood unit ID

Specify the cord blood unit identification number used by the cord blood bank to identify and track the unit. If reporting confirmatory typing on the cord blood unit, continue with question 4. If reporting maternal HLA typing, continue with question 12.

Question 4: Is cord blood unit maternal HLA typing available?

Maternal HLA that is not inherited by the fetus, or non-inherited maternal antigens (NIMAs), may be used to select between comparable mismatched cord blood units. Studies have found that NIMA-matched cord blood transplantation may be associated with improved outcomes when compared to equivalent
NIMA-mismatched cord blood transplantation.

Indicate if the maternal HLA typing is available and continue with question 7; if yes, also complete Form 2005 reporting maternal HLA typing. The form will not come due on its own, so must be added by the data manager.

**Question 5: Specify recipient’s biological relative and typing**

If confirmation of HLA typing is being reported on a donor who is biologically related to the recipient, specify their relationship.

- **Mother:** The HLA typing is being reported on a donor who is the recipient’s biological mother.
- **Father:** The HLA typing is being reported on a donor who is the recipient’s biological father.
- **Sibling:** The HLA typing is being reported on a donor who shares the same biological mother and father.
- **Syngeneic twin:** The HLA typing is being reported on a donor who is the recipient’s monozygotic (identical) twin. Monozygotic twins arise from the division of a single implanted egg, resulting in two embryos that share the same chromosomal profile.
- **Fraternal twin:** The HLA typing is being reported on a donor who is the recipient’s dizygotic twin. Dizygotic twins arise from two eggs being independently fertilized and implanted, resulting in two embryos that are the same age but are unlikely to share the same chromosomal profile.
- **Child:** The HLA typing is being reported on a donor who is the recipient’s biological child.
- **Aunt:** The HLA typing is being reported on a donor who is the recipient’s biological parent’s sister.
- **Uncle:** The HLA typing is being reported on a donor who is the recipient’s biological parent’s brother.
- **Cousin:** The HLA typing is being reported on a donor who is the child of the recipient’s aunt or uncle.
- **Other biological relative:** The HLA typing is being reported on a donor who does not fit the definition of other biological relatives specified above. Specify the other biological relative’s relationship to the recipient (do not report the donor’s name) and if preliminary or confirmatory typing was done in question 6.

**Questions 7-8: Date of birth (donor/infant)**

Indicate whether the donor’s or infant cord donor’s date of birth is “known” or “unknown.” If “known,” report the date of birth in question 8. If the date of birth is known, it is not necessary to complete questions 9-10 specifying the donor’s or infant cord donor’s age. If “unknown,” continue with question 9.

**Questions 9-10: Age (donor/infant)**

Indicate whether the donor’s or infant cord donor’s age at the time of HLA typing is “known” or “unknown.” If “known,” report the donor’s or infant cord donor’s age in question 10. If the infant’s age is less than one year, report as months rounded to the nearest whole month. If the HLA typing was done at birth or
prenatally, report “0” months. If “unknown,” continue with question 11.

**Question 11: Sex (donor/infant)**

Indicate the biological sex of the donor or infant cord donor.

**Question 12: Was the person for whom this typing is being done used as the donor?**

Indicate if the reported typing is for the recipient’s biological relative selected as the donor. Reporting typing done on family members not selected as donors is optional, but may be beneficial for additional HLA studies.
Q13-35: HLA Typing by DNA Technology

Complete this section for all typing done by DNA based methods. Examples of HLA typing by DNA technology may include: sequence-specific primer (SSP), sequence-specific oligonucleotide probe (SSOP), and sequence-based typing (SBT).

DNA technology can be used to type for a single allele, combinations of alleles (allele strings), or a “generic” allele designation similar to a serologic typing result. For this reason, the number of digits reported, as well as the number of alleles, will vary.

Laboratories may use “/”, “-” or a combination of numbers and letters on the typing report as a shorthand notation for the results. Transcribe the information onto the form as directly as possible. The letters, called allele codes, will be 1 or more characters in length and represent a combination of possible alleles at a locus. The same allele combination may be reported several different ways (e.g., DRB1*01:01 or 01:02, DRB1*01:01/01:02, DRB1*01:01/02, or DRB1*01:AB).

There will be two alleles reported for each locus, unless the individual is presumed homozygous (i.e., carries two copies of the same allele) at a locus. Transcribe the first allele designation in the first box, and the second allele designation in the second box. If the person is homozygous, leave the second box blank.

Question 13: Was documentation submitted to the CIBMTR (e.g., lab report)?

Indicate if a copy of the HLA typing report is attached. Use the “Add Attachment” feature to attach a copy of the HLA typing report in FormsNet. Attaching a copy of the laboratory report assists in confirming the reporting of HLA typing and reduces the need for later data queries.

Class I

Questions 14-15: Locus A

Indicate whether the allele designations at HLA-A are “known” or “unknown.” If known, report the first A* allele and second A* allele designations in question 15; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 16. If question 14 is “unknown,” then question 36 (“A” antigens defined by serologic typing) is required.
Questions 16-17: Locus B

Indicate whether the allele designations at HLA-B are “known” or “unknown.” If known, report the first B* allele and second B* allele designations in question 17; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 18. If question 16 is “unknown,” then question 39 (“B” antigens defined by serologic typing) is required.

Questions 18-19: Locus C

Indicate whether the allele designations at HLA-C are “known” or “unknown.” If known, report the first C* allele and second C* allele designations in question 19; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 20.

Class II

Questions 20-21: Locus DRB1

Indicate whether the allele designations at HLA-DRB1 are “known” or “unknown.” If known, report the first DRB1* allele and second DRB1* allele designations in question 21; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 22.

Class II (Optional)

Questions 22-23: Locus DRB3

Indicate whether the allele designations at HLA-DRB3 are “known” or “unknown.” If known, report the first DRB3* allele and second DRB3* allele designations in question 23; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 24.

Questions 24-25: Locus DRB4

Indicate whether the allele designations at HLA-DRB4 are “known” or “unknown.” If known, report the first DRB4* allele and second DRB4* allele designations in question 25; report a single allele, a string of alleles,
or an allele code.

If “unknown,” continue with question 26.

Questions 26-27: Locus DRB5

Indicate whether the allele designations at HLA-DRB5 are “known” or “unknown.” If known, report the first DRB5* allele and second DRB5* allele designations in question 27; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 28.

Questions 28-29: Locus DQB1

Indicate whether the allele designations at HLA-DQB1 are “known” or “unknown.” If known, report the first DQB1* allele and second DQB1* allele designations in question 29; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 30.

Questions 30-31: Locus DPB1

Indicate whether the allele designations at HLA-DPB1 are “known” or “unknown.” If known, report the first DPB1* allele and second DPB1* allele designations in question 31; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 32.

Questions 32-33: Locus DQA1

Indicate whether the allele designations at HLA-DQA1 are “known” or “unknown.” If known, report the first DQA1* allele and second DQA1* allele designations in question 33; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 34.

Questions 34-35: Locus DPA1

Indicate whether the allele designations at HLA-DPA1 are “known” or “unknown.” If known, report the first DPA1* allele and second DPA1* allele designations in question 35; report a single allele, a string of alleles, or an allele code.
If “unknown,” continue with question 36.
Q36-41: Antigens Defined by Serologic Typing

Complete this section for all serologic typing. If serologic typing was not performed, leave this section blank. Report broad antigens only when your laboratory was not able to confirm typing for a known split antigen.

Each HLA locus has a serologically defined “X” antigen specificity: AX, BX, CX, DRX, DPX, and DQX. At this time, an “X” specificity is defined as “unknown but known to be different from the other antigen at that locus.” This is different from a blank specificity, which is assumed to be the same as the other antigen at that locus.” When comparisons between recipient and donor antigens involve an “X” or “blank” specificity, the “X” or “blank” is assumed to be homozygous for the antigen reported at the locus. In other words, the search algorithm treats typing containing “blank” or “X” antigens in the same manner as known homozygous typing.

Questions 36-38: Number of A antigens provided

Indicate if one or two HLA-A antigens were tested. If one antigen was tested, report the first antigen specificity in question 37 and continue with question 39.

If two antigens were tested, report the first antigen specificity in question 37 and the second antigen specificity in question 38. Continue with question 39.

Questions 39-41: Number of B antigens provided

Indicate if one or two HLA-B antigens were tested. If one antigen was tested, report the first antigen specificity in question 40 and continue with question 42.

If two antigens were tested, report the first antigen specificity in question 40 and the second antigen specificity in question 41. Continue with question 42.
Q42-58: Optional Antigen Reporting

Questions 42-44: Number of C antigens provided

Indicate if one or two HLA-C antigens were tested. If one antigen was tested, report the first antigen specificity in question 43 and continue with question 45.

If two antigens were tested, report the first antigen specificity in question 43 and the second antigen specificity in question 44. Continue with question 45.

Question 45: Specificity Bw4 present?

Bw4 refers to an epitope expressed by HLA-B alleles; epitopes are presented on the surface of the antigen and are recognized by the immune system. Bw4 and Bw6 are mutually exclusive and may confer reactivity with lymphocytes. Select “yes” if Bw4 specificity is present. Leave blank if specificity for Bw4 was not tested.

Question 46: Specificity Bw6 present?

Bw6 refers to an epitope expressed by HLA-B alleles; epitopes are presented on the surface of the antigen and are recognized by the immune system. Bw4 and Bw6 are mutually exclusive and may confer reactivity with lymphocytes. Select “yes” if Bw6 specificity is present. Leave blank if specificity for Bw6 was not tested.

Questions 47-49: Number of DR antigens provided

Indicate if one or two HLA-DR antigens were tested. If one antigen was tested, report the first antigen specificity in question 48 and continue with question 50.

If two antigens were tested, report the first antigen specificity in question 48 and the second antigen specificity in question 49. Continue with question 50.

Question 50: Specificity DR51 present?

HLA-DR51 is an HLA-DR variant that recognizes antigens from HLA-DRB5. Select “yes” if DR51 specificity is present. Leave blank if specificity for DR51 was not tested.

Question 51: Specificity DR52 present?

HLA-DR52 is an HLA-DR variant that recognizes antigens from HLA-DRB3. Select “yes” if DR52 specificity is present. Leave blank if specificity for DR52 was not tested.
**Question 52: Specificity DR53 present?**

HLA-DR53 is an HLA-DR variant that recognizes antigens from HLA-DRB4. Select “yes” if DR53 specificity is present. Leave blank if specificity for DR53 was not tested.

**Questions 53-55: Number of DQ antigens provided**

Indicate if one or two HLA-DQ antigens were tested. If one antigen was tested, report the first antigen specificity in question 54 and continue with question 56.

If two antigens were tested, report the first antigen specificity in question 54 and the second antigen specificity in question 55. Continue with question 56.

**Questions 56-58: Number of DP antigens provided**

Indicate if one or two HLA-DP antigens were tested. If one antigen was tested, report the first antigen specificity in question 57 and continue with the signature section.

If two antigens were tested, report the first antigen specificity in question 57 and the second antigen specificity in question 58. Continue with the signature section.
2006: Hematopoietic Stem Cell Transplant (HCT) Infusion

All recipients on the Comprehensive Report Form track must complete the Form 2006. Recipients on the Transplant Essential Data track must complete the Form 2006 for each product when the following product types are infused as part of the transplant:

- NMDP donor products
- NMDP and non-NMDP cord blood units

Additionally, all transplant centers (TED-only and Comprehensive Report Form) participating in the Related Sample Repository must complete the Form 2006 for all non-NMDP donor products when a research sample is collected.

For more information see General Instructions, Center Type and Data Collection Forms.

The Form 2006 is designed to capture product- and infusion-specific information for all products given to a recipient as part of a Hematopoietic Stem Cell Transplant (HCT). This includes cells given prior to the HCT for reasons other than engraftment. In addition to use in research, this information is used for quality assurance measures, both by the NMDP and the Cord Blood Banks.

If more than one type of HCT product is infused, each product type must be analyzed and reported on a separate form. Two different products from the same donor (for example, PBSC and bone marrow), require two 2006 forms; one for each product.

However, a series of collections from the same donor that uses the same collection method and mobilization cycle, even if the collections are performed on different days, should be considered a single product.

For more information see Appendix D and Appendix E.

Q1-15: Donor/Cord Blood Unit Identification
Q16-27: Pre-Collection Therapy
Q28-42: Production Collection
Q43-56: Product Transport and Receipt
Q57-108: Product Processing/Manipulation
Q109-157: Autologous Products Only
Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please [click here](#) or reference the retired manual section on the [Retired Forms Manuals](#) webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
</table>
| 2/27/19    | 2006: Hematopoietic Stem Cell Transplant (HCT) Infusion | Add                 | Added additional instruction (in red below) regarding T-Cell depletion under questions 73-95:  
**T-Cell depletion:** T-cell depletion removes some or all of the T cells in an effort to minimize GVHD. Methods of T-cell depletion include antibody affinity column, antibody-coated plates, antibody-coated plates and soybean lectin, antibody + toxin, immunomagnetic beads, CD34 affinity column plus sheep red blood cell resetting, and T-cell receptor alpha / beta depletion. |
| 2/2/18     | 2006: Hematopoietic Stem Cell Transplant (HCT) Infusion | Modify              | Removed text (struck out below) from the instructions for question 272.                                                                                                                                   |
| 1/23/18    | 2006: Hematopoietic Stem Cell Transplant (HCT) Infusion | Modify              | Added text (highlighted red below) to the instructions for question 272 to clarify hospitalization scenarios.  
*Indicate “Yes” if the donor was hospitalized for complications during or after the collection for any reason. Indicate “No” if the donor was not hospitalized as an inpatient or if the donor was admitted to an observation unit and discharged in less than 24 hours.* |
| 4/6/17     | 2006: Hematopoietic Stem Cell Transplant (HCT) Infusion | Modify              | Updated the following text on the 2006 Title Page: All recipients on the Comprehensive Report Form track must complete the Form 2006. Recipients on the Transplant Essential Data track must complete the Form 2006 for each product when the following product types are infused as part of the transplant:  
- NMDP donor products  
- NMDP and non-NMDP cord blood units |
| 12/7/15    | 2006: Hematopoietic Stem Cell                       | Modify/Add          | Edited the text regarding manipulation of products in [questions 73-95: Steps in Manipulation](#)  
If the manipulation consists of several steps, individual steps do not need to |
<table>
<thead>
<tr>
<th>Date</th>
<th>Origin</th>
<th>Action</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/3/15</td>
<td>Transplant (HCT) Infusion</td>
<td>Add</td>
<td>be reported as separate manipulations. For example, washing that is part of CD34+ expansion selection does not need to be reported as a separate manipulation. Similarly, T-cell depletion that is part of expansion does not need to be reported. If dilution is performed as part of washing, dilution does not need to be reported. In the cases above, if T-cell depletion and/or washing are done as stand-alone manipulations, they should be reported.</td>
</tr>
<tr>
<td>8/3/15</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Add</td>
<td>Added additional product analysis reporting instructions to question 158: To assist centers in reporting product analysis timepoints, the CIBMTR has developed guidelines specific to the product type being reported. … This may be different than the date testing for cell counts or cell viability was performed. [see text for full detail]</td>
</tr>
<tr>
<td>8/3/15</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Remove</td>
<td>Removed the following information bubble in question 158: This instruction is under review. If the product is thawed, but not retested prior to infusion, you can report the values prior to cryopreservation as “at infusion.” If a viability assessment is completed, ensure that it is reported accurately for the at infusion time point.</td>
</tr>
<tr>
<td>6/12/15</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Add</td>
<td>Added the following text to question 96: If antibodies were used during product manipulation, select “yes” and continue with question 97. However, it is not necessary to report antibody use as part of CD34+ enrichment using the CliniMacs, Isolex, or Miltenyi devices. If antibodies were not used, select “no” and continue with question 109.</td>
</tr>
<tr>
<td>05/16/2015</td>
<td>2006: Hematopoietic Stem Cell Transplant (HCT) Infusion</td>
<td>Add</td>
<td>Added to “Cultured (ex-vivo expansion)” under questions 73-95: If the product is expanded, also report the expansion protocol under “other” in addition to checking “cultured.”</td>
</tr>
</tbody>
</table>
**Q1-15: Donor/Cord Blood Unit Identification**

**Question 1: Specify Donor:**

Indicate the donor type for this product.

An **autologous** product has cells collected from the recipient for his/her own use.

- If the product was **autologous** (marrow, PBSC, other product), select “autologous” and continue with question 16.
- If the product was an **autologous cord blood unit**, select “autologous cord blood unit” and continue with question 5.

An **unrelated donor (allogeneic, unrelated)** is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or stepparents/children. Distinguish if the product is an NMDP product or a non-NMDP product. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank, Anthony Nolan, and StemCyte International Cord Blood Center.

- If the product was an **NMDP unrelated cord blood unit**, select “NMDP unrelated cord blood unit” and continue with question 2.
- If the product was from an **NMDP unrelated donor** (marrow, PBSC, other product), select “NMDP unrelated donor” and continue with question 3.
- If the product was from a **non-NMDP unrelated donor** and was facilitated through another registry, select “non-NMDP unrelated donor” and continue with question 4.
- If the product was a **non-NMDP cord blood unit**, select “non-NMDP cord blood unit” and continue with question 5.

A **related donor (allogeneic or syngeneic, related)** is a blood-related relative. This includes monozygotic (identical twins), non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc.

- If the product was from a **related donor** (marrow, PBSC, other product), select “related donor” and continue with question 10.
- If the product was a **related cord blood unit**, select “related cord blood unit” and continue with question 5.
Question 2: NMDP Cord Blood Unit ID:

Report the NMDP Cord Blood Unit ID. This information is included on the product label, the product insert accompanying the product, and within the NMDP search/product documentation. The ID is always numeric and begins with “9” (e.g., 9000-0000-0). If the product ID does not begin with a “9,” the product may not be an NMDP cord blood unit and the source of the product should be double-checked. Continue with question 15.

Question 3: NMDP Donor ID:

Report the NMDP Donor ID (e.g., 0000-0000-0). This ID is unique for each donor and is assigned by the NMDP. This information is included on the product label, the product insert accompanying the product, and within the NMDP search/product documentation. Continue with question 15.

Question 4: Non-NMDP unrelated donor ID: (**not applicable for related donor**)

Report the non-NMDP unrelated donor ID. Do not complete this field if the recipient has an NMDP donor, a related donor, or a cord blood donor. This ID is often located on the product label, the product insert accompanying the product, and the registry-specific search/product documentation. Continue with question 8.

Question 5: Non-NMDP cord blood unit ID: (**include related and autologous CBUs**)

Report the non-NMDP cord blood unit ID. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank and StemCyte International Cord Blood Center. This ID is often located on the product label, the paperwork accompanying the product, and registry specific search/product documentation. Enter the non-NMDP cord blood ID. Note that some cord blood banks can ship their units either through the NMDP or directly to the transplant center. Carefully review the accompanying documentation to determine which is appropriate for your unit. You may wish to consult with your center’s Transplant Coordinator, as he or she will have insight as to how the product was acquired.

Question 6: Is the CBU ID also the ISBT DIN number?

Report “yes” if the non-NMDP CBU ID is the same as the International Society of Blood Transfusion (ISBT) Donation Identification Number (DIN) and continue with question 8. If the product has an ISBT label on it, the ISBT DIN number is in the upper left-hand corner and consists of a letter followed by 12 numbers, two numbers on the end, and a letter in a box. Example below:
Please find additional information regarding the ISBT DIN numbers and traceability at http://www.iccbba.org/docs/public/introduction_traceability.pdf. For example, you may see a barcode with an alphanumeric string below it.

If the CBU ID is not the same as the ISBT DIN number, select “no” and continue with question 7.

**Question 7: Specify the ISBT DIN number:**

If you answered “yes” to question 6, report the ISBT DIN number using the letter, 12 digits, 2 numbers on end, and the letter in the box.

If you answered “no” to question 6 (the product does not have an ISBT DIN number), leave this field blank, override the error, and continue with question 8.

**Question 8: Registry or UCB Bank ID:**

Specify the registry used to obtain the adult donor or umbilical cord blood unit. The Bone Marrow Donors Worldwide (BMDW) codes have been adopted to avoid submitting the entire name and address of the donor registry.

The registry code for NMDP donors is **USA1** and for NMDP cord units is **U1CB**.

Some common banks that do not list with BMDW have been added to the FormsNet list for version 4, including St Louis Cord Blood Bank (SLCBB) and Viacord (VIAC).

If the donor was found through DKMS, report the registry that facilitated the HCT. Some registries may be listed more than once with BMDW (once for marrow/PBSC products and differently for cord blood products). Ensure that the appropriate code for the product was selected, because distribution of data is dependent on the code.

If the registry code cannot be determined using the BMDW website, select “other registry” and continue to question 9.
**Question 9: Specify Other Registry or UCB Bank:**

If the BMDW website does not list a match code for the adult donor registry or cord blood bank, provide the registry’s official name in the “Specify other registry” field.

Please ensure that the registry you are entering under “other” is not already listed in the pull-down list for question 8. Entries such as NMDP adult donors, NMDP cords, and New York Cord Bank each have their own entries above.

**Questions 10 & 11: Date of Birth (donor/infant):**

Report if the donor’s/infant’s date of birth is “known” or “unknown” for question 10. If the donor’s/infant’s date of birth is known, report the date of birth (YYYY-MM-DD) in question 11. If the donor’s/infant’s date of birth is unknown, continue with question 12.

**Questions 12 & 13: Age (donor/infant):**

Report if the donor’s/infant’s age is “known” or “unknown” for question 12. If the donor’s/infant’s age is known, report the donor’s/infant’s age at the time of product collection in question 13. Report the age in months if the recipient is less than 1 year old, otherwise report the age in years. If the donor’s/infant’s age at collection is unknown, continue with question 14.

**Question 14: Sex (donor/infant):**

Indicate the donor’s biological sex as “male” or “female.” For cord blood units, report the infant’s sex.

**Question 15: Was the product derived from an NMDP adult donor, NMDP cord blood unit, or non-NMDP cord blood unit?**

If the source of the product was an NMDP adult donor, NMDP cord blood unit, or non-NMDP cord blood unit, select “yes” and continue with question 43. If the product does not meet those criteria, select “no” and continue with question 16 in the Pre-Collection Therapy section.
Q16-27: Pre-Collection Therapy

Question 16: Did the donor receive therapy, prior to any stem cell harvest, to enhance the product collection for this HCT?

Stem cells do not typically circulate in the blood stream. Therefore, in order to increase the quantity of cells for collection, an agent is frequently given to the allogeneic donor or autologous donor-recipient. The purpose of the agent is to move the stem cells from the bone marrow into the peripheral blood where the cells can be collected by apheresis. This practice is often referred to as mobilization or priming. Occasionally, a donor may be primed using a growth factor prior to collection of bone marrow.

If the donor (including autologous donor-recipients) received therapy (such as growth factors, mobilizing agents, chemotherapy, etc.), select “yes” and continue with question 17.

If the donor did not receive therapy to enhance the stem cell product, select “no” and continue with question 28.

Question 17: Growth and mobilizing factor(s)

Examples of growth and mobilizing factors include, but are not limited to, the following:

- Epidermal growth factor – EGF
- Erythropoietin – EPO
- Fibroblast growth factor – FGF
- Granulocyte-colony stimulating factor – G-CSF
- Granulocyte-macrophage colony stimulating factor – GM-CSF
- Growth differentiation factor-9 – GDF9
- Hepatocyte growth factor – HGF
- Insulin-like growth factor – IGF
- Platelet-derived growth factor – PDGF
- Thrombopoietin – TPO
- Transforming growth factor alpha – TGF-α
- Transforming growth factor beta – TGF-β

If the donor or autologous donor-recipient received growth factors prior to the stem cell harvest to enhance the stem cell product select “yes” and continue with question 18.

If the donor or autologous donor-recipient did not receive growth factor(s), select “no” and continue with question 24.
Questions 18-23: Specify therapy(s)

Report if any of the following products were given. Select "yes" or "no" for each question.

- **G-CSF** (granulocyte-colony stimulating factor, [filgrastim, Neupogen®](#))
- **Pegylated G-CSF** ([pegfilgrastim, Neulasta®](#))
- **GM-CSF** (granulocyte macrophage-colony stimulating factor, [sargramostim, Leukine®](#))
- **Plerixafor (Mozobil®)** *

If the growth or mobilizing factor that was given is not included in the above list, select “yes” for question 22 and specify the generic name for the growth or mobilizing factor in question 23.

**Question 24: Systemic therapy (chemotherapy) (autologous only)**

Indicate if the autologous donor-recipient received systemic therapy prior to the stem cell harvest to enhance the stem cell product. Although the intended purpose of this therapy may not be to treat the recipient’s disease, occasionally there is a disease response. Therefore, also record this therapy on the Pre-HCT Disease Specific Form (Forms 20xx) as a line of therapy, if applicable.

Systemic therapies used to enhance the stem cell product may include cyclophosphamide or ICE chemotherapy ([ifosfamide, carboplatin, and etoposide](#)).

If the autologous donor-recipient received systemic therapy prior to the stem cell harvest, select “yes” and continue with question 25. If systemic therapy was not received, select “no” and continue with question 26.

**Question 25: Anti-CD20 (rituximab, Rituxan) (autologous only)**

Indicate if Anti-CD20 monoclonal antibodies (rituximab) were used during the collection of the autologous product. Although the intended purpose of this therapy may not be to treat the recipient’s disease, occasionally there is a disease response. Therefore, also record this therapy on the Pre-HCT Disease Specific Form (Forms 20xx) as a line of therapy, if applicable.

An example of systemic therapies using anti-CD20 monoclonal antibodies to enhance stem cell products is R-ICE (rituximab, ifosfamide, carboplatin, and etoposide).

**Questions 26-27: Other therapy**

If the donor or autologous donor-recipient received any other treatment prior to the stem cell harvest to enhance the stem cell product, select “yes” and specify the treatment administered in question 27.
If the donor or autologous donor-recipient did not receive any other treatment, select “no” and continue with question 28.
**Q28-42: Product Collection**

*Multiple collections versus multiple products:*
This form collects information for a single product. PBSC collected from a single mobilization event (a mobilization event is the planned administration of growth factors or systemic therapy designed to enhance stem cell collection), even when collected over several days, is considered one product.

Multiple products are collected when, for example, the donor requires another mobilization to collect a product at a later date. The collection from the second mobilization event is considered a different product and should be reported on an additional 2006 form. Also, if the mobilization method changes (e.g., plerixafor is required starting on Day 3 of collection) this is considered a different product and an additional 2006 form must be completed for the product collected with the new mobilization method.

**Question 28: Date of first collection for this mobilization:**
Report the date the stem cell collection was performed. If a collection event occurred over multiple days, enter the date the collection started (i.e., Day 1).

**Example 1:** An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. Since the collection and mobilization methods remained the same over the duration of the collection, this collection is considered one product. Report the collection start date as the date of product collection.

**Example 2:** An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. Then the recipient was given plerixafor to enhance the mobilization. Due to the change in mobilization method, this is considered two separate products, and two Form 2006s should be submitted. The date of product collection should be the first day of collection of mobilization method for which the form is being completed.

**Question 29: Was more than one collection required for this HCT?**
If more than one day of collection was required for this mobilization event, select “yes” and continue with question 30.

Do not report days of collection for a different product, as each product is reported on a separate 2006 form.

If more than one day of collection was not required, select “no.”
**Question 30: Specify the number of subsequent days of collection in this episode:**

Report the number of collection days for this product excluding the first day of collection. For example, if a collection occurred over three days, “2” should be reported for this question. For an HCT that includes multiple products, only report the total number of collection days excluding the first day for the product being reported on this form.

Complete a separate Form 2006 for each subsequent mobilization cycle. A separate Form 2006 does not need to be filled out for each collection day from the same mobilization cycle.

**Question 31: Were anticoagulants added to the product during collection?**

If anticoagulants were used during collection, select “yes” and continue with question 32. Anticoagulants are typically documented on the product bag label. Anticoagulants are often added to PBSC products.

If anticoagulants were not used during collection, select “no” and continue with question 37.

**Questions 32-36: Specify anticoagulant(s):**

More than one anticoagulant may be added to a product. Select all the anticoagulants added to the reported product. Do not leave any responses blank.

If an anticoagulant added to the product is not listed on the form, check “yes” for question 35, and specify the anticoagulant’s name in question 36.

**Question 37: Were anticoagulants added to the product before freezing?**

Report any anticoagulants that were added to the product after collection but prior to cryopreservation. This does not include anticoagulants that were added during collection and already reported on questions 31-36. Anticoagulants are typically documented on the product bag label. Anticoagulants are often added to PBSC products.

If anticoagulants were added after collection and prior to freezing, select “yes” and continue with question 38.

If anticoagulants were not added after collection and prior to freezing, select “no” and continue with question 43.

**Questions 38-42: Specify anticoagulant(s)**

More than one anticoagulant may be added to a product. Select all the anticoagulants added to the reported product. Do not leave any responses blank.
If an anticoagulant added to the product is not listed on the form, check “yes” for question 41 and specify the anticoagulant’s name in question 42.
Q43-56: Product Transport and Receipt

Question 43: Was this product collected off-site and shipped to your facility?

If the product was shipped to the transplant center from an off-site collection center, select "yes." In general, the “yes” option will be used for unrelated donors.

However, there may be circumstances where the donor resides in the same geographic location as the recipient and the collection occurred at the same facility as the transplant; in this case, the “no” option should be used.

If the product was not shipped to the transplant center from an outside facility, or if the product was collected on site then shipped off site for laboratory processing, select “no” and continue with question 57. The “no” option usually applies to autologous collections and related donors.

Question 44: Date of receipt of product at your facility:

The intent of this question is to determine the date that the transplant center assumed responsibility for the product from the collection center. Enter the date your institution became responsible for the product.

If multiple bags of the same product arrived on different days, report the date the first bag arrived at your facility.

If a contract laboratory processes the product prior to arrival at the transplant facility, report the date the product arrived at the contract laboratory.

Question 45: Time of receipt of product (24-hour clock):

Enter the exact time your institution or off-site laboratory received and became responsible for the product. Report the time using a 24-hour clock and indicate if daylight savings time or standard time was in effect. If the location of your institution or off-site laboratory does not observe daylight savings time, report the time as standard time. For more information about daylight savings time schedules, go to http://www.timeanddate.com/time/dst/.

Questions 46-47: Specify the shipping environment of the product(s):

Indicate the shipping environment of the product. If the recipient’s product was shipped in a way other than described on the list, select “other shipping environment” and specify the shipping environment in question 47. It is not necessary to provide the specific temperature of the product during shipment.
If the product is a cord blood unit, continue with question 48. For all other products, continue with question 57.

**Question 48: Was there any indication that the environment within the shipper was outside the expected temperature range for this product at any time during shipment? (Cord blood units only)**

Indicate if there was any indication that the environment within the shipper was outside the expected temperature range for this product at any time during shipment. The temperature of the shipper is generally constant and tracked using a data-logger. Mishandling of the product shipper or spikes in temperature could impact the integrity of the product.

If there was any indication that the environment within the shipper was outside the expected temperature range upon arrival at your center, a product complaint form (Form 3010) must be completed.

**Question 49: Were the secondary containers (e.g., insulated shipping containers and unit cassette) intact when they arrived at your center? (Cord blood units only)**

Indicate if the secondary containers were intact upon receipt of the cord blood unit by your center.

If the secondary containers *were not* intact upon arrival, a product complaint form (Form 3010) must be completed.

**Question 50: Was the cord blood unit stored at your center prior to thawing? (Cord blood units only)**

If the cord blood unit was stored at your center prior to thawing, select “yes” and continue with question 51.

If the cord blood unit was not stored at your center prior to thawing, select “no” and continue with question 54.

**Question 51: Specify the storage method used for the cord blood unit:**

Indicate the storage method used for the cord blood unit. The storage method is generally standard and should be documented within the laboratory at your center. Note: *liquid nitrogen* is also known as *liquid phase*.

**Question 52: Temperature during storage:**

Indicate the storage temperature used for the cord blood unit. The storage temperature is generally standard and should be documented within the laboratory at your center.

**Question 53: Date storage started:**

Report the date the cord blood unit was first stored at your center prior to thawing.
The values reported for questions 54 and 55 are from documentation supplied by the cord blood bank. Report the absolute number of cells, not per mL or per kg.

**Question 54: Total Nucleated cells: (Cord blood units only)**

Report the total nucleated cells for the cord blood product. This information is available within the documentation received with the product shipment and from the search documentation performed to select the product. These values are from the Cord Blood Bank and should not represent post-thaw values assessed at your center’s lab.

**Questions 55-56: CD34+ cells: (Cord blood units only)**

Indicate if the cord blood bank quantified CD34+ cells in the product. If the CD34+ cells were quantified, select “done” and report the total CD34+ cells for the cord blood product in question 56. This information is available within the documentation received with the product shipment and from the search documentation performed to select the product. These values are from the Cord Blood Bank and should not represent post-thaw values assessed at your center’s lab.

If the CD34+ cells were not quantified by the cord blood bank, report “not done” and continue with question 57.
**Q57-108: Product Processing/Manipulation**

**Question 57: Was a fresh product received (e.g., not frozen)? (NMDP products only)**

The intent of this question is to determine if the product shipped to the transplant center was ever cryopreserved. Indicate “yes” if the product was received fresh (and never cryopreserved) and continue with question 58. If the product was frozen, select “no” and continue with question 59. If the product was a cord blood unit, select “not applicable (cord blood unit)” and continue with question 59.

**Question 58: Was the entire fresh product cryopreserved at your facility prior to infusion? (NMDP products only)**

Indicate if the fresh NMDP product that arrived at your center was cryopreserved prior to infusion. If the entire fresh product was cryopreserved prior to infusion, select “yes” and continue with question 59. Select “no” if the product was not cryopreserved prior to infusion. Also select “no” in situations where the product is split and the fresh product will be infused without ever having been cryopreserved, even if the remaining portions are cryopreserved for future use.

**Question 59: Was the product thawed from a cryopreserved state prior to infusion?**

If any portion of the product was thawed prior to this infusion, select “yes” and continue with question 60. If the product was never cryopreserved, select “no” and continue with question 71.

**Question 60: Was the entire product thawed?**

A product may have been collected as a single product bag and then cryopreserved and stored in compartments. For example, the product could be stored in a 500mL bag with five 100mL cryopreserved compartments, or it could be stored in multiple separate product bags that have been cryopreserved. If the entire product (all compartments or all product bags) was thawed, select “yes” and continue with question 64. If the entire product was not thawed, select “no” and continue with question 61. If this infusion is using “leftover” cells from a previous infusion, the “leftover” portion is now considered the *entire product*. Therefore, if all of the “leftover” cells were thawed, select “yes.” If a portion of the “leftover” cells were not used and remain frozen, select “no.”
**Question 61: Was only a compartment of the bag thawed? (cord blood units only)**

Large product bags (units, fraction) are often comprised of several compartments (chambers). The compartments can be removed from the larger bag and thawed individually.

Indicate if compartment(s) from within the larger product bag was(were) thawed.

**Question 62: Were there multiple product bags?**

Indicate if the product consisted of multiple product bags. If “yes,” go to question 63. If “no,” go to question 64.

**Question 63: Specify number of bags thawed:**

Of the total number of product bags, indicate the number of bags thawed. This number should be less than the total number of bags cryopreserved.

**Question 64: Date thawing process initiated:**

Report the date the thawing process began.

**Question 65: Time at initiation of thaw (24-hour clock):**

Report the time the product thaw began. Report the time using a 24-hour clock and indicate if daylight savings time or standard time was in effect. If the location of your institution or off-site laboratory does not observe daylight savings time, report the time as standard time. For more information about daylight savings time schedules, go to [http://www.timeanddate.com/time/dst/](http://www.timeanddate.com/time/dst/).

If multiple bags of the same product are thawed, report the time the first bag begins thawing. The exact time should be documented within the patient record or the stem cell laboratory processing record.

**Question 66: Time product ready for infusion or expansion (24-hour clock):**

Report the time the thawed product was ready for infusion or expansion. This time is frequently when the product thaw is completed. Show the time using a 24-hour clock and indicate if daylight savings time or standard time was in effect. If the location of your institution or off-site laboratory does not observe daylight savings time, report the time as standard time. For more information about daylight savings time schedules, go to [http://www.timeanddate.com/time/dst/](http://www.timeanddate.com/time/dst/).

If multiple bags of the same product are thawed, report the time the last bag was finished thawing, even if the date is not the same as the date reported in question 64. The exact time should be documented within the patient record or the stem cell laboratory processing record.
Question 67: Was the primary container (e.g., cord blood unit bag) intact upon thawing?

Indicate if the primary container was intact upon thawing. The primary container refers to the product bag, not the shipping container.

If the cord blood unit primary container was not intact upon thawing, a product complaint form (Form 3010) must be completed.

Questions 68-69: What method was used to thaw the product?

Report the thawing method used to thaw the product. If a method other than “waterbath” or “electric warmer” was used, select “other method” and specify the method in question 69.

Question 70: Did any adverse events, incidents, or product complaints occur while preparing or thawing the product?

Indicate if any incidents occurred regarding the product during the thawing process. If any product complaints were found while preparing or thawing the product, a product complaint form (Form 3010) must be completed. Possible complaints include, but are not limited to: broken bags, a clot in the product, or missing documentation used to identify the product.

Question 71: Was the product manipulated prior to infusion?

If any part of the product was manipulated in any way prior to infusion at the transplant center, select “yes.” Do not report cryopreservation (including plasma removal as part of cryopreservation) as a method of manipulation; cryopreservation of the product(s) is reported in questions 57-58, if applicable.

If the product was shipped to your facility, do not report manipulation of the product performed at the collection center.

If the product was not manipulated, select “no.” For an autologous product, continue with question 109. For an allogeneic product, continue with question 158.

Question 72: Specify portion manipulated:

Indicate the portion of the product that was manipulated. If the entire product was manipulated, select “entire product” and continue with question 73. If a portion of the product was removed and manipulated, select “portion of product” and continue with question 73.

If multiple portions of the product were manipulated in different ways, select “portion of product” to indicate that the manipulation was not performed on the entire product. All of the manipulations for each portion of the product should be reported in this section.
Questions 73-95: Specify all methods used to manipulate the product:

Indicate the method(s) of stem cell manipulation. Answer each question as “yes” or “no” and do not leave any responses blank.

Steps in Manipulation

If the manipulation consists of several steps, individual steps do not need to be reported as separate manipulations. For example, washing that is part of CD34+ selection does not need to be reported as a separate manipulation. Similarly, T-cell depletion that is part of expansion does not need to be reported. If dilution is performed as part of washing, dilution does not need to be reported. In the cases above, if T-cell depletion and/or washing are done as stand-alone manipulations, they should be reported.

Washed: Washing is performed to remove cryoprotectant (such as DMSO) from the product.

Diluted: Dilution is performed to reduce the cell concentration.¹

Buffy coat enriched: Buffy coat enrichment is performed to reduce/remove mature erythrocytes and plasma.¹

B cell reduced: B cell reduction is performed to reduce/remove the quantity of B cells in the product.¹

CD8 reduced: CD8 reduction is performed to reduce/remove the population of CD8 cells in the product.¹ The removal of CD8 cells may mitigate the risk of GVHD.

Plasma reduced (removal): Plasma reduction is performed to remove plasma via sedimentation or centrifugation.¹ Plasma reduction may be done in order to minimize the risks associated with ABO mismatched products or to prevent volume overload. Previous versions of the Form 2006 made a distinction between plasma removal and volume reduction; for the purpose of this form, both volume reduction and plasma removal should be reported here.

Plasma reduction/removal that is part of the cryopreservation process should not be reported as manipulation.

RBC reduced: RBC reduction is performed to reduce/remove mature erythrocytes from the product.¹
**Cultured (ex-vivo expansion):** Ex-vivo expansion is a method of culturing cells to “activate, expand, or promote development of a specified cell population in the presence of specific additive(s).” (ISBT, 2012) If the product is expanded, also report the expansion protocol under “other” in addition to checking “cultured.”

**Genetic manipulation (gene transfer/transduction):** Gene manipulation refers to any method used to modify the genes in the product cells. Gene transduction refers to the transfer of genes from one cell to another. Using genetic manipulation is still in the “research” stage.

**PUVA treated:** Treatment with psoralen and ultraviolet light (PUVA).

**CD34 enriched (CD34+ selection):** CD34+ selection is a manipulation method also known as “positive selection.” This method identifies and selects stem cells that have a CD34+ marker on the cell surface.

**CD133 enriched:** CD133 enrichment identifies and selects stem cells that have a CD133 marker on the cell surface.

**Monocyte enriched:** Monocyte enrichment identifies and selects monocytes.

**Mononuclear cells enriched:** Mononuclear cell enrichment identifies and selects mononuclear cells.

**T-cell depletion:** T-cell depletion removes some or all of the T cells in an effort to minimize GVHD. Methods of T-cell depletion include antibody affinity column, antibody-coated plates, antibody-coated plates and soybean lectin, antibody + toxin, immunomagnetic beads, CD34 affinity column plus sheep red blood cell resetting, and T-cell receptor alpha / beta depletion.

If a method of manipulation was performed on the product, but is not listed above, select “yes” for question 94 and specify the method in question 95. Do not report cryopreservation (or processing used in the cryopreservation process) as manipulation.


**Question 96: Were antibodies used during product manipulation?**

If antibodies were used during product manipulation, select “yes” and continue with question 97. However, it is not necessary to report antibody use as part of CD34+ enrichment using the CliniMacs, Isolex, or Miltenyi devices. If antibodies were not used, select “no” and continue with question 109.
Questions 97-108: Specify antibodies:

Specify the antibodies used for product manipulation. Do not leave any responses blank. If antibodies were used during product manipulation, but are not listed above, select “yes” for question 107 and specify in question 108.
Q109-157: Autologous Products Only

The following section refers to autologous products only, including autologous cord blood. If this is not an autologous HCT, continue with the Product Analysis section at question 158.

Question 109: Were tumor cells detected in the recipient or autologous product prior to HCT?

Indicate if tumor cells (e.g., plasma cells in a myeloma patient, lymphoma cells, or breast cancer cells) were detected in the circulating blood stream or bone marrow within the period between the last systemic therapy and collection, or if tumor cells were present in the product. If tumor cells were detected, select “yes” and continue with question 110. If no tumor cells were found in the circulating blood cells, bone marrow (between last systemic therapy and collection), or product (before purging), select “no” and continue with question 136.

Do not report the presence of tumor markers (e.g., SPEP, IFE, and free light chains), as they do not necessarily indicate the presence of a tumor cell.

Do not report the presence of a tumor (i.e., solid tumor) in the recipient prior to HCT on this form; the disease status of the recipient is recorded on the recipient forms.

Questions 110-135: Specify tumor cell detection method used and site(s) of tumor cells:

For each method of tumor cell detection, indicate “yes” if tumor cells were detected. If yes, continue with the subsequent questions regarding site(s) of tumor cells. If no tumor cells were located, continue with the next detection method. Do not leave any responses blank.

- **Routine histopathology** includes a review of histological and morphological findings in the circulating blood, bone marrow, or autologous product.

- **Polymerase chain reaction (PCR)** is a molecular method used to detect known molecular abnormalities using markers for specific diseases.

- **Other molecular techniques** include gene expression profiling techniques such as microarray. Specify the method used in question 119.

- **Immunohistochemistry** is a technique used to evaluate surface markers on cellular material. Flow cytometry is an example of immunohistochemistry.

- **Cell culture technique** is a technique used to detect malignant cell proliferation in cell culture medium.
Other techniques should be reported if the method used to detect tumor cells is not one listed above. Specify the technique in question 132.

If tumor cells were detected using one of the methods listed above, specify the site(s) of detection. Select “yes” if the site was tested and tumor cells were detected. Select “no” if the site was tested and tumor cells were not detected. Select “not done” if the site was not tested for tumor cells.

Circulating blood cells are evaluated after peripheral blood collection.

Bone marrow may be tested to detect tumor cells in the interval between the most recent systemic treatment and the stem cell collection.

Collected cells are in the product that will be used for transplant. Detection of disease in the collected cells should be reported prior to removing malignant cells (purging).

Question 136: Was the product treated to remove malignant cells (purged)?

This type of negative selection manipulation removes malignant cells from the collected product.

If the product was purged, select “yes” and continue with question 137. If the product did not have malignant cells to remove and/or was not purged, select “no” and continue with question 158.

Questions 137-150: Specify method(s) used:

Specify all methods used to purge the product. Answer each question as “yes” or “no,” being sure not to leave any question blank. \( ^{123} \)

Monoclonal antibody: a negative selection method in which antibodies destroy malignant T- or B-cells.

4-hydroperoxycyclophosphamide (4HC) and Mafosfamide: a negative selection method in which derivatives of cyclophosphamide destroy malignant cells.

Elutriation: a method in which cells are separated based on size, potentially allowing malignant cells to be separated from non-malignant cells.

Immunomagnetic Column: a selection method in which monoclonal antibodies and magnetic beads attach to targeted cells, allowing for the separation of malignant and non-malignant cells using a magnet.

Toxin: a negative selection method in which a toxin or toxin-derivative may be combined with a monoclonal antibody to destroy malignant cells.
**CD34 selection (other than preparation of mononuclear fraction):** a positive selection method in which only CD34 cells for transplant are identified and collected. Select this option if this method was used to separate malignant cells from cells for transplant. Do not select this option if the product was CD34 selected for other reasons.


**Questions 151-157: Specify if tumor cells were detected in the graft after purging by each method used:**

For each of the detection methods listed (and described above in questions 110-135), indicate whether tumor cells were detected in the product after the purging was completed. Answer each question as “yes” or “no,” being sure not to leave any question blank.
Q158-195: Product Analysis (All Products)

Product Analysis
The “at infusion” timepoint is a critical timepoint and should reflect the values of the infused product (i.e., what was given to the patient). As long as the values specific to the volume of product infused are known, the analysis at this timepoint is the only analysis required by the CIBMTR. All other timepoints are not required. However, for NMDP products, reporting analysis for the “product arrival” timepoint is recommended for quality assurance purposes. Additionally, for cord blood products, the “post-thaw” timepoint is the most indicative of the quality of the product. If there are sufficient cells to obtain a post-thaw/pre-wash sample, it is recommended to report this analysis as well.

Report the product analysis results for each timepoint that testing was performed.
If the product is contained in multiple bags and infused together, add the cell counts from each bag to get the total cell count. To calculate the percent viability, average the viability of all bags/products.

Question 158: Specify the timepoint in the product preparation phase that the product was analyzed:

Indicate the timepoint at which product analysis was reported. A maximum of four timepoints may be reported. Each timepoint can only be reported once.

Product arrival: Assessment of fresh product at the transplant facility. This may include arrival of fresh product from an apheresis or collection center, or product collected from an autologous or related donor at your site.

Pre-cryopreservation: Assessment of fresh product prior to cryopreservation at your center.

Post-thaw: Assessment after the product has been thawed, but prior to any post-thaw manipulation, including washing the cells to remove cryoprotectant.

At infusion: Must be reported if values specific to the volume of product infused are known. If the product was manipulated after thawing, report the post-manipulation analysis under the “at infusion” timepoint.

If the product is analyzed upon arrival at the receiving transplant center, the product is not manipulated or cryopreserved prior to infusion, and no additional analyses are performed, then the timepoint of analysis should be reported as “at infusion” instead of “product arrival.”

The “at infusion” timepoint should only report the values for the actual product volume infused. Therefore, if
analysis was performed on the entire product but only a portion of the product was infused, the “at infusion” values reported should represent only the portion of product infused. If product analysis values of the entire product are known and the values specific to only the volume of product infused cannot be determined, then the “at infusion” may be reported using the known volume (and additional details including viability, culture results, CFU assessment results, etc.), but the cell counts may be reported as “not done.” An additional timepoint such as “pre-cryopreservation” or “post-thaw” should be reported if the product was analyzed at your center.

**Example 1 – entire product infused**: The entire product is analyzed at arrival and does not undergo any manipulation, cryopreservation, or additional analyses. The entire product volume is infused. The values from the product analysis should be reported for the “at infusion” timepoint.

**Example 2 – portion of product infused**: The entire product is analyzed prior to infusion and the values from this analysis are reflective of the entire product. Only a portion of this product is infused. The counts specific to the volume of product analyzed are proportional to the volume infused and can be calculated. The results of the analysis performed on the entire product should be reported for the appropriate timepoint (e.g., product arrival, pre-cryopreservation, or post-thaw).

If the product arrives at your center (or is collected at your center), is tested, and then cryopreserved, report these values as “at arrival.” If the product arrives, and is tested several times, and then cryopreserved, report the first testing results as “at arrival” and the last test results prior to cryopreservation as “pre-cryopreservation.”

To assist centers in reporting product analysis timepoints, the CIBMTR has developed guidelines specific to the product type being reported. The following instructions are meant to guide center reporting practices based on common product testing scenarios. They do not cover all possible scenarios and centers are encouraged to contact their CRC for further clarification as necessary.

**Cord Blood Units**: Centers are reminded to only report product testing performed by their laboratory. Product testing performed by the cord blood bank is captured in the Product Transport and Receipt section of this form and should not be reported in the Product Analysis section. For all washed cord blood units, testing performed prior to washing should be reported under “post-thaw” while testing performed after washing should be reported under “at infusion.” If the transplant center only tests for viability, report the timepoint, date of analysis, product volume, and viability.

**Fresh Marrow or PBSC**: Product processing and manipulation will determine which timepoints the center is able to report. For a fresh product that is not manipulated, report all testing under the “at infusion” timepoint. If only a portion of the product is infused, adjust the “at infusion” counts as indicated above.

**Cryopreserved Marrow or PBSC, collected at an outside facility**: Centers are reminded to only report
product testing performed by their laboratory. Testing will be reported under “post-thaw” and/or “at infusion”
timepoints. If a product is thawed, tested, and infused without being manipulated, report all testing under “at
infusion.” For washed products, testing performed prior to washing should be reported under “post-thaw”
while testing performed after washing should be reported under “at infusion.” If the transplant center only
tests for viability, report the timepoint, date of analysis, product volume, and viability.

**Cryopreserved Marrow or PBSC, collected at the transplant center:** If the transplant center does a
complete analysis post-thaw, report this testing under the “at infusion” timepoint. A common scenario is for
the transplant center to perform a complete analysis prior to cryopreservation, with only viability testing
performed post-thaw. In this case, the center should report an “at arrival” or “pre-cryopreservation” timepoint
in addition to the required “at infusion” timepoint. The “at arrival” or “pre-cryopreservation” timepoint will
capture all cell counts, viability, sterility, etc. performed prior to freezing the product. If repeat testing is not
performed post-thaw, the “at infusion” cell counts must be reported based on testing performed prior to
cryopreservation and adjusted for the volume actually infused. This information is typically documented on
the infusion report. The “at infusion” timepoint must also capture post-thaw viability testing if performed. The
date of the “at infusion” product analysis timepoint will be the date of infusion. This may be different than the
date testing for cell counts or cell viability was performed.

**Question 159: Date of product analysis:**

Report the date of the product analysis for each timepoint reported. In situations where the product is being
collected at your center and the “product arrival” timepoint is being used, report the first date of collection as
the date of product analysis if the collection spans multiple days.

**Question 160: Total volume of product plus additives:**

Enter the total volume of the product plus additives in the bag(s) for each timepoint. Report the volume in
either milliliters (mL) or grams (g).

**Questions 161-176: Report the total number of cells (not cells per kilogram) not corrected for viability.**

For each of the cell types, report “done” if the cell type was quantified at the specified timepoint. Report the
absolute number of the cells, not cells per kg.

**Total nucleated cells (TNC):** the total nucleated cell count includes nucleated red and nucleated white
blood cells. *See note below*

**Nucleated white blood cells:** (also known as leukocytes) the nucleated cell count includes the
neutrophils, eosinophils, basophils, lymphocytes, and monocytes. *See note below*

**Mononuclear cells:** the total mononuclear cell count includes lymphocytes and monocytes.
**Nucleated red blood cells**: (also known as normoblasts) the total count of red blood cells containing a nucleus. *See note below*

**CD34+ cells**: the total count of cells with CD34+ markers on the surface.

**CD3+ cells**: the total count of cells with CD3+ markers on the surface.

**CD3+CD4+ cells**: the total count of cells with CD3+CD4+ markers on the surface. The lab report may display this value as “CD4+.”

**CD3+CD8+ cells**: the total count of cells with CD3+CD8+ markers on the surface. The lab report may display this value as “CD8+”

Since total nucleated cells consist of both nucleated red and white blood cells, it is possible to calculate a missing value if the two other values are present on lab reports. Centers do not need to calculate and report these lab values if they don’t appear on the laboratory paperwork.

Occasionally, cell differential results may be “corrected” in order to remove cells such as nRBCs. The CIBMTR would like to have uncorrected data submitted in these fields. Some labs report corrected cell counts, others report uncorrected cells counts. Some even report both. If your lab report does not clearly indicate whether the TNC is corrected or uncorrected, ask someone in the lab to help you determine which is correct. This will most likely be the same every time, so you would not need to check for each patient. If this information is not clearly indicated on the lab report, please ensure this is somewhere in your center SOPs. If the only value available to you is the corrected TNC, you may calculate the uncorrected TNC with the formula below. Please be sure to carefully check your math and the units reported to ensure that the information on the form is correct. To determine the uncorrected TNC count, use the following formula (Adapted from *Essential Laboratory Mathematics* by CW Johnson, DL Timmons, PE Hall (2003), pg 175.):

- **If the corrected WBC is in cells/mL:**
  \[
  (\text{corrected WBC per mL}) \times (\text{volume of product}) \times ((\text{nRBCs per 100 WBCs}) + 100) / 100 = \text{Total Uncorrected TNC}
  \]

- **If the corrected WBC is in cells/kg:**
  \[
  (\text{corrected WBC per kg}) \times (\text{recipient kg}) \times ((\text{nRBCs per 100 WBCs}) + 100) / 100 = \text{Total Uncorrected TNC}
  \]

- **If the corrected WBC is an absolute cell count:**
  \[
  (\text{total corrected WBC}) \times ((\text{nRBCs per 100 WBCs}) + 100) / 100 = \text{Total Uncorrected TNC}
  \]
For example, if the corrected WBC is 17.96×10⁶/mL, the product volume is 390 mL, and the nRBCs per 100 WBCs is 12.8 (using the formula above when considering cells/mL):

\[(17.96 \times 10^{6}) \times (390 \text{ mL}) \times (12.8 + 100) / 100 = 79 \times 10^{8} \text{ Uncorrected TNC}\]

If the cell type was not quantified at that specific timepoint, report “not done” and continue with the next cell type.

**Questions 177-178: Viability of cells:**

If the viability of the cells was quantified, select “done” and report the percentage of viable cells in question 178. If your center’s laboratory assay only measures viable cells, report the number of viable cells in questions 161-176 along with a viability number of 100% in question 178. If the assay measures all cells and then checks viability, report the total number and report the percent of cells that are viable.

**Questions 179-180: Method of testing cell viability:**

Indicate the method of testing viability

- **7-AAD** (7-aminoactinomycin D) and **Propidium iodide** are compounds that can stain dead cells but will not cross the membrane of living cells. Cytometric techniques are used to calculate the percentage of viable cells in a sample.

- **Trypan Blue** is a technique where the dead cells become stained when in contact with the compound, but living cells remain impermeable to the dye. Cells are counted under a microscope to determine the percentage of viable cells in a sample.

**If both methods of viability testing are performed, report 7-AAD results.**

If the cell viability was tested using a different method, select “other method” and specify the method in question 180.

**Question 181: Were the colony-forming units (CFU) assessed after thawing? (cord blood units only)**

CFUs have been shown to be a predictor of engraftment. Indicate whether CFUs were assessed after thawing. If the CFUs were assessed, continue with question 182. If no CFU assessments were performed, continue with question 187.

**Question 182: Was there growth?**

If CFUs were assessed after thawing, indicate whether growth was detected.
Questions 183-184: Total CFU-GM

Indicate if the total CFU-GM (granulocyte/macrophages) was quantified. If the CFU-GM was quantified, report “done” and continue with question 184. Report the total CFU as documented on the laboratory report. Do not report CFU per dish, per bag, or per kg.

Questions 185-186: Total BFU-E

Indicate if the total BFU-E (burst forming unit – erythroid) was assessed. BFU-E indicates the presence of erythroid precursor cells. If the BFU – E was quantified, report “done” and continue with question 186. Report the total BFU-E as documented in the laboratory report. Do not report BFU per dish, per bag, or per kg.

Question 187: Were cultures performed before infusion to test the product(s) for bacterial or fungal infection? (complete for all cell products)

If cultures were performed, select “yes” and continue with question 188.

If cultures were not performed, select “no” and continue with question 196.

Questions 188-195: Specify results and organism code(s)

If a single product was split into multiple bags and one or more bags are contaminated, then all bags should be considered contaminated for the purposes of reporting data to the CIBMTR.

If multiple products are infused, and only one product is contaminated, then report the infection on the Form 2006 for the product that was contaminated (i.e., the uninfected product will be reported on a separate Form 2006).

If cultures were performed on the product, indicate the results as “positive,” “negative,” or “unknown.”

If the results were positive, select the isolated organism(s) using the pull down options in FormsNet.
Q196-249: Product Infusion

Questions 196: Date of this product infusion:

Report the date this product was infused. If the product was infused over multiple days, report the first date of infusion.

If this Form 2006 is completed for additional cells not intended to produce engraftment, (i.e., question 198 was reported as “no”) report the date the additional cells were infused. However, the Key Field “Date of this HCT” must be reported as date of the actual HCT (clinical day 0) intended to produce engraftment.

Question 197: Was more than one product infused? (e.g., marrow and PBSC, PBSC and cord blood, two different cords, etc.)

Indicate if more than one product was infused as part of this transplant event. Previous transplants should not be reported here. Multiple bags from the same collection are not considered different products and should not be reported here. If “yes,” continue with question 198. If “no,” continue with question 199.

Question 198: Was the product described on this insert intended to produce hematopoietic engraftment?

If an infusion of additional cells (not intended to produce engraftment) was given prior to the actual HCT (i.e., clinical day 0), the cells must be reported as a product on the Pre-TED Form 2400 and on a separate Form 2006. If the additional cells were infused after the actual HCT, for any reason other than those pertaining to the original HCT graft, they should be reported as a DCI on the appropriate follow-up form. Reporting the additional cells (given pre-HCT and not intended to produce engraftment) on the Form 2006 is the only mechanism the CIBMTR has in place to collect this data and ensure that the quality assurance data is reported to cord blood banks, if applicable.

If the product reported on this form was intended to produce engraftment, select “yes.” If the product was not intended for engraftment, select “no.”

Question 199: Date infusion started:

Report the date the product was infused. If multiple bags from the same product were infused, report the start date of the first bag.

If multiple products were infused, enter the initiation date of the product for which this form is being completed.
**Question 200: Time product infusion initiated (24-hour clock):**

Report the start time of the infusion. If multiple bags were infused, report the start time of the infusion of the first bag. Show the time using a 24-hour clock and indicate if daylight savings time or standard time was in effect. If the location of your institution does not observe daylight savings time, report the time as standard time. For more information about daylight savings time schedules, go to [http://www.timeanddate.com/time/dst/](http://www.timeanddate.com/time/dst/).

If **multiple products** were infused, enter the initiation time of the **product for which this form is being completed**.

**Question 201: Date infusion stopped:**

Report the date the infusion was completed. If multiple bags of the same product were infused, report the stop date of the last bag.

If **multiple products** were infused, enter the stop date of the **product for which this form is being completed**.

**Question 202: Time product infusion completed (24-hour clock):**

If **multiple bags** of the same product were infused, report the completion time of the last bag.

If **multiple products** were infused, enter the completion time of the **product for which this form is being completed**.

Enter the completion time of the infused product using a 24-hour clock and indicate if daylight savings time or standard time was in effect. If the location of your institution does not observe daylight savings time, report the time as standard time. For more information about daylight savings time schedules, go to [http://www.timeanddate.com/time/dst/](http://www.timeanddate.com/time/dst/).

**Question 203: Total volume of product plus additives intended for infusion:**

Report the total volume of the infused product, including any additives.

In most cases, this value will be the same as the “total volume of product” (question 160) for the “at infusion” timepoint (question 158).

The total volume reported may be from pooled products. If products are pooled prior to infusion, report the total volume of the pooled product that was infused. It is important to be aware that the timing of the pool determines how the data is reported. See the examples below.
Example 1 – with manipulation: If a single product consisted of two collections and the products were pooled prior to any manipulation (e.g., CD34+ selection), the pooled volume prior to manipulation would be reported in question 160 only. The final infused product volume post manipulation would be reported in question 204.

Example 2 – without manipulation: If a single product consisted of two collections and the products were pooled and infused without any manipulation, the total volume would be reported in question 160 and question 204. These volumes should be the same unless there were additives post pooling.

Question 204: Was the entire volume of product infused?
Indicate “yes” if the entire volume of the product received was infused. Indicate “no” if only a portion of the product received was infused.

Questions 205-206: Specify what happened to the reserved portion:
Report if the product was “discarded,” “cryopreserved for future use,” or “other fate.” If “other fate” is selected, report the outcome of this product.

Questions 207-208: Specify the route of product infusion:
Report the route by which the product was infused. Intravenous refers to infusion into the veins – examples include infusion via central line or via catheter. Intramedullary refers to infusion into the marrow cavity within a bone, such as directly into the left or right iliac crest. Intraperitoneal refers to infusion within the peritoneal cavity. If the route of infusion is not one of the above options, select “other route of infusion” and specify the infusion route in question 208.

The following questions refer to all stem cell products except for autologous marrow or autologous PBSC products. If this HCT used an autologous marrow or autologous PBSC product, continue with the signature lines at the end of the form.

Question 209: Were there any adverse events or incidents associated with the stem cell infusion?
Indicate whether any adverse events or incidents occurred as a result of the stem cell infusion. Report all adverse events regardless of the grade or severity.

If an adverse event occurred, select “yes” and continue with question 210. If an adverse event did not occur, select “no” and continue with question 250.

A serious adverse event is defined as an event which:
• led to death,
• was considered life-threatening,
• required prolongation of hospitalization,
• led to persistent or significant disability/incapacity,
• or led to a congenital anomaly/birth defect.

If any of the above happened, an Adverse Event Form (Form 3001) must also be completed. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Please review Adverse Event reporting at the CIBMTR website: http://www.cibmtr.org/DataManagement/TrainingReference/Pages/AdverseEvents.aspx

Questions 210-249: Specify the following adverse event(s)

Indicate “yes” or “no” for each adverse event listed. Do not leave any responses blank. If the recipient experienced an expected (in the physician’s opinion) adverse event that was not listed, specify the other expected adverse event in question 245. If the recipient experienced an unexpected adverse event (i.e., not one of the options listed above, or an “other expected AE”), specify the unexpected adverse event in questions 247-248.

For each adverse event that occurred, indicate if the medical director believes the adverse event(s) to be directly related to the infusion of the product.
Q250-285: Donor/Infant Demographic Information

The Donor Demographic Information section (questions 250-270) is to be completed for all non-NMDP allogeneic donors. If the stem cell product was from an NMDP donor or an autologous donor, continue with the signature lines at the end of the form.

**Question 250: Was the donor ever pregnant?**

If the donor has ever been pregnant, select “yes” and continue with question 251.

If the donor has never been pregnant, select “no” and continue with question 253.

If there is no documentation regarding whether or not the donor has ever been pregnant, select “unknown” and continue with question 253.

If the product is a cord blood unit or was from a male donor, select “Not Applicable (male donor or cord blood unit)” and continue with question 253.

**Questions 251-252: Number of pregnancies**

Indicate if the number of pregnancies is known or unknown. If “known,” specify the total number of pregnancies in question 252.

If the total number of pregnancies is not known, select “unknown” and continue with question 253.

**Question 253: Specify blood type:**

Report the donor’s blood type.

**Question 254: Specify Rh factor:**

Report the donor’s Rh factor as “negative” or “positive.”

**Question 255: Did this donor have a central line placed?**

If the donor had a central line placed during the donation process, select “yes” and continue with question 256.

If the donor did not have a central line, select “no” and continue with question 258.
If the product is a cord blood unit or marrow, select “not applicable (cord blood unit or marrow product)” and continue with question 258.

Questions 256-257: Specify the site of the central line placement:

Indicate the location of the donor’s central line. If “other site” is selected, complete question 257 to specify the location of central line placement.

Question 258: Donor’s ethnicity:

Indicate the donor’s ethnicity. For more information regarding ethnicity, see Appendix I.

Questions 259-260: Donor’s race and detail: (Mark the group(s) in which the donor is a member. Check all that apply.)

Indicate the race of the donor, marking all that apply. For more information regarding race, see Appendix I.

Copy questions 259-260 to report more than one race.

Questions 261-263: What is the biological relationship of the donor to the recipient?

From the perspective of the recipient, indicate the biological relationship of the donor. If the recipient and donor are not biologically related, select “unrelated” and continue with question 264. If the recipient and donor are related, but the relationship is not best characterized by one of the options for question 261, select “other biological relative” and specify in question 262. If the biological relationship is not listed among the options, select “other biological relative” and specify the biological relationship in question 263 (i.e., maternal grandmother).

Question 264: Was the donor/product tested for potentially transplantable genetic diseases?

If the donor and/or product were tested for genetic disease, select “yes” and continue with question 265. If the donor and/or product were not tested, or if there is no documentation of genetic testing, select “no” or “unknown,” respectively, and continue with question 272 for related donors or the signature lines at the end of the form for all other donor types.

Questions 265-271: Specify disease(s) tested:

For each of the diseases listed, indicate whether testing was done. Indicate “yes” or “no” and specify the results in the following question. Do not leave any responses blank. If the donor was tested for a potentially transplantable disease, but it was not listed in questions 265-268, select “yes” for “other disease” and specify the disease and the results in questions 270-271.
Question 272: Was the donor hospitalized (inpatient) during or after the collection?

Indicate “Yes” if the donor was hospitalized for complications during or after the collection. Indicate “No” if the donor was not hospitalized as an inpatient or if the donor was admitted to an observation unit and discharged in less than 24 hours.

Questions 273-274: Did the donor experience any life-threatening complications during or after the collection?

Examples of life-threatening complications include, but are not limited to the following:

- Allergic reaction to filgrastim
- Reaction to anesthesia
- PBSC donors: Low platelet counts (<30,000)
- Marrow donors: Injury to bone, nerve, or muscle during collection

If the donor experienced life-threatening complications during or after the collection, select “yes” and specify the complication(s) in question 274.

If the donor did not experience life-threatening complications during or after the collection, select “no” and continue with question 275.

Question 275: Did the donor receive blood transfusions as a result of the collection?

Indicate if the donor received blood transfusions as a result of the collection. If the donor received any blood products as a result of the collection, select “yes” and continue with question 276. If the recipient did not receive blood transfusions as a result of the collection, select “no” and continue with question 280.

Questions 276-277: Was the blood transfusion product autologous?

If the recipient received transfusions of their own blood that had been previously collected and stored, even once, indicate “yes” and specify the number of units received in question 277.

If the recipient received no autologous blood transfusions, indicate “no” and continue with question 278.
Questions 278-279: Was the blood transfusion product allogeneic (homologous)?

If the recipient received blood transfusions (excluding autologous blood product), indicate “yes” and specify the number of units received in question 279.

If the recipient did not receive any blood transfusions (excluding autologous products), indicate “no” and continue with question 280.

Questions 280-281: Did the donor die as a result of the collection?

If the donor died as a result of the collection, select “yes” and specify the cause of death in question 281. If the donor did not die as a result of the collection, select “no” and continue with question 282.

Questions 282-283: Did the recipient submit a research sample to the NMDP/CIBMTR repository? (Related donors only)

There are a select number of transplant centers participating in the Related Specimen Repository. If your center is one of the participating centers, and the recipient provided a research sample, select “yes” and provide the recipient ID in question 283. The ID number is located on the bar code that is attached to the sample tube.

If the recipient did not provide a research sample, select “no” and continue with question 284.

Questions 284-285: Did the donor submit a research sample to the NMDP/CIBMTR repository? (Related donors only)

If the donor provided a research sample, select “yes” and provide the donor ID in question 285.

If the donor did not provide a research sample, select “no” and continue with the signature lines.
2100: Post-HCT Follow-Up

A transplant center designated as a Comprehensive Report Form center will submit data on the Pre-TED and Pre-TED Disease Classification Forms, followed by either the Post-TED Form or the Comprehensive Report Forms. The type of follow-up forms required for a specific recipient is determined by the CIBMTR’s form selection algorithm (see see Section 1 in the Center Reference Guide).

The Post-HCT Form (2100) must be completed at the following time points: 100 days, 6 months, annually for 6 years post-HCT, and biennially thereafter. This form should be completed as closely to these time points as possible. The following recipient data should be collected from an actual examination (or other recipient contact) by the transplant center physician or the local physician who is following the recipient post-HCT: vital status, hematopoietic reconstitution post-HCT, neutrophil recovery, platelet recovery, current hematologic findings, immune reconstitution, chimerism studies, engraftment syndrome, acute Graft-versus-Host Disease (GVHD), chronic GVHD, infections, organ function, new malignancy, functional status, and subsequent HCT.

Subsequent HCT:
If a recipient receives a subsequent HCT between time points (100 day, 6 months, annually), the CRF form sequence will start over again with another Pre-TED.

However, if the recipient receives an autologous HCT as a result of a poor graft or graft failure, the CRF form sequence will not start over again. Generally this type of infusion (autologous rescue) is used to treat the recipient’s poor graft response, rather than to treat the recipient’s disease, and is, therefore, not considered a subsequent HCT.

Contact your center’s CIBMTR CRC if the subsequent Pre-TED does not come due automatically.

* If the recipient received a subsequent transplant (excluding an autologous rescue), the answers to all questions should reflect the clinical status of the recipient the day prior to the start of the preparative regimen or, if no preparative regimen was given, the answers to all questions should reflect the clinical status of the recipient the day prior to HCT infusion.

Lost to Follow Up:
Occasionally, centers may lose contact with recipients for a variety of reasons, including the recipient’s moving, changing physicians, or death. If contact with a recipient appears lost, please consider calling the recipient at home or work, sending a letter, communicating with the treating or referring physician, or
contacting the hospital billing department. If your center receives documented information that a recipient is alive or dead, the form should be filled out with the recipient survival status. If no documentation exists and several unsuccessful attempts have been made to contact the recipient, they are considered lost to follow-up and the form may be marked as such using the Lost to Follow-Up Tool in FormsNet3 for each reporting period in which no contact exists.

Links to Sections of the Form:

Q1-5: Vital Status
Q6-12: Granulopoiesis / Neutrophil Recovery
Q13-18: Megakaryopoiesis / Platelet Recovery
Q19-58: Growth Factor and Cytokine Therapy
Q49-63: Current Hematologic Findings
Q64-88: Immune Reconstitution
Q89-107: Chimerism Studies
Q108-130: Engraftment Syndrome
Q131-233: Acute Graft vs. Host Disease
Q234-406: Chronic Graft vs. Host Disease
Q407-427: Infection Prophylaxis
Q428-440: Infection
Q441-645: Organ Function
Q616-639: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder
Q640-664: Functional Status
Q665-672: Subsequent HCT

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/18/18</td>
<td>2100: Post-HCT Follow-Up Data</td>
<td>Add</td>
<td>Added the following reporting instruction for Questions 486-487: Please indicate “no” if the patient received endotracheal intubation or mechanical ventilation during surgery.</td>
</tr>
<tr>
<td>7/</td>
<td>2100:</td>
<td>Modify</td>
<td>Version 4 of the 2100: Post-HCT Follow-Up Data Form (Form 2100) (formerly</td>
</tr>
<tr>
<td>25/18</td>
<td><strong>Post-HCT Follow-Up Data</strong></td>
<td>100 Day Post-HSCT Data Form) section of the Forms Instructions Manual released. Version 4 corresponds to revision 5 of the Form 2100.</td>
<td></td>
</tr>
</tbody>
</table>
Q1-5: Vital Status

The date of actual contact with the recipient to determine medical status for this follow-up report is based on a medical evaluation conducted by a clinician with responsibility for the recipient’s care. Report the date of the medical evaluation performed closest to the designated time period of the form (e.g., Day+100, 6 months, or annual follow-up visit). Time windows are provided to guide selection of dates for reporting purposes. Recipients are not always seen within the time windows used for reporting follow-up dates, and some discretion is therefore required when determining which date to report. If the recipient is not seen within the time windows, report the date closest to the date of contact within reason.

If the Post-HCT Follow-Up Form reports a subsequent transplant, report the date of latest follow-up as the day prior to the start of the preparative regimen. If no preparative regimen or conditioning was given, report the day prior to infusion as the date of contact.

Question 1: Date of actual contact with the recipient to determine the medical status for this follow-up report

Enter the date of actual contact with recipient to determine medical status for this follow-up report. Acceptable evaluations include those from the transplant center, referring physician, or other physician currently assuming responsibility for the recipient’s care. If an evaluation was not performed at Day+100, at 6 months, or on the HCT anniversary, choose the date of the visit closest to the actual time point.

If the recipient has not been seen by a clinician during the reporting period but the survival status is known, submit the Post-HCT Data Form reporting only the survival status.

In general, the date of contact should be reported as close to the 100 day, 6 month, or annual anniversary to transplant as possible. Report the date of actual contact with the recipient to evaluate medical status for the reporting period. In the absence of contact with a clinician, other types of contact may include a documented phone call with the recipient, a laboratory evaluation, or any other documented recipient interaction on the date reported. If there was no contact on the exact time point, choose the date of contact closest to the actual time point. Below, the guidelines show an ideal approximate range for reporting each post-transplant time point:
<table>
<thead>
<tr>
<th>Time Point</th>
<th>Approximate Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 days</td>
<td>+/- 15 days (Day 85-115)</td>
</tr>
<tr>
<td>6 months</td>
<td>+/- 30 days (Day 150-210)</td>
</tr>
<tr>
<td>Annual</td>
<td>+/- 30 days (Months 11-13, 23-25, 35-37, etc)</td>
</tr>
</tbody>
</table>

Recipients are not always seen within the approximate ranges and some discretion is required when determining the date of contact to report. In that case, report the date closest to the date of contact within reason. The examples below assume that efforts were undertaken to retrieve outside medical records from the primary care provider, but source documentation was available.

**Example 1.** *The 100 day date of contact doesn't fall within the ideal approximate range.*

The autologous recipient was transplanted on 1/1/13 and is seen regularly until 3/1/13. After that, the recipient was referred home and not seen again until 7/1/13 for a restaging exam and 7/5/13 for a meeting to discuss the results.

What to report:

100 Day Date of Contact: 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)

6 Month Date of Contact: 7/5/13 (note the latest disease assessment would likely be reported as 7/1/13)

**Example 2.** *The 100 day date of contact doesn't fall within the ideal approximate range and the recipient wasn't seen again until 1 year post-HCT.*

The autologous recipient was transplanted on 1/1/12 and is seen regularly until 3/1/12. After that, the recipient was referred home and not seen again until 1/1/13 for a restaging exam and 1/4/13 for a meeting to discuss the results.

What to report:

100 Day Date of Contact: 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)

6 Month Form: Indicate the recipient is lost to follow-up in FormsNet3

1 Year Date of Contact: 1/4/13 (note the latest disease assessment would likely be reported as 1/1/13)

Additional Information

- A date of contact should never be used multiple times for the same recipient’s forms.
  - For example, 6/1/13 should not be reported for both the 6 month and 1 year form. Instead, determine the best possible date of contact for each reporting period; if there is not a suitable date of contact for a reporting period, this may indicate that the recipient was lost to follow-up.
If the recipient has a disease evaluation just after the ideal date of contact, capturing that data on the form may be beneficial.

- For example, if the recipient’s 90 day restaging exam was delayed until day 115 and the physician had contact with the recipient on day 117, the restaging exams can be reported as the latest disease assessment and day 117 would be the ideal date of contact, even though it is just slightly after the ideal approximate range for the date of contact.

Date of Contact & Death

In the case of recipient death, the date of death should be reported as the date of contact regardless of the time until the ideal date of contact. The date of death should be reported no matter where the death took place (inpatient at the transplant facility, at an outside hospital, in a hospice setting, or within the recipient’s home).

If the death occurred at an outside location and records of death are not available, the dictated date of death within a physician note may be reported. If the progress notes detailing the circumstances of death are available, request these records. These records are useful for completing required follow-up data fields and the cause of death data fields on this form. If the exact date of death is not known, use the processed described for reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Example 3. The recipient has died before their six month anniversary.

The recipient is transplanted on 1/1/13, was seen regularly through the first 100 days. They had restaging exams on 4/4/13 and was seen on 4/8/13, and then died on 5/13/13 in the hospital emergency room.

What to report:

100 Day Date of Contact: 4/8/13 (note the latest disease assessment would likely be reported as 4/4/13)
6 Month Date of Contact: 5/13/13 (though the death does not occur within the ideal approximate range for 6 months)

Example 4. The recipient has died after their six month anniversary.

The recipient is transplanted on 1/1/13, was seen regularly through the first 100 days. They had restaging exams on 4/22/13 and was seen on 4/23/13. Based on findings in the restaging exam, the recipient was admitted for additional treatment. The disease was found to be refractory on a 6/25/13 restaging exam, and the recipient was discharged to hospice on 7/8/13. The hospital was notified via telephone that the recipient died on 7/16/13.

What to report:

100 Day Date of Contact: 4/23/13 (note the latest disease assessment would likely be reported as 4/22/13)
6 Month Date of Contact: 7/16/13 (note the latest disease assessment would likely be reported as 6/25/13)

**Date of Contact & Subsequent Transplant**
If the recipient has a subsequent HCT, report the date of contact as the day before the preparative regimen begins for the subsequent HCT. If no preparative regimen is given, report the date of contact as the day before the subsequent HCT. In these cases, actual contact on that day is **not** required, and the day prior to the initiation of the preparative regimen (or infusion, if no preparative regimen) should be reported. This allows every day to be covered by a reporting period, but prevents overlap between transplant events.

**Example 5. The recipient had a 2nd transplant with a preparative regimen.**
The recipient has their first transplant on 1/1/13 and a planned second transplant on 2/1/13. The recipient was admitted on and received their first dose of chemotherapy for the preparative regimen for HCT #2 on 1/28/13.

What to report:
100 Day Date of Contact: 1/27/13 (regardless of actual contact on that date)

**Example 6. The recipient had a subsequent transplant without a preparative regimen.**
Following their first transplant on 1/1/13, a recipient with SCID required a subsequent allogeneic transplant due to poor graft function. The recipient has remained inpatient following the first transplant. The physician planned the second transplant for 5/31/13, and proceeded without a preparative regimen.

What to report:
100 Day Date of Contact: 4/11/13 (+/- 15 days)
6 Month Date of Contact: 5/30/13

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 2: Specify the recipient’s survival status at the date of last contact:**
Indicate the clinical status of the recipient on the date of actual contact for follow-up evaluation. If the recipient has died, answers to subsequent questions should reflect the recipient’s clinical status between the date of last report and their death. The center must also complete a Recipient Death Data Form (Form 2900).

**Question 3: Did the recipient receive a subsequent HCT since the date of last report?**
Indicate whether the recipient received a second (or third, etc.) hematopoietic stem cell infusion.
Hematopoietic stem cells are defined as mobilized peripheral blood stem cells, bone marrow, or cord blood. The source of the hematopoietic stem cells may be allogeneic unrelated, allogeneic related, or autologous. For more information on how to distinguish infusion types (example: HCT versus DCI), see Appendix D.

If the recipient has received a subsequent HCT since the date of the last report, ensure the date of actual contact reported in question 1 is the date immediately prior to the start of the preparative regimen for the subsequent HCT. If no preparative regimen was given, report the date prior to infusion.

Questions 4: Has the recipient received a cellular therapy since the date of last report? (e.g., DCI)

Therapy Over Multiple Reporting Periods
If course of cellular therapy carries over an HCT reporting period, and has already been reported on a prior form, do not re-report that course of cellular therapy. For example, if a course of cellular therapy includes three infusions, and the third infusion overlaps from the one year to two year HCT reporting period, do not report a cellular therapy since the date of the last report on the two year HCT follow up form.

Indicate whether the recipient received a cellular therapy for any reason within the reporting period. The most common type of post-HCT cellular therapy would be a donor cellular infusion (DCI) or donor lymphocyte infusion (DLI). These infusions are not intended to promote hematopoiesis. If the recipient received additional cells due to engraftment issues, or if they received an infusion of unmanipulated CD34+ cellular product (stimulated peripheral blood stem cells, bone marrow, or cord blood), report as a subsequent HCT rather than a cellular therapy. For more information on how to distinguish infusion types (example: HCT versus DCI), see Appendix D.

A DCI is a form of cellular therapy that uses cells from the original donor, and is commonly used to create a graft-versus-leukemia / tumor (GVL / GVT) effect. The recipient does not receive a preparative regimen prior to receiving the donor cells because the purpose of a DCI is to activate the immune system rather than repopulate the marrow. The recipient may, however, be given therapy prior to the infusion for the purpose of disease control. The types of cells used in a DCI include, but are not limited to: lymphocytes, unstimulated peripheral blood mononuclear cells, dendritic cells, and / or mesenchymal cells.

Other forms of cellular therapy may include cytotoxic T-lymphocytes (CTLC) to treat infections or chimeric antigen receptor T-cells (CAR T-cells) to treat persistent, progressive or recurrent disease.

Question 5: Date of cellular therapy:

Report the date of cellular therapy infusion. If multiple infusions were received in the reporting period, report the earliest. If infusions are continuing from a previous instance of DCI, only report in the period during which the first infusion was received.
Absolute neutrophil recovery (ANC) recovery is defined as an ANC of \( \geq 500/\text{mm}^3 \) (or \( \geq 0.5 \times 10^9/\text{L} \)) for three consecutive laboratory values obtained on different days.* Date of ANC recovery is the date of the first of three consecutive laboratory values where the ANC is \( \geq 500/\text{mm}^3 \). At some institutions, the laboratory reports display the ANC value once there are sufficient white blood cells to perform a differential count. At other institutions, the laboratory reports do not display the ANC, and it must be calculated from the white blood cell count (WBC) and the percent of segmented and band neutrophils (if the differential was performed on a machine, the percent neutrophils will include both segmented and band neutrophils). If the laboratory report displays an automated ANC value of exactly 500/\( \text{mm}^3 \), the actual ANC value should be calculated from the manual differential if available. The calculated value from the manual differential will determine ANC recovery. If your institution’s laboratory reports do not display the ANC value, use the following calculation to determine the ANC:

**Example 1: Calculating Absolute Neutrophil Count (ANC)**

\[
\frac{% \text{segmented neutrophils} + % \text{band neutrophils}}{% \text{neutrophils}} \times \frac{\text{white blood cell count}/\text{mm}^3}{\text{absolute neutrophil count}/\text{mm}^3}
\]

**Example:**

(Divide percentage by 100 to convert to decimal)

\[
0.45 \text{segmented neutrophils} + 0.05 \text{band neutrophils} = 0.50 \text{neutrophils} \\
\times \frac{1000/\text{mm}^3 \text{white blood cell count}}{500/\text{mm}^3 \text{absolute neutrophil count}}
\]

\[
\text{ANC } 500/\text{mm}^3 = 0.5 \times 10^9/\text{L} = 0.5 \times 10^9/\text{mL} = 0.5 \times 10^3/\text{mm}^3
\]

Traditionally, the definition of ANC recovery required selecting the first date of three consecutive days in
which the recipient’s ANC was ≥ 0.5×10^9/L (500/mm^3). For various reasons it may not be possible to obtain daily laboratory values. Under those circumstances, report ANC recovery based upon three consecutive laboratory values (drawn more than a day apart) as long as the ANC remains ≥ 0.5×10^9/L (500/mm^3).

Tracking the date of ANC recovery may not always be straightforward. In some cases the ANC may fluctuate for a period of time before the recipient fully recovers. In other cases the ANC may remain above ≥ 500/mm^3 for several days immediately post-HCT and then fall below ≥ 500/mm^3. Do not begin counting ANC values of ≥ 500/mm^3 towards recovery until the ANC has dropped to the lowest level (nadir) post-HCT. If the recipient was transplanted using a non-myeloablative (NST) or reduced intensity (RIC) regimen, or was transplanted for an immunodeficiency (e.g., SCID, WAS), the recipient’s ANC may never drop below ≥ 500/mm^3. If this is the case, an ANC recovery date will not be reported, and the “not applicable” option should be chosen. However, if the recipient’s ANC drops below ≥ 500/mm^3 for even one day, this should be considered the nadir and “not applicable” should not be chosen. See the following example for more information regarding tracking the date of ANC recovery.

To report dates in this section, use the first of 3 consecutive laboratory values obtained on different days.

**Example 2: Tracking ANC Recovery**

*Transplant Date = May 6  
Contact Date = August 15*

<table>
<thead>
<tr>
<th>Date</th>
<th>WBC</th>
<th>%Neutrophils</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 7</td>
<td>900</td>
<td>0.6</td>
<td>540</td>
</tr>
<tr>
<td>May 8</td>
<td>850</td>
<td>0.59</td>
<td>502</td>
</tr>
<tr>
<td>May 9</td>
<td>720</td>
<td>0.7</td>
<td>504</td>
</tr>
<tr>
<td>May 10</td>
<td>300</td>
<td>0.45</td>
<td>135</td>
</tr>
<tr>
<td>May 11</td>
<td>15</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 12</td>
<td>30</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 13</td>
<td>50</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 14</td>
<td>250</td>
<td>0.4</td>
<td>100</td>
</tr>
<tr>
<td>May 15</td>
<td>800</td>
<td>0.7</td>
<td>560</td>
</tr>
</tbody>
</table>

*Date of initial recovery: ANC ≥ 500/mm^3 (report this date in question 7)*

<table>
<thead>
<tr>
<th>Date</th>
<th>WBC</th>
<th>%Neutrophils</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 16</td>
<td>1050</td>
<td>0.8</td>
<td>840</td>
</tr>
<tr>
<td>May 17</td>
<td>1000</td>
<td>0.7</td>
<td>700</td>
</tr>
</tbody>
</table>
### Example 3: Initial Recovery with Subsequent Decline and Recovery

**Transplant Date = May 6**  
**Contact Date = August 15**

<table>
<thead>
<tr>
<th>Date</th>
<th>WBC</th>
<th>%Neutrophils</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 7</td>
<td>900</td>
<td>0.6</td>
<td>540</td>
</tr>
<tr>
<td>May 8</td>
<td>850</td>
<td>0.59</td>
<td>502</td>
</tr>
<tr>
<td>May 9</td>
<td>720</td>
<td>0.7</td>
<td>504</td>
</tr>
<tr>
<td>May 10</td>
<td>300</td>
<td>0.45</td>
<td>135</td>
</tr>
<tr>
<td>May 11</td>
<td>15</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 12</td>
<td>30</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 13</td>
<td>50</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 14</td>
<td>250</td>
<td>0.4</td>
<td>100</td>
</tr>
<tr>
<td>May 15</td>
<td>800</td>
<td>0.7</td>
<td>560</td>
</tr>
<tr>
<td>May 16</td>
<td>1050</td>
<td>0.8</td>
<td>840</td>
</tr>
<tr>
<td>May 17</td>
<td>1000</td>
<td>0.7</td>
<td>700</td>
</tr>
<tr>
<td>May 18</td>
<td>1800</td>
<td>0.6</td>
<td>1080</td>
</tr>
<tr>
<td>May 19</td>
<td>2000</td>
<td>0.55</td>
<td>1100</td>
</tr>
<tr>
<td>May 20</td>
<td>2500</td>
<td>0.53</td>
<td>1325</td>
</tr>
<tr>
<td>May 21</td>
<td>2250</td>
<td>0.43</td>
<td>968</td>
</tr>
<tr>
<td>May 22</td>
<td>1500</td>
<td>0.45</td>
<td>675</td>
</tr>
<tr>
<td>May 23</td>
<td>800</td>
<td>0.6</td>
<td>480</td>
</tr>
<tr>
<td>May 24</td>
<td>850</td>
<td>0.41</td>
<td>349</td>
</tr>
</tbody>
</table>
Question 6: Was there evidence of initial hematopoietic recovery?

Indicate whether or not there was evidence of initial ANC recovery following this HCT.

Check only one response:

- If “yes, ANC ≥ 500/mm$^3$ (or ≥ 0.5 × 10$^9$/L) achieved and sustained for 3 laboratory values,” continue with question 7.
- If “no, ANC ≥ 500/mm$^3$ (or ≥ 0.5 × 10$^9$/L) was not achieved,” continue with question 13.
- Check “not applicable” if the recipient’s ANC never dropped below 500/mm$^3$ (or ≥ 0.5 × 10$^9$/L) at any time after the start of the preparative regimen. Continue with question 8.
- Check “previously reported,” if the recipient’s initial hematopoietic recovery was recorded on a previous report. Continue with question 13.

Question 7: Date ANC ≥ 500/mm$^3$ (first of 3 lab values):

Enter the first date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm$^3$ (or ≥ 0.5 × 10$^9$/L). For an example of tracking ANC, see Example 2 and Example 3 above.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 8: Following the initial hematopoietic recovery, was there subsequent decline in ANC to < 500/mm$^3$ for ≥ 3 days since the date of last report?

Report if there was subsequent decline in ANC < 500/mm$^3$ (or < 0.5 × 10$^9$/L) (three consecutive laboratory
values obtained on different days where the ANC declined to < 500/mm$^3$. If “yes,” continue with question 9. If “no,” continue with question 13.

**Multiple Recoveries and Declines**
The form does not allow for multiple recoveries and declines in the same reporting period. If the recipient’s ANC initially recovers and then declines, followed by another recovery and another decline, report the date of the first (initial) recovery (question 7), the first decline (question 9), and the last recovery (question 12).

**Question 9: Date of decline in ANC < 500/mm$^3$ for ≥ 3 days (first of 3 days that the ANC declined):**

Enter the first date of the three consecutive laboratory values obtained on different days where the ANC declined to < 500/mm$^3$ (or < 0.5 × 10$^9$/L).

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

**Question 10: Did recipient recover and maintain ANC ≥ 500/mm$^3$ following the decline?**

Indicate whether there was evidence of ANC recovery following the decline (three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm$^3$ (or ≥ 0.5 × 10$^9$/L). If “yes,” continue with question 11. If “no,” continue with question 13.

**Question 11-12: Date of ANC recovery:**

Report if the date of ANC recovery following the decline is “known” or “unknown.” If the date of recovery is “known,” continue with question 12 and enter the first date of the three consecutive laboratory values obtained on different days where the ANC recovered to ≥ 500/mm$^3$ (or ≥ 0.5 × 10$^9$/L) following the decline. See [Example 3](#) above. If the date of recovery following decline is “unknown,” continue with question 13.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).
Q13-18: Megakaryopoiesis / Platelet Recovery

The following questions refer to initial platelet recovery following the HCT for which this form is being completed. All dates should reflect no platelet transfusions administered for seven consecutive days. Report the date of the first of three consecutive laboratory (≥ 20 × 10⁹/L and ≥ 50 × 10⁹/L) obtained on different days, as shown in Example 10 below. Note that platelet recovery may take place well after the recipient has returned to the referring physician for care. It is essential that information and laboratory values be obtained from the referring physician.

Transfusions temporarily increase platelet counts. When the data is later used for analysis, it is important to be able to distinguish between a recipient whose own body was creating the platelets and a recipient who required transfusions to support the counts.

The following example illustrates the procedure to follow for reporting platelet recovery.

**Example 1: Reporting Platelet Recovery**

<table>
<thead>
<tr>
<th>Transfusion</th>
<th>Day</th>
<th>Platelet Count</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>10,000</td>
<td>1/1/2008</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>35,000</td>
<td>1/2/2008</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>30,000</td>
<td>1/3/2008</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>25,000</td>
<td>1/4/2008</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>10,000</td>
<td>1/5/2008</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>15,000</td>
<td>1/6/2008</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>19,000</td>
<td>1/7/2008</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>23,000</td>
<td>1/8/2008</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>25,000</td>
<td>1/9/2008</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>40,000</td>
<td>1/10/2008</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>50,000</td>
<td>1/11/2008</td>
</tr>
</tbody>
</table>

Report 1/8/08 as date platelet count ≥ 20 × 10⁹/L

**Example 2: Reporting Platelet Recovery (≥ 20 × 10⁹/L and ≥ 50 × 10⁹/L)**

<table>
<thead>
<tr>
<th>Date</th>
<th>Day</th>
<th>Platelet Count</th>
<th>Date of last platelet transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 13</td>
<td>0</td>
<td>10,000</td>
<td></td>
</tr>
</tbody>
</table>

Questions 13-18 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.
### Question 13: Was an initial platelet count ≥ 20 × 10^9/L achieved?

Indicate whether or not there was evidence of initial platelet recovery following this HCT.

Check only one response:

- If “yes,” continue with question 14.
- If “no,” continue with question 19.
- Check “not applicable,” if the recipient’s platelets never dropped below 20 × 10^9/L at any time post-HCT and a platelet transfusion was never required. If the recipient’s platelet count drops below

<table>
<thead>
<tr>
<th>Date</th>
<th>Day</th>
<th>Value (cells/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 14</td>
<td>1</td>
<td>30,000</td>
</tr>
<tr>
<td>June 15</td>
<td>2</td>
<td>25,000</td>
</tr>
<tr>
<td>June 16</td>
<td>3</td>
<td>10,000</td>
</tr>
<tr>
<td>June 17</td>
<td>4</td>
<td>15,000</td>
</tr>
<tr>
<td>June 18</td>
<td>5</td>
<td>19,000</td>
</tr>
<tr>
<td>June 19</td>
<td>6</td>
<td>23,000</td>
</tr>
<tr>
<td>June 20</td>
<td>7</td>
<td>25,000</td>
</tr>
<tr>
<td>June 21</td>
<td>8</td>
<td>40,000</td>
</tr>
<tr>
<td>June 22</td>
<td>9</td>
<td>50,000</td>
</tr>
<tr>
<td>June 23</td>
<td>10</td>
<td>56,000</td>
</tr>
<tr>
<td>June 24</td>
<td>11</td>
<td>65,000</td>
</tr>
<tr>
<td>June 25</td>
<td>12</td>
<td>72,000</td>
</tr>
</tbody>
</table>

This section relates to initial platelet recovery. All dates should reflect no transfusions in the previous 7 days. To report dates in this section, use the first of 3 consecutive laboratory values obtained on different days.

1st of 3 consecutive laboratory values ≥ 20 × 10^9/L (report this date in question 15)

1st of 3 consecutive laboratory values ≥ 50 × 10^9/L (report this date in question 18)
20 × 10⁹/L and/or the recipient received a platelet transfusion even once, do not use this option. This option is only applicable in the 100-day reporting period. Continue with question 16.

- Check “previously reported” if this is the 6 month or annual follow-up, and initial platelet recovery has already been reported on a previous form. Continue with question 16.

**Question 14-15: Date platelet ≥ 20 × 10⁹/L**

Enter the **first** date of three consecutive laboratory values obtained on different days where the platelet count was ≥ 20 × 10⁹/L. Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in Example 1 above, when determining the recovery date.

If three laboratory values were not obtained on consecutive days, but a sequential rise of ≥ 20 × 10⁹/L is demonstrated, follow the examples below when determining an estimated date.

**Reporting Scenarios:**

**A.** The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is 22 × 10⁹/L on January 2, 24 × 10⁹/L on January 3, and 28 × 10⁹/L on January 4. The recipient does not come into the clinic for evaluation until one month later. The recipient has not received any more platelet transfusions and the platelet count is well above 20 × 10⁹/L. Report January 8 (day seven post-platelet transfusion) for the date of platelet recovery.

**B.** The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is ≥ 20 × 10⁹/L on January 2, January 3, and January 4. The recipient is then discharged back to their primary care physician. The transplant center receives a follow-up note from the primary care physician that states “recipient recovered their platelets in January of 2011.” Report an estimated date of recovery using the guidelines available in General Instructions, [General Guidelines for Completing Forms](#).

**Question 16: Was an initial platelet count ≥ 50 × 10⁹/L achieved?**

Indicate whether a platelet count of ≥ 50 × 10⁹/L was achieved following this HCT.

Check only **one** response:

- If “yes,” continue with question 17.
- If “no,” continue with question 19.
- Check “not applicable,” if the platelet count never dropped below 50 × 10⁹/L at any time post-HCT.
Continue with question 19.

- Check “previously reported,” if a platelet count of ≥ 50 \( \times 10^9 \)/L was achieved and reported previously.

Continue with question 19.

**Question 17-18: Date platelets ≥ 50 \( \times 10^9 \)/L:**

Enter the **first** date of three consecutive laboratory values obtained on different days where the platelet count was ≥ 50 \( \times 10^9 \)/L. Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in **Example 2** above, when determining the recovery date.

If three laboratory values were not obtained on consecutive days, but a sequential rise of ≥ 50 \( \times 10^9 \)/L is demonstrated, follow the examples included in the instructions for questions 14-15 above.
Q19-48: Growth Factor and Cytokine Therapy

Questions 19-48 can only be completed on the 100 day follow-up form. These questions will be skipped for all subsequent reporting periods.

Question 19: Did the recipient receive hematopoietic, lymphoid growth factors or cytokines after the start of the preparatory regimen?

A growth factor is a substance that stimulates cell growth, differentiation, and proliferation. Cytokines can act as growth factors or have an inhibitory effect on cell growth.

Indicate whether the recipient received hematopoietic growth factors, lymphoid growth factors, or cytokines between the start of the preparative regimen and 100 days post-HCT. If “yes,” continue with question 20. If “no,” continue with question 49.

Questions 20-48: Specify agents and provide dates for the first course of each agent given in this reporting period.

Report all agents given during the reporting period. For each agent administered during the reporting period, report the start date and the reason it was given.


**Erythropoietin (EPO)**: Alternate names: Epogen, Procrit, darbepoietin alfa (Aranesp). EPO stimulates red blood cell production.

**KGF** (keratinocyte growth factor): Alternate names: palifermin, Kepivance. KGF acts to stimulate the growth of cells that line the surface of the mouth and intestinal tract. KGF may also be given to treat oral mucositis or as GVHD prophylaxis. Report if administered to stimulate cell growth or to treat oral mucositis. If KGF is administered as GVHD prophylaxis, report in the Acute Graft vs. Host Disease section of this form.

**Blinded growth factor or cytokine trial**: If the recipient is on a blinded randomized trial, specify the trial agent administered. Additionally, update this form (2100) once the trial is over to specify whether the
recipient received the trial drug or placebo.

**Other agent:** Specify any other hematopoietic growth factor, lymphoid growth factor, or cytokine administered.
Questions 49-63: Current Hematologic Findings

Questions 49-63 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.

Questions 49-63: Provide the most recent laboratory values recorded

These questions are intended to determine the hematological status of the recipient after the HCT. Testing may be performed multiple times within the reporting period; however, report only the most recent (closest to the contact date) laboratory values.

Report the laboratory value and unit (if applicable) for each hematologic finding. If a value is not known, select “unknown” and continue with the next laboratory value.

For hematocrit, check the box if red blood cells were transfused within 30 days prior to the testing.

For platelets, check the box if platelets were transfused within seven days prior to the testing.
Q64-88: Immune Reconstitution

These questions are intended to determine whether the recipient recovered their immune function post-HCT. Along with hematopoietic recovery, the infused hematopoietic progenitor cells (HPCs) also generate a new immune system. This process may be slowed by immunosuppressants given to prevent GVHD.

Questions 64: Date sample collected:

Report the date when the most recent immunoglobulin sample was collected. If no immunoglobulin testing was performed during the reporting period, leave question 64 blank and override the validation error using the “Not Tested” option.

Question 65: Did the recipient receive supplemental intravenous immunoglobulins (IVIG)?

IVIG is a product made from pooled human plasma and primarily contains IgG. It is used to provide immune-deficient recipients with antibody function to prevent infection. It may be administered intravenously or subcutaneously and IVIG given via either route should be reported in this section of the form.

Indicate whether the recipient received IVIG during the reporting period. If “yes,” continue with question 66. If “no,” continue with question 69.

*IVIG Given without Immunoglobulin Testing*

In some cases, IVIG may be given for low immune function without immunoglobulin testing. The transplant center should verify that Ig levels were not tested at another facility, as it is unusual for IVIG to be given without knowing what the IgG level is. In these cases, question 65 should be answered “yes” and question 66 should be answered “no” (even though testing was not done). Answer question 67 as “prophylaxis for low IgG…” because the recipient is receiving IVIG for decreased immune function even though there is not a laboratory value to document a low IgG level. Report “unknown” for questions 69, 71, and 73.
Question 66: Was supplemental IVIG received in the 30 days prior to the date the sample was collected?

Indicate whether the recipient received IVIG ≤30 days prior to the immunoglobulin testing reported in questions 69-74. If IVIG is given within 30 days of immunoglobulin testing, the IgG level would not represent the recipient’s native IgG.

Question 67-68: Specify the indication for which IVIG was given:

Specify the indication(s) for which IVIG was given to the recipient. If the indication is unclear, consult with the transplant physician. If “other indication” is selected, specify the indication for use of IVIG in question 68.

Question 69-74: Specify the immunoglobulin values from the most recent testing:

Antibodies are produced by the immune system in response to foreign substances such as bacteria, viruses, or fungi. There are several types of immunoglobulins; the CIBMTR requests information on IgG, IgM, and IgA.

- IgG antibodies are present in all body fluids. They play a key role in fighting bacterial and viral infections.
- IgM antibodies are present in blood and lymph fluid. They are the first type of antibody produced by the immune system in response to an infection.
- IgA antibodies are present in the nose, airway, digestive tract, ears, eyes, saliva, tears, and blood. They protect surfaces of the body that are exposed to outside foreign substances.

Report if the value for each immunoglobulin (antibody) is “known” or “unknown.” If “known,” specify the value and unit from the most recent test performed during the reporting period. Report “unknown” if testing was not performed during the reporting period or the results cannot be obtained.

Question 75-76: Were lymphocyte analyses performed?

Lymphocyte analyses are often performed post-HCT to evaluate the reconstitution of the immune system. Certain lymphocyte groups repopulate earlier than others post-HCT. Indicate whether lymphocyte analyses were performed. If “yes,” report the date the sample was collected in question 76. If “no,” continue with question 89.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.
Questions 77-88: Results of Lymphocyte Analysis

Test for CD16+ Cells
If testing is not performed for CD56+ cells, but is performed for CD16+ cells, report the CD16+ result in questions 87-88.

Report the value and specify the unit for each lymphocyte subset if known. If the subset was not tested on the date specified in question 76 or the result is not known, select “unknown” and continue with the next subset.

If the results show the absolute lymphocyte count, but only percentages of lymphocyte subsets, it is necessary to calculate the absolute value of each lymphocyte subset for reporting purposes. This can be done by multiplying the percentage of each subset by the absolute lymphocyte count. See the example below:

**Example 1: Calculating lymphocyte counts**

*Absolute Lymphocyte Count: 4.8 × 10^9/L*

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Lab Report Percentage</th>
<th>Calculation (Percentage x ALC)</th>
<th>Absolute Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3</td>
<td>74%</td>
<td>0.74 × 4.8</td>
<td>CD3: 3.55 × 10^9/L</td>
</tr>
<tr>
<td>CD3CD4</td>
<td>40%</td>
<td>0.40 × 4.8</td>
<td>CD4: 1.92 × 10^9/L</td>
</tr>
<tr>
<td>CD3CD8</td>
<td>34%</td>
<td>0.34 × 4.8</td>
<td>CD8: 1.63 × 10^9/L</td>
</tr>
<tr>
<td>CD19</td>
<td>NT</td>
<td>—</td>
<td>CD19: Unknown</td>
</tr>
<tr>
<td>CD20</td>
<td>NT</td>
<td>—</td>
<td>CD20: Unknown</td>
</tr>
<tr>
<td>CD56</td>
<td>NT</td>
<td>—</td>
<td>CD56: Unknown</td>
</tr>
</tbody>
</table>
Q89-107: Chimerism Studies

**Autologous Transplants**
If this was an autologous HCT, continue with the Engraftment Syndrome section starting with question 108. Chimerism testing and graft-versus-host disease sections should only be completed for allogeneic HCTs.

**Syngeneic Transplants**
If this was a syngeneic HCT, continue with the Engraftment Syndrome section starting with question 108. Chimerism testing is not collected for syngeneic HCTs.

**Questions 89-107 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.**

Chimerism studies are performed to determine the percent of blood or marrow cells post-transplant that are produced from donor hematopoietic stem cells and the percent that are produced from host (recipient) hematopoietic stem cells. Different types of blood cells and a variety of laboratory tests can be used to determine if a chimera (presence of both donor- and host-derived cells) exists. If cytogenetic testing was performed to look for disease markers, and the donor and recipient are different sexes, the test may also be used to determine if a chimera exists. If the donor and recipient are of the same sex, cytogenetic testing using the common staining technique, known as giemsa banding (G-banding), cannot be used to determine if there is a chimera. However, quinicrine banding (Q-banding) can be used to identify if the cells are of donor origin or not in a same-sex transplant, as this staining technique highlights inherited chromosome polymorphisms on certain human chromosomes including 3, 4, 13, 15, 21, 22, and Y. This is not a commonly used staining technique and is only helpful when the polymorphism is documented pre-HCT.

**Chimerism Studies**
If chimerism studies were attempted, but no evaluable results were obtained, do not report the test.
When a multi-donor chimerism exists and includes a donor (or donors) from a previous HCT, report as a multi-donor chimerism though there may only be one donor for the current transplant.
**Question 89-90: Were chimerism studies performed post-HCT? (Allogeneic HCTs only)**

Indicate whether chimerism studies were performed within the reporting period. If “yes,” continue with question 90 and indicate whether documentation was submitted to CIBMTR (e.g., chimerism laboratory reports).

If chimerism studies were not performed within the reporting period, select “no,” and continue with question 108.

**Question 91: Were chimerism studies assessed for more than one donor / multiple donors?**

Indicate whether this HCT included product(s) from multiple donors. When a multi-donor chimerism exists and includes a donor or donors from a previous HCT, report as a multi-donor chimerism even though there may only be one donor for the current transplant.

**Questions 92-107: Provide date(s), method(s) and other information for all chimerism studies performed prior to the date of contact (question 1)**

Transplant centers may perform frequent chimerism studies. If there is a need to reduce the number of chimerism study results reported due to volume, ensure that the following are reported at a minimum:

- Studies performed on or at approximately Day+28
- Most recent studies performed prior to the date of contact, particularly for Day+100
- Most recent studies performed prior to and after an intervention (such as a donor cellular infusion)
- The first result to show complete / 100% donor chimerism

### Chimerism – Single Donor

<table>
<thead>
<tr>
<th>Data Field</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>92. NMDP donor ID</td>
<td>If the donor or one of the donors was an NMDP PBSC or marrow donor, enter the 9 digit NMDP donor ID.</td>
</tr>
<tr>
<td></td>
<td>Description</td>
</tr>
<tr>
<td>---</td>
<td>------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>93.</td>
<td>NMDP cord blood unit ID If the donor or one of the donors was an NMDP cord blood unit, enter the 9 digit NMDP cord blood unit ID.</td>
</tr>
<tr>
<td>94.</td>
<td>Non-NMDP unrelated donor ID If the donor or one of the donors was a non-NMDP unrelated PBSC or marrow donor, enter the non-NMDP registry donor ID.</td>
</tr>
<tr>
<td>95.</td>
<td>Non-NMDP cord blood unit ID If the donor or one of the donors was a non-NMDP cord blood unit, enter the non-NMDP registry donor ID.</td>
</tr>
<tr>
<td>96.</td>
<td>Date of birth or age If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry, provide the date of birth, if known; if date of birth is not known, provide the donor’s age at donation.</td>
</tr>
<tr>
<td>97.</td>
<td>Sex If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry, provide the biological sex.</td>
</tr>
<tr>
<td>98.</td>
<td>Date sample collected Enter the date the sample was collected for the chimerism test.</td>
</tr>
<tr>
<td>99-100.</td>
<td>Method Report the test method used for the reported chimerism study. Cytogenetic testing methods include karyotyping and fluorescent in situ hybridization (FISH). Cytogenetic methods are only valid for sex mismatched transplants with the exception of quinicrine banding. VNTR / STR is one of the most common molecular methods for assessing chimerism. See the Chimerism Methods table below for additional details on chimerism testing methods.</td>
</tr>
<tr>
<td>101.</td>
<td>Cell source Report whether the specimen taken for chimerism testing was from a marrow or peripheral blood source.</td>
</tr>
<tr>
<td>102-103.</td>
<td>Cell type Indicate the cell type tested. If the specimen was not sorted for a specific cell line, indicate “unsorted / whole.” See the Chimerism Cell Types table below for additional details on cell markers unique to certain cell lines.</td>
</tr>
<tr>
<td>104.</td>
<td>Total cells examined Cytogenetic testing methods include karyotyping and fluorescent in situ hybridization (FISH), each of which examines a specific and relatively low number of cells – generally 15 to 200, depending on specimen and test method. If a cytogenetic method was used, enter the total number of cells that were examined. If a non-cytogenetic test was used, leave these boxes blank.</td>
</tr>
<tr>
<td>105.</td>
<td>Number of donor cells Cytogenetic methods, karyotyping and FISH, examine a specific and relatively low number of cells – generally 15 to 200, depending on specimen and test method. If a cytogenetic method was used, enter the total number of cells that were examined and found to be of donor origin. If a non-cytogenetic test was used, leave these boxes blank.</td>
</tr>
<tr>
<td>106.</td>
<td>Were donor cells detected? Molecular testing methods include RFLP and VNTR / STR. If a molecular method was used, indicate whether donor cells were detected. Report “yes,” if the testing identified any percentage of cells as being of donor origin.</td>
</tr>
</tbody>
</table>
| 107. | Percent donor cells Molecular testing methods include VNTR / STR, RFLP, and AFLP. Report the percentage of donor cells identified by molecular testing. If the test result did not detect any recipient cell population within the sensitivity of the assay, report 100% donor cells. If the test detected recipient
cells, but indicated donor cells “> n%,” report “n + 1” percent donor cells. If the test detected donor cells but indicated donor cells “< n%,” report “n – 1” percent donor cells.

Chimerism Methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karyotyping for XX / XY</td>
<td>Cells are grown in culture, stained, and examined under a microscope to identify the number of cells matching the sex of the donor. This method is only valid when donor and recipient are sex mismatched.</td>
</tr>
<tr>
<td>Fluorescent in situ hybridization (FISH) for XX / XY</td>
<td>Cells are exposed to fluorescent DNA probes which attach to X and Y chromosomes. A microscope is used to identify the number of cells matching the sex of the donor. This method is only valid when donor and recipient are sex mismatched. Do not report FISH testing for disease-specific abnormalities in the chimerism section of the Post-TED.</td>
</tr>
<tr>
<td>Restricted fragment length polymorphisms (RFLP)</td>
<td>A restriction fragment is a portion of DNA which has been cut out by an enzyme. RFLP testing begins by isolating DNA from the sample. Enzymes are used to cut the DNA at specific loci resulting in many unique restriction fragments. The fragments are separated according to size by electrophoresis. The unique pattern of separation is used to identify the percent donor DNA present in the sample.</td>
</tr>
<tr>
<td>Variable number tandem repeat (VNTR), micro- or minisatellite</td>
<td>VNTR refers to a portion of DNA containing a repeating sequence of base pairs (micro- or minisatellite). The number of times a micro- or minisatellite repeats within specific loci can differ between individuals. These differences are used to distinguish donor DNA from recipient DNA. VNTR testing involves obtaining samples from the recipient and donor prior to transplant. Specific loci are compared to determine which loci contain VNTRs unique to the donor. After transplant, DNA is isolated from recipient samples. Donor-specific VNTRs are amplified by PCR techniques. The sample is then analyzed to determine the percent donor DNA present.</td>
</tr>
<tr>
<td>Small tandem repeat (STR), micro- or minisatellite</td>
<td>STR also refers to a portion of DNA containing a repeating sequence of base pairs (micro- or minisatellite). The number of times a micro- or minisatellite repeats within specific loci can differ between individuals. These differences are used to distinguish donor DNA from recipient DNA. STR testing involves obtaining samples from the recipient and donor prior to transplant. Specific loci are compared to determine which loci contain STRs unique to the donor. After transplant, DNA is isolated from recipient samples. Donor-specific STRs are amplified by PCR techniques. The sample is then analyzed to determine the percent donor DNA present.</td>
</tr>
<tr>
<td>Amplified fragment length polymorphisms (AFLP)</td>
<td>A restriction fragment is a portion of DNA which has been cut out by an enzyme. AFLP testing begins by isolating DNA from the sample. Enzymes are used to cut the DNA at specific loci resulting in many unique restriction fragments. Many restrictions fragments are amplified using PCR techniques. The fragments are separated according to size by electrophoresis. The unique pattern of separation is used to identify the percent donor DNA present in the sample. Report AFLP testing using the VNTR/STR method option on the 2450 form.</td>
</tr>
</tbody>
</table>

Chimerism Cell Types

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
<td>Description</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Unsorted / whole</td>
<td>The peripheral blood or bone marrow sample has not been sorted or selected for a certain cell line.</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>Also known as RBCs or erythrocytes; carry the CD235a cell marker</td>
</tr>
<tr>
<td>Hematopoietic progenitor cells</td>
<td>Includes CD34+ cells</td>
</tr>
<tr>
<td>Total mononuclear cells</td>
<td>Total mononuclear cells would be a specimen containing only and both lymphocytes and monocytes</td>
</tr>
<tr>
<td>T cells</td>
<td>Includes CD3+, CD4+, and / or CD8+ cells</td>
</tr>
<tr>
<td>B cells</td>
<td>Includes CD19+ or CD20+ cells</td>
</tr>
<tr>
<td>Granulocytes</td>
<td>Also known as polymorphonuclear leukocytes (PMNs, PMLs) and includes neutrophils, eosinophils, and basophils. Includes CD33+ cells</td>
</tr>
<tr>
<td>NK cells</td>
<td>Includes CD56+ cells</td>
</tr>
<tr>
<td>Other, specify</td>
<td>Use this option to report cell types that do not fit in a category above.</td>
</tr>
</tbody>
</table>
Engraftment syndrome typically occurs during neutrophil recovery post-HCT and is characterized by capillary leak syndrome, non-infectious fever, erythrodermatous skin rash, and non-cardiogenic pulmonary edema. Engraftment syndrome is usually seen following autologous transplants, but can occur after allogeneic transplants. It is associated with increased transplant mortality, generally from pulmonary and associated multi-organ failure. Corticosteroid therapy is often an effective treatment for engraftment syndrome, mainly for the treatment of pulmonary symptoms.

Indicate whether the recipient developed engraftment syndrome.

If the recipient developed engraftment syndrome during the reporting period, report “yes” and indicate the date of diagnosis in question 109. If the recipient did not develop engraft syndrome, report “no” and continue with question 131.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 110-119: Specify symptoms of engraftment syndrome

Indicate whether the recipient developed the symptoms listed. If “other symptom” is selected, specify symptom in question 119.

Question 120: Was a biopsy performed?

If a biopsy was performed to evaluate engraftment syndrome, report “yes” and specify the site(s) in questions 121-125. If no biopsies were done to evaluate for engraftment syndrome, report “no” and continue with question 126.

Question 121-125: Specify site:

From the options listed, report the biopsy site. If “other site” is selected, specify the location of the biopsy in question 124. Indicate whether documentation (pathology report) was attached to the form in FormsNet3 or
otherwise submitted to the CIBMTR in question 125. For further instructions on how to attach documents in FormsNet3, refer to the training guide.

**Question 126: Was therapy given for engraftment syndrome?**

Report if therapy was given for engraftment syndrome. If therapy was given for engraftment syndrome, report “yes” and continue with question 127. If therapy was not given, report “no” and continue with question 130.

**Question 127-129: Specify therapy given for engraftment syndrome (systemic corticosteroids, other therapy)**

Report any treatment given for engraftment syndrome. If “other therapy” is chosen, specify the treatment(s) in question 129.

**Question 130: Did engraftment syndrome resolve?**

Indicate whether engraftment syndrome resolved during the reporting period. If engraftment syndrome was still present on the date of contact, report “no.”
Graft vs. Host Disease (GVHD) is an immunological phenomenon resulting from the reaction of donor immune cells against major or minor histocompatibility antigens of the recipient. GVHD is primarily caused by donor-derived T-cells. Very rarely, GVHD may occur due to autologous reactivity (autologous GVHD), third party transfusions, or with identical twin (syngeneic) transplantation.

Factors influencing the severity of GVHD are related to three main categories: 1) donor or graft, 2) recipient, and 3) treatment. Influential risk factors include the degree of genetic disparity between the donor and the recipient (HLA match), female donor to male recipient, donor parity, older donors, and T-cell dose. The occurrence of acute GVHD becomes a risk factor for the development of chronic GVHD. Recipient age and prior infections are also factors.

In the past, GVHD was classified as acute or chronic based on its time to diagnosis following transplant, and other clinical and histological (biopsy or post-mortem) features. Today, there has been increased recognition that acute and chronic GVHD are not dependent upon the time since HCT, so determination of acute or chronic should rest on clinical and histological features. However, organ staging and overall grade should only be calculated from the clinical picture, not histology. Acute GVHD usually begins between 10 and 40 days after HCT but can appear earlier or later. The organs most commonly affected by acute GVHD are the skin, gut, and/or liver. Other sites, such as the lung, may be involved.

GVHD Prophylaxis
ATG, cyclophosphamide, and alemtuzumab given prior to and including Day 0 as GVHD prophylaxis should be reported in the preparative regimen section on the Baseline Form and on the Pre-TED Form.
Question 131: Was specific therapy used after the start of the preparative regimen to prevent acute GVHD? (Note: do not include growth factors reported in questions 19-48, or ex vivo T-cell depletion reported on the Product Insert. Do not include drugs given as part of the preparative regimen)

Following an allogeneic HCT, specific immunosuppressive therapy may be administered to prevent GVHD or to immunosuppress the host marrow, thereby promoting engraftment of the donor hematopoietic stem cells. Most transplant centers have specific GVHD prophylaxis protocols and graft rejection protocols. Any agent a recipient receives as a result of these protocols should be included in this section.

The prophylactic drug options listed on the form are intended to be systemic (IV or oral administration). If the recipient received one of the listed drugs in a topical form, report the drug in the “other, specify” category.

Do not include growth factors reported in question 19, or ex vivo T-cell depletion reported on the Product Insert. Do not include drugs given as part of the preparative regimen.

The Post-Transplant Follow-Up Data Form (Form 2100) lists the generic immune suppression drug names. The following website provides the trade names under which generic drugs are manufactured: http://www.rxlist.com/drugs/alpha_a.htm.

If GVHD prophylaxis is used for a syngeneic (monozygotic or identical twin) or autologous HCT, fax or e-mail an explanation to your center’s CIBMTR CRC, and request it be scanned as part of the form documentation.

If specific therapy was given after the start of the preparative regimen to prevent acute GVHD, report “yes” and continue with question 132. See the GVHD Prophylaxis note above for additional instructions on how to report ATG, cyclophosphamide, and alemtuzumab. If specific therapy to prevent acute GVHD was not given after the start of the preparative regimen, report “no” and continue with question 157.
Questions 132-156:

For each agent listed, indicate whether it was used to prevent acute GVHD or graft rejection, and answer any additional question(s) for each prophylactic therapy used.

**ALG (Anti-Lymphocyte Globulin), ALS (Anti-Lymphocyte Serum), ATG (Anti-Thymocyte Globulin)**

**ATS (Anti-Thymocyte Serum):** Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes. Also report the animal source. If “other” is selected, specify the source.

**Bortezomib (Velcade):** A proteasome inhibitor.

**Corticosteroids (systemic) (e.g., prednisone, dexamethasone):** Usually combined with cyclosporine when used for prophylaxis. Only report systemic steroids in this section. If topical steroids are used prophylactically, report in questions 155-156 and provide an explanation regarding how the site for topical application was selected.

**Cyclosporine (CSA, Neoral, Sandimmune):** Calcineurin inhibitor which decreases cytokine production by T-cells. Usually given for ≥ 3 months.

**Cyclophosphamide (Cytoxan):** Given in high doses near the date of infusion as single agent prophylaxis.

**Extra-corporeal photopheresis (ECP):** The recipient’s blood is removed from the body, exposes to psoralen and ultraviolet light, and re-infused.

**FK 506 (Tacrolimus, Prograf):** Inhibits the production of interleukin-2 by T-cells.

**In vivo monoclonal antibody:** Antibody preparations that are infused in the recipient following HSCT. Specify the antibody used as: anti CD25 (Zenapax, Daclizumab, AntiTAC), alemtuzumab (Campath), entanercept (Enbrel), infliximab (Remicade), and / or rituximab (Rituxan).

**In vivo immunotoxin:** Antibody preparations linked to a toxin that is infused in the recipient following HCT. Specify the immunotoxin.

**Methotrexate (MTX) (Amethopterin):** Inhibits the metabolism of folic acid. It is most often used with cyclosporine and is usually for a short duration of time.

**Mycophenolate mofetil (MMF) (CellCept, Myfortic):** Inhibits the de novo pathway used for lymphocyte
proliferation and activation.

**Sirolimus (Rapamycin, Rapamune):** Inhibits the response to interleukin-2, blocking the activation of T-cells.

**Blinded randomized trial:** If the recipient is on a blinded randomized trial, specify agent being studied in the trial. Additionally, update the Post-HCT Data Form (Form 2100) once the trial is over to specify whether the recipient received the trial drug or placebo.

**Other agent:** Specify the other agent being given as GVHD prophylaxis.

- Do not include ex vivo T-cell depletion. Report ex vivo T-cell depletion on the HCT Infusion Form (Form 2006).
- Do not include agents used to prevent infection. Report infection prophylaxis agents in the infection section, questions 407-427.

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**Acute / Chronic GVHD**

If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 157-233). Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section.

Report any **new or persistent** acute GVHD symptoms occurring on or after the onset of chronic GVHD only in the chronic GVHD section. If chronic GVHD was diagnosed in a prior reporting period, report “no” for questions 157 and 159 in each subsequent reporting period. See Acute GVHD Diagnosis Scenarios included in the instructions for question 157.

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**Question 157: Did acute GVHD develop since the date of the last report?**

Questions 157 and 159 on the Post-HCT Follow-Up Data Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 157 or question 158 must be answered “yes” unless there has been a prior / concurrent diagnosis of chronic GVHD (refer to the note above question 157). There will not be a situation where “yes” is reported for both question 157 and question 159. If question 157 is answered yes and a diagnosis date has been reported in question 158, question 159 will be disabled in FormsNet3SM.

Centers should report “yes” for question 157 to indicate the recipient developed acute GVHD in the following scenarios:

- Acute GVHD is diagnosed for the first time during the reporting period.
• An acute GVHD flare is diagnosed during the current reporting period and all of the following conditions are met:
  ◦ The recipient’s prior acute GVHD symptoms did not persist from the prior reporting period into the beginning of the current reporting period.
  ◦ The flare is diagnosed after at least 30 days without any active acute GVHD symptoms.
  ◦ The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 157).

If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report “no” for question 157 and “yes” for question 159. Question 159 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer questions 157 and 159.

Report “no” for questions 157 and 159 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 157).

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

**Acute GVHD Diagnosis Scenarios:**

**A.** A recipient receives a HCT on 1/1/2015 and develops acute GVHD which is clinically diagnosed on 2/1/2015. At least one of their symptoms, attributed to acute GVHD, persists beyond the 100 day date of contact which is 4/5/2015. Treatment continues and symptoms completely resolve on 5/1/2015. Immunosuppression is tapered until a flare of acute GVHD is diagnosed on 5/25/2015. Immunosuppression is given and symptoms quickly resolve with no active acute GVHD beginning 6/10/2015. The six month date of contact is 6/20/2015. Another flare of acute GVHD is clinically diagnosed on 8/15/2015.

**100 Day Post-Infusion Data Form:**

Question 157: Report “yes” to indicate a new clinical diagnosis of acute GVHD.
Question 158: Report the initial date of diagnosis (2/1/2015).
Question 159: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 158.
Questions 160-175: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

_Six Month Post-Infusion Data Form:_

Question 157: Report “no” to indicate acute GVHD persists from a previous report. Note, the flare of acute GVHD was < 30 days from symptoms resolution so it doesn’t count as a new reportable episode. Question 158: Leave blank. This question will be skipped whenever question 157 is answered “no.” Question 159: Report “yes” to indicate GVHD persists from a previous report. Questions 160-175: Leave blank. Answering “yes” for question 159 prevents the center from re-reporting diagnosis information already captured on the 100 day form.

_One Year Post-Infusion Data Form:_

Question 157: Report “yes” to indicate a flare of acute GVHD occurred at least 30 days after resolving during a prior reporting period. Question 158: Report the diagnosis date of the flare occurring during the reporting period (8/15/2015). Question 159: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 158. Questions 160-175: Answer these questions based on the assessments performed at the time of diagnosis of the flare of acute GVHD (8/15/2015).

_B._ A recipient receives a HCT on 1/1/2015 and develops acute skin GVHD on 2/1/2015 and then chronic eye GVHD on 3/1/2015. Both acute and chronic symptoms resolve by the 100 day date of contact (4/5/2015). While tapering their immunosuppression, the recipient has a flare of their acute skin GVHD on 5/30/2015. Treatment continues and symptoms completely resolve by the six month date of contact (6/20/2015).

_100 Day Post-Infusion Data Form:_

Question 157: Report “yes” to indicate a new clinical diagnosis of acute GVHD. Question 158: Report the initial date of diagnosis (2/1/2015). Question 159: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 158. Questions 160-175: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015). Questions 176-233: Answer these questions based on any symptoms and treatment documented from the onset of acute GVHD (2/1/2015) up to the diagnosis of chronic GVHD (3/1/2015). This instruction is provided in the note box above question 157.
Six Month Post-Infusion Data Form:

Question 157: Report “no” to indicate acute GVHD did not develop during the reporting period.
Question 158: Leave blank. This question will be skipped whenever question 157 is answered “no.”
Question 159: Report “no” to indicate acute GVHD did not persist from a previous report.

*If chronic GVHD has been diagnosed in a prior reporting period, report “no” for questions 157 and 159. Any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD must be reported in the chronic GVHD section of the form. Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section. This instruction has been provided in the note above question 157.*

**Question 158: Date of acute GVHD diagnosis**

Report the date of clinical diagnosis of acute GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed a rash one week prior to the physician clinically diagnosing acute skin GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of acute GVHD in the same reporting period, report the date of onset of the first episode of acute GVHD.

If the date of diagnosis is **unknown**, leave question 158 blank and override the validation error using the code “Unknown.” However, question 158 may **not** be left blank if treatment for acute GVHD (question 185) is reported “Yes.” If the exact clinical diagnosis date is unknown, but the treatment start date is known, report the date treatment started as the date of acute GVHD diagnosis.

For more information regarding reporting partial or unknown dates, see General Instructions. [General Guidelines for Completing Forms.](#)

**Question 159: Did acute GVHD persist since the date of the last report?**

Question 159 will only be enabled in FormsNet3SM if the center has reported “no” for question 157 and, therefore, has not reported a date of diagnosis in question 158. If prompted to answer question 159, report “yes” if acute GVHD was diagnosed in a prior reporting period and **any** of the following conditions are met:

- The recipient’s acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).
- The recipient’s acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred within **30 days** of symptom resolution / quiescence.
• The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 157).

Report “no” for questions 157 and 159 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 157).

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

**Question 160: Was acute GVHD evaluated by biopsy (histology)? (at diagnosis)**

Histological tests may be performed to confirm the clinical diagnosis of GVHD; however, the staging and grading of GVHD should be based on clinical evidence, not histological results.

Indicate whether a biopsy was used to diagnose acute GVHD. If “yes,” specify the site(s) / result(s) in questions 161-168. If “no,” continue with question 169.

**Questions 161-168: Specify result(s)**

For each organ listed, indicate the test result documented on the pathology report as either “positive,” “suggestive,” “negative,” or “inconclusive / equivocal.” “Suggestive” or “inconclusive / equivocal” should be reported if in the final diagnosis or comments section of the pathology report those words are used. If a biopsy was not completed for a specific organ, select “not done” and continue with the next organ. If “other site” is selected, specify the site biopsied in question 167.

Indicate whether documentation was submitted to the CIBMTR (e.g., pathology report) in question 168. For further instructions on how to attach documents in FormsNet3, refer to the training guide.

**Question 169: Overall grade of acute GVHD at diagnosis:**

Indicate the overall grade of acute GVHD at the time of diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic). The acute GVHD grading scale is based on clinical evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on clinical severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, overall grading remains clinical and is based on the criteria published by Przepiorka et al., Bone Marrow Transplant 1995; 15(6):825-8, see the GVHD Grading and Staging table below.
If acute GVHD was present, but the grade at diagnosis was not documented and it cannot be determined from the grading and staging table, report “not applicable.” Examples may include:

- Only elevated liver function tests without increased bilirubin
- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios lower intestinal tract involvement description below

**Upper GI GVHD**
If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

GVHD Grading and Staging

<table>
<thead>
<tr>
<th>Extent of Organ Involvement</th>
<th>Skin</th>
<th>Liver</th>
<th>Gut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Skin</td>
<td>Liver</td>
<td>Gut</td>
</tr>
</tbody>
</table>
| 1                            | Rash on <25% of skin  | Bilirubin 2-3 mg/dl | Diarrhea > 500 ml/day or persistent nausea

Pediatric: 280-555 ml/m²/day or 10-19.9 mL/kg/day

| 2                            | Rash on 25-50% of skin | Bilirubin 3-6 mg/dl | Diarrhea >1000 ml/day

Pediatric: 556-833 ml/m²/day or 20-30 mL/kg/day

| 3                            | Rash on >50% of skin   | Bilirubin 6-15 mg/dl | Diarrhea >1500 ml/day

Pediatric: >833 ml/m²/day or > 30 mL/kg/day

| 4                            | Generalized erythroderma with bullous formation | Bilirubin >15 mg/dl | Severe abdominal pain, with or without ileus, and / or grossly blood stool |

Grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>Stage 1-2</th>
<th>Stage 3</th>
<th>Stage 1</th>
<th>Stage 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>None</td>
<td>Stage 1</td>
<td>Stage 1</td>
<td>—</td>
</tr>
<tr>
<td>II</td>
<td>Stage 3</td>
<td>—</td>
<td>Stage 2-3</td>
<td>Stages 2-4</td>
</tr>
<tr>
<td>III</td>
<td>—</td>
<td>Stage 4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>IV</td>
<td>Stage 4</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

1 Use “Rule of Nines” (see Percent Body Surfaces table below) or burn chart to determine extent of rash.

2 Range given as total bilirubin. Downgrade one stage if an additional cause of elevated bilirubin has been documented.
Volume of diarrhea applies to adults. For pediatric patients, the volume of diarrhea should be based on body surface area. Downgrade one stage if an additional cause of diarrhea has been documented.

Persistent nausea with or without histologic evidence of GVHD in the stomach or duodenum.

Criteria for grading given as minimum degree of organ involvement required to confer that grade.

Grade IV may also include lesser organ involvement with an extreme decrease in performance status.

**Question 170-175: Indicate the stage for each organ involvement at time of diagnosis of acute GVHD**

Report the stage of each organ at diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic).

**Skin:** Select the stage that reflects the body surface area involved with a maculopapular rash attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. See Table 5 below to determine the percent of body surface area involved with a rash. Do not report ongoing rash not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

**Percent Body Surfaces**

<table>
<thead>
<tr>
<th>Body Area</th>
<th>Percent</th>
<th>Total Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each Arm</td>
<td>9%</td>
<td>18%</td>
</tr>
<tr>
<td>Each Leg</td>
<td>18%</td>
<td>36%</td>
</tr>
<tr>
<td>Chest &amp; Abdomen</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Back</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Head</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Pubis</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Lower intestinal tract (use mL/day for adult recipients and mL/m²/day for pediatric recipients):**

Select the stage that reflects the volume of diarrhea attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Use mL/day for adult recipients and mL/m²/day for pediatric recipients. Input and output records may be useful in determining the volume of diarrhea. Do not report diarrhea ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, report “stage 0” for lower intestinal tract involvement. In this case, report “Not Applicable” for the overall grade unless stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in...
performance status was also documented at the time point being reported (at diagnosis or maximum grade during the reporting period). Report an overall grade of IV if stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status is documented at the time point being reported (see GVHD Staging and Grading Table). Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.

**Upper intestinal tract:** Select the stage that reflects the presence of persistent nausea or vomiting attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report nausea or vomiting ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

**Liver:** Select the stage that reflects the bilirubin level attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report hyperbilirubinemia ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

For recipients who have a normal bilirubin level with elevated transaminase levels attributed to acute GVHD, report this in “Other clinical organ involvement.”

**Other site(s) involved with acute GVHD:** Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 175. If reporting transaminitis under “other site,” write in “transaminitis” rather than “liver” when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under “other site.”

**Question 176: Maximum overall grade of acute GVHD**

Indicate the overall maximum grade of acute GVHD since the date of the last report. Grading is based on clinical evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on clinical severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, overall grading remains clinical and is based on the criteria published by Przepiorka et al., *Bone Marrow Transplant* 1995; 15(6):825-8, see the GVHD Grading and Staging table above.

If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. See question 157 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.
Report the recipient’s maximum acute GVHD grade in the reporting period; this may differ from the grade at diagnosis or may be the same. If acute GVHD was present, but the maximum grade was not documented and it cannot be determined from the grading and staging table, report “not applicable.” Examples may include:

- Only elevated liver function tests without increased bilirubin
- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios lower intestinal tract involvement description above

**Upper GI GVHD**

If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

**Acute GVHD Grading Scenarios:**

**A.** A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging / grading can be determined based on the skin involvement alone.

**B.** A recipient developed acute liver GVHD with elevated LFTs (i.e., transaminases) with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in the GVHD Grading and Staging Table; “not applicable” would be the best option to report.

**C.** A recipient developed stage 2 skin involvement, which showed improvement in response to topical steroids. However, the recipient then developed hyperbilirubinemia attributed to stage 1 liver involvement; the skin involvement at that time was stage 1. In this case, grade II would be reported (assuming this was the extent of the recipient’s acute GVHD in the reporting period).

**D.** A recipient developed stage 2 skin involvement which resolved in response to topical steroids. Later in the reporting period, the recipient was diagnosed with mild chronic eye GVHD. Shortly thereafter, they were diagnosed with a stage 3 flare of acute skin GVHD. In this case, grade I would be reported. Do not consider any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD when completing the acute GVHD section of the form.
Question 177: Date maximum overall grade of acute GVHD

Report the date of maximum acute GVHD involvement, based on clinical grade. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date. If "not applicable" was reported for question 176, question 177 must be left blank.

Question 178-183: Specify organ involvement at time of maximum grade

Report the stage of involvement for each organ on the date reported in question 177. Refer to the GVHD Grading and Staging Table above for staging guidelines. Also, see additional information included for each organ in the instructions for questions 170-175 above.

Corticosteroids

Corticosteroids are captured differently depending on whether they are used topically or systemically. Use the following guidelines when determining how to report corticosteroids used to treat acute GVHD:

Topical Creams for Skin: Do not report topical ointments or creams used to treat skin GVHD including corticosteroid creams such as Triamcinolone or Hydrocortisone.

Other Topical Treatments: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. If these treatments are given for acute GI GVHD during the reporting period, report “Yes” for question 184. If these treatments were given for other organ involvement of GVHD, contact your liaison to determine the best option for reporting this therapy.

Systemic Treatments: Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in questions 197-198).

Question 184: Were corticosteroids (topical GI) used to treat acute GVHD?

Report “yes” if topical corticosteroids were used to treat GI GVHD. Do not report topical therapies used for skin or lung GVHD in this question. Also, do not report systemic corticosteroids such as prednisone or dexamethasone. Systemic therapies are captured in questions 185-233.

Question 185-233: Was specific therapy given for acute GVHD?

Fecal Microbiota Transplant

Fecal microbiota transplant (FMT) is under investigation as a viable therapy to treat acute or chronic steroid-refractory gastrointestinal GVHD. This procedure involves collecting fecal matter from a pre-screened donor and transferring it to a recipient by the oral or rectal route (for example by nasogastric tube or enema) in order to restore intestinal microbial flora. If an FMT was performed to treat acute GVHD, report “Yes” for “Other agent” and specify “Fecal Microbiota Transplant.” The date started will be the date of the FMT. If multiple FMTs
Indicate whether systemic therapy was used to treat acute GVHD during the reporting period. If “yes,” continue with question 186. Report any prophylactic drugs as therapy for acute GVHD if they were continued after the date of diagnosis. If no therapy was given, indicate “no” and continue with question 233. If systemic therapy was given to treat acute GVHD during the reporting period, specify the drugs given in questions 186-233.

When reporting the total dose, report the total delivered dose of each drug during the reporting period. **Do not report the prescribed doses or daily doses.** For example, if 50 mg/kg of ATGAM was given for 5 days, the center should report a total dose of 250 mg/kg. Drug doses must be reported in whole numbers. If the total dose includes a decimal, round to the nearest whole number.

When reporting the date started, report the first day the drug as given on or after the GVHD diagnosis date (reported in question 158). For **prophylaxis medications** continued after the date of diagnosis of acute GVHD, report the date of diagnosis as the date started. If an acute GVHD treatment has continued from a previous reporting period, report the original start date and override the error in FormsNet3SM using the code “verified correct.”
Q234-406: Chronic Graft vs. Host Disease (GVHD)

Report any chronic graft-versus-host disease occurring in this reporting period in response to allogeneic HCT or cellular therapy. Chronic GVHD affects 25-50% of long-term survivors of allogeneic transplants and usually develops after day 100. However, it has been documented as occurring as early as day 60. Chronic GVHD may result in response to transplant or donor cellular infusion. The mechanism of tissue damage differs from acute GVHD and a greater variety of organs may be affected. For further information on acute GVHD, refer to the Acute GVHD section of the manual.

Question 234: Did chronic GVHD develop since the date of the last report?

Indicate whether a new clinical diagnosis of chronic GVHD was documented during the reporting period. If chronic GVHD was diagnosed during the reporting period, report “yes” and continue with question 235.

If the recipient had a flare of chronic GVHD occurring after at least a 30 day period of symptom quiescence, report “yes” and continue with question 235. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent chronic GVHD which is captured in question 236.

Report “no” if chronic GVHD was not clinically diagnosed – initially or as a flare – in the reporting period; this includes instances where chronic GVHD persists from a prior reporting period.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

Question 235: Date of chronic GVHD diagnosis

Report the date of clinical diagnosis of chronic GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed shortness of breath one month prior to the clinical diagnosis of pulmonary chronic GVHD). If the clinical diagnosis is documented, but the diagnosis
date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of chronic GVHD in the same reporting period, report the date of onset of the first episode of chronic GVHD.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 236: Did chronic GVHD persist since the date of last report?**

Indicate whether chronic GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive chronic GVHD, or a prior history of GVHD. If “yes,” continue with question 302; questions concerning chronic GVHD at the time of diagnosis will be skipped. See question 234 for instructions on reporting a chronic GVHD flare.

If the recipient has no active symptoms during the reporting period, report “no” continue with question 400.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

**Question 237: Onset of chronic GVHD was:**

Indicate whether the onset of chronic GVHD was:

- Progressive – acute GVHD present within 2 weeks prior to onset of chronic GVHD
- Interrupted – acute GVHD resolved for greater than 2 weeks, then chronic GVHD developed
- De novo – acute GVHD never developed

**Question 238: Were signs of acute GVHD present at the time of chronic GVHD diagnosis (overlap syndrome)?**

Chronic GVHD can be separated into two different categories; classical chronic GVHD and overlap syndrome. Overlap syndrome is a condition where there are features of both acute and chronic GVHD at the time of diagnosis. Indicate whether signs of acute GVHD were present at the time of diagnosis of chronic GVHD (overlap syndrome). Refer to question 157 for instructions on how to complete the acute and chronic GVHD sections for recipients with overlap syndrome.

**Question 239-241: Karnofsky/Lansky score at time of chronic GVHD diagnosis**

The Karnofsky Scale is designed for recipients aged 16 years and older, and is not appropriate for children
under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. If the recipient is less than one year old, leave questions 239-241 blank.

Indicate the score (10-100) that best represents the recipient’s activity status at diagnosis of chronic GVHD. The only valid scores are 10-100, zero is not a valid response for this scale, nor are values not ending in zero, such as “85.” The Karnofsky/Lansky scale can be found in Appendix L, Karnofsky/Lansky Performance Status.

For further information on reporting Karnofsky / Lansky Scores refer to the instructions for Questions 651-653 below.

**Question 242: Platelets (at diagnosis of chronic GVHD):**

Report the lowest platelet count recorded within 14 days (+ / -) of the diagnosis of chronic GVHD whether or not the recipient has received a platelet transfusion. Indicate the units.

**Question 243: Total serum bilirubin (at diagnosis of GVHD):**

Report the highest total serum bilirubin value (and units) within 14 days (+ / -) of the diagnosis of chronic GVHD. Indicate the units.

**Question 244: Was chronic GVHD evaluated by biopsy (histology)? (at diagnosis)**

Histological tests may be performed to confirm the clinical diagnosis of GVHD; however, the scoring of GVHD should be based on clinical evidence, not histological results.

Indicate whether a biopsy was used to diagnose chronic GVHD. If “yes,” specify the site(s) / result(s) in questions 245-251. If “no,” continue with question 252.

**Question 245-251: Specify result(s):**

For each organ listed, indicate the result documented on the laboratory report as either “positive,” “suggestive,” “negative,” or “inconclusive / equivocal.” If a biopsy was not completed for a specific organ, select “not done” and continue with the next organ. If “other site” is selected, specify the site biopsied in question 251.

**Question 252-301: Organ involvement and NIH scoring at diagnosis of chronic GVHD**

Report the organ involvement and NIH score of chronic GVHD for each organ / system listed at the time of diagnosis. For each involved organ, specify any features present at time of diagnosis. Refer to the Organ Scoring of Chronic GVHD Table below for the NIH Consensus Criteria, 2014 for organ scoring of chronic GVHD.
Signs or symptoms occurring at the time of diagnosis may be partially or entirely attributed to GVHD. Alternatively, reportable features may be observed at diagnosis, but attributed entirely to non-GVHD causes. In any case, report "yes" for organ involvement if any reportable signs / symptoms are documented during the reporting period regardless of whether those features are attributed to GVHD. Features entirely explained by non-GVHD causes will be excluded when determining the overall severity of chronic GVHD, but are still collected on the form. Spaces have been provided to document non-GVHD causes.

Specify all features observed at the time of diagnosis and report the score for each organ using the criteria from the Organ Scoring of Chronic GVHD Table below. If any reported features are attributed entirely to non-GVHD causes, specify the non-GVHD cause(s) in the appropriate field. If a sign or symptom is caused by a combination of chronic GVHD and other causes, then the section on "non-GVHD causes" does not need to be completed. Further instruction has been provided under each organ below.

If a recipient has signs / symptoms of both acute and chronic GVHD during the reporting period, refer to question 157 for additional instructions. Scenarios C and D below have also been provided for further clarification.

**GVHD Reporting Scenarios:**

**A.** A recipient developed a maculopapular rash covering 25% BSA as well as deep sclerotic features. Both features are attributed to chronic GVHD. In this case, report “yes” and “score 3” for skin involvement (based on findings of deep sclerotic features).

**B.** A recipient developed a maculopapular rash covering 25% BSA as well as diarrhea without significant weight loss. Both findings were identified and diagnosed at the same time. The skin rash was attributed to acute GVHD while diarrhea was entirely attributed to chronic GVHD. In this case, report “yes” and “Score 2” for skin involvement. Report “yes” and “score 1” for GI involvement. Any acute findings identified on or after the date of chronic GVHD diagnosis must be reported in the chronic GVHD section. The skin rash would not be reported in the acute GVHD section of the form unless identified and diagnosed prior to any findings of chronic GVHD.

**C.** A recipient developed a maculopapular rash covering 25% BSA. This was diagnosed as acute GVHD, treated, and completely resolved during the 100 day reporting period. During the six month reporting period, the recipient developed mild dry eyes which was diagnosed as chronic GVHD. Shortly thereafter, the recipient was also diagnosed with an acute flare of skin GVHD.

**100 Day Post-HCT Data Form:** Report the acute GVHD findings (maculopapular rash) in the acute GVHD section of the form. Report “no” for questions 234 and 235 to indicate chronic GVHD was not diagnosed during the 100 day reporting period.
6 Month Post-HCT Data Form: Report acute and chronic GVHD findings in the chronic GVHD section of the form. Report “no” for questions 157 and 159 to indicate no acute GVHD symptoms were identified during the reporting period. Even though acute skin GVHD was diagnosed, it is not necessary to report these symptoms in both acute and chronic sections of the form. Once a chronic GVHD diagnosis is made, report all signs / symptoms of GVHD (acute and chronic) in the chronic GVHD section of the form.

D. A recipient is diagnosed with acute skin GVHD early in the reporting period. This is treated and quickly resolves. During the same reporting period, the recipient later develops chronic GVHD of the gut. Shortly after the diagnosis of chronic GVHD, the recipient has a flare of their skin GVHD.

Acute GVHD data fields: Report any signs or symptoms of acute GVHD documented prior to the diagnosis of chronic GVHD in the acute GVHD section of the form (Questions 157-183). In this case, the initial diagnosis of skin GVHD as well as any treatments initiated prior to the diagnosis of chronic GVHD will be reported in acute GVHD data fields.

Chronic GVHD data fields: Report any signs or symptoms of GVHD (acute or chronic) documented on or after the diagnosis of chronic GVHD in the chronic GVHD section of the form (Questions 234-323). In this case, the initial diagnosis of gut GVHD as well as the subsequent flare of skin GVHD will be reported in chronic GVHD data fields. Any treatments continued or initiated on or after the date of diagnosis of chronic GVHD will be reported in chronic GVHD data fields.

E. A recipient developed a maculopapular rash covering 25% BSA as well as diarrhea without significant weight loss. The skin rash was entirely attributed to a drug reaction while the diarrhea was attributed to chronic GVHD and an ongoing CMV infection. In this case, report “yes” and “score 2” for skin involvement. The center should also specify the observed rash was entirely attributed to a drug reaction in questions 259-260. Report “yes” and “score 1” for GI involvement. Do not specify CMV as a non-GVHD cause in questions 273-274 because the observed symptoms were not entirely explained by this diagnosis.

F. A recipient developed maculopapular rash covering 55% BSA as well as superficial sclerotic features of the skin. The rash is attributed to a drug reaction and the sclerotic findings are entirely attributed to chronic GVHD. In this case, report “yes” and “score 3” as well as “superficial sclerotic features” for skin involvement. The center should also specify the observed rash was entirely attributed to a drug reaction in questions 259-260.

Organ Scoring of Chronic GVHD

<table>
<thead>
<tr>
<th>Organ</th>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin %</td>
<td>No BSA</td>
<td>1-18% BSA</td>
<td>19-50% BSA</td>
<td>&gt;50% BSA</td>
</tr>
<tr>
<td>BSA&lt;sup&gt;1&lt;/sup&gt;</td>
<td>involved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>----------</td>
<td>----------------</td>
<td>----------------</td>
<td></td>
</tr>
<tr>
<td><strong>Skin Features</strong></td>
<td>No sclerotic features</td>
<td>N/A</td>
<td>Superficial sclerotic features, but not &quot;hidebound&quot;</td>
<td>Deep sclerotic features; &quot;hidebound;&quot; impaired mobility; ulceration</td>
</tr>
<tr>
<td><strong>Mouth</strong></td>
<td>No symptoms</td>
<td>Moderate symptoms with disease signs with partial limitation of oral intake</td>
<td>Severe symptoms with disease signs with major limitation of oral intake</td>
<td></td>
</tr>
<tr>
<td><strong>Eyes</strong></td>
<td>No symptoms</td>
<td>Mild dry eye symptoms not affecting ADL (requiring lubricant drops \leq 3x/day)</td>
<td>Moderate dry eye symptoms partially affecting ADL (requiring lubricant drops &gt; 3x/day or punctal plugs) WITHOUT new vision impairment due to keratoconjunctivitis sicca (KCS)</td>
<td>Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) OR unable to work because of ocular symptoms OR loss of vision due to keratoconjunctivitis sicca (KCS)</td>
</tr>
<tr>
<td><strong>GI Tract</strong></td>
<td>No symptoms</td>
<td>Symptoms without significant weight loss (&lt; 5%)</td>
<td>Symptoms associated with mild to moderate weight loss (5-15%) within 3 months OR moderate diarrhea without significant interference with daily living</td>
<td>Symptoms associated with significant weight loss (&gt; 15%) within 3 months, requires nutritional supplement for most calorie needs OR esophageal dilation OR severe diarrhea with significant interference with daily living.</td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td>Normal total bilirubin and ALT or AP &lt; 3 x ULN</td>
<td>Normal total bilirubin with ALT \geq 3 to 5 x ULN or AP \geq 3 x ULN</td>
<td>Elevated total bilirubin but \leq 3 mg / dL or ALT &gt; 5 x ULN</td>
<td>Elevated total bilirubin &gt; 3 mg / dL</td>
</tr>
<tr>
<td><strong>Lungs Symptom Score:</strong></td>
<td>No symptoms</td>
<td>Mild symptoms (SOB after climbing one flight of steps)</td>
<td>Moderate symptoms (SOB after walking on flat ground)</td>
<td>Severe symptoms (SOB at rests; requires O2)</td>
</tr>
<tr>
<td><strong>Lungs Lung Score:</strong></td>
<td>FEV1 \geq 80%</td>
<td>FEV1 60-79%</td>
<td>FEV1 40-59%</td>
<td>FEV1 \leq 39%</td>
</tr>
<tr>
<td><strong>Joints and Fascia</strong></td>
<td>No symptoms</td>
<td>Mild tightness of arms or legs, normal or mild decreased range of motion AND not affecting ADL</td>
<td>Tightness of arms or legs OR joint contractures, erythema thought to be due to fasciitis, moderate decrease of range of motion AND mild to moderate limitation of ADL</td>
<td>Contractures WITH significant decrease of range of motion AND significant limitation of ADL (unable to tie shoes, button shirts, dress self, etc.)</td>
</tr>
</tbody>
</table>
**Genital Tract**

<table>
<thead>
<tr>
<th>Features</th>
<th>No signs</th>
<th>Mild signs and females with or without discomfort on exam</th>
<th>Moderate signs and may have signs of discomfort on exam</th>
<th>Severe signs with or without symptoms</th>
</tr>
</thead>
</table>

**Other Features**

<table>
<thead>
<tr>
<th>Features</th>
<th>No GVHD</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>

**NIH Consensus Criteria, 2014**

1. Features to be scored by BSA: Maculopapular rash, lichen planus-like features, sclerotic features, papulosquamous lesions or ichthyosis, keratosis pilaris-like GVHD.

2. Scoring is based on severity of the signs instead of symptoms, based on limited available data and the opinions of experts. Female or male genital GVHD is not scored if a practitioner is unable to examine the patient.

3. May include ascites, pericardial effusion, pleural effusion(s), nephrotic syndrome, myasthenia gravis, peripheral neuropathy, polymyositis, weight loss without GI symptoms, eosinophilia > 500/μL, platelets < 100,000/μL, others.

**Skin:** Ranges from skin discoloration to severe scarring and tightness. Includes, but is not limited to:

- Sclerosis: thickening of the skin, which may cause loss of suppleness
- Maculopapular rash / erythema: reddish skin with small confluent bumps / redness
- Lichen planus-like features: erythematous / violaceous flat-topped papules or plaques with or without surface reticulations or a silvery or shiny appearance.
- Papulosquamous lesions or ichthyosis: dry, scaly, or thickened skin
- Keratosis pilaris: small acne-like bumps and rough patches
- Poikiloderma: atrophy, pigmentary changes, and telangiectasia

If any skin abnormalities were present, but explained entirely by non-GVHD causes, specify any documented causes in question 260.

**Mouth:** Refers to white plaques, scarring, and ulcers occurring in the mouth and throat.

- Lichen planus-like features: whitish lacy patches that usually appear first on inner cheeks, but can involve roof of mouth, gums, and / or tongue

If any mouth abnormalities were present, but explained entirely by non-GVHD causes, specify any documented causes in question 265.
Eyes: Recipients may have dry eyes and corneal ulcers due to keratoconjunctivits sicca.

- Keratoconjunctivitis sicca (KCS): dry eye syndrome

If any eye abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes in question 270.

Gastrointestinal tract (GI):

- Esophageal web / proximal stricture or ring: extension of esophageal tissue
- Dysphagia: difficulty swallowing
- Anorexia
- Nausea
- Vomiting
- Diarrhea
- Weight loss: weight loss ≥ 5%
- Failure to thrive

If any GI abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes in question 274.

Liver: Record all types of liver abnormalities either clinical or histological.

- Liver involvement may be manifested by elevation of any of the liver function tests (bilirubin, particularly the direct component: alkaline phosphatase; GGT; SGOT [AST]; SGPT [ALT]).

If any liver abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes in question 286.

Lung: This ranges from mild impairment on pulmonary function tests to severe disorders.

If pulmonary function tests were performed, specify FEV1 percent in question 290.

If any lung abnormalities were present, but explained entirely by non-GVHD documented causes, specify causes in question 292.

Joints and fascia:

- Contractures: loss of joint mobility due to skin or fascia changes
If any joint or fascia abnormalities were present, but explained entirely by non-GVHD causes, specify causes in question 296.

**Genital tract:**

- Female: Vaginitis / stricture: pain, ulceration, inflammation, eventually scarring / narrowing of the vaginal opening.
- Male: Pain, burning sensation, lichen planus or lichen sclerosis features, scarring, stenosis.

If any genital tract abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes in question 301.

**Question 302: Maximum grade of chronic GVHD: (according to best clinical judgment)**

Report the maximum chronic GVHD involvement since the date of last report, based on clinical grade, as documented by the recipient’s primary care provider. The intent of this question is to capture the maximum grade based on the best clinical judgment. If the maximum clinical grade is not documented, request documentation from the recipient’s primary care provider.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period. Please note, questions 303 and 304 must still be answered if question 302 is reported as “unknown.”

**Question 303: Specify if chronic GVHD was limited or extensive:**

The grading system for chronic GVHD is divided into two categories: limited and extensive. Definitions are based on Sullivan KM, Blood 1981; 57:267.

Report the extent of chronic GVHD since the date of last report. Report “limited” if chronic GVHD includes only localized skin involvement and/or liver dysfunction. Report “extensive” if any of the following symptoms are attributed to chronic GVHD:

- Generalized skin involvement and / or liver dysfunction
- Liver histology showing chronic aggressive hepatitis, bridging necrosis, or cirrhosis
- Involvement of the eye: Schirmer’s test with < 5 mm wetting, or
- Involvement of minor salivary glands or oral mucosa, or
- Involvement of any other target organ
**Question 304: Date of maximum grade of chronic GVHD:**

Report the date of maximum chronic GVHD involvement since the date of last report, based on clinical grade. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 305-323: Indicate whether there was organ specific manifestations with chronic GVHD since the date of last report:**

Report if there were any organ specific manifestations associated with chronic GVHD. If “yes,” answer any additional questions. If “no,” continue with the next option.

**Sclerosis of skin:**

- Scleroderma: thickening of the skin, which may cause loss of suppleness
- Fasciitis: inflammation of the fascia of a muscle or organ
- Morphea: thickening or hardening patches of the skin which are discolored

**Erythematous skin rash:** skin rash characterized by redness.

**Join contractures:** loss of joint mobility due to skin or fascia changes.

**Other skin or hair involvement:** other skin or hair involvement, includes, but is not limited to:

- Ulcers
- Pruritus: itching of the skin
- Dyspigmentation: change in color of the skin. Usually erythema (redness) or vitiligo (loss of skin color)
- Alopecia: scalp hair loss
- Lichenoid skin changes: purplish rash

**Eyes:** Dry eyes and corneal ulcers due to keratoconjunctivitis sicca.

- Xerophthalmia: dry eyes
- Abnormal Schirmer’s test: a measure of tear production, decreased wetting <5 mm
- Abnormal slit lamp: The binocular slit lamp examination provides stereoscopic magnified view of the eye structures in detail
- Corneal erosion / conjunctivitis: ulcers on the cornea, usually quite painful, or inflammation of thin
membrane covering the eye and inner lids

**Mouth:** Refers to white plaques, red inflammation, scarring, and ulcers occurring in the mouth and throat.

- Lichenoid changes: whitish lacy patches that usually appear first on inner cheeks, but can involve roof of mouth, gums, and/or tongue
- Mucositis / ulcers: similar to cold sores but they can involve any part of the mouth, important not to confuse with herpes simplex infections
- Erythema: redness

**Bronchiolitis obliterans:** scarring of the small airways. Usually diagnosed by lung biopsy or pulmonary function tests (showing obstruction of airflow). Symptoms include shortness of breath (dyspnea), dry cough, and wheezing. **If bronchiolitis obliterans was a manifestation of chronic GVHD, also complete the Pulmonary Function section, questions 441-489.**

**Other lung involvement:** includes related pulmonary disorders here. Do not report interstitial pneumonitis (IPn). Report IPn in the Pulmonary Function section, questions 441-489.

**Upper gastrointestinal tract:**

- Esophageal: may have difficulty swallowing (dysphagia), pain when swallowing (odynophagia), narrowing of esophagus (esophageal web), poor motility (food does not move down esophagus normally).
- Chronic nausea / vomiting: either nausea or vomiting that occurs on at least 25% of days (1 out of 4 days) or occurs frequently enough to interfere with functioning and lifestyle.

**Lower gastrointestinal tract:**

- Chronic diarrhea: occurs on at least 25% of days (1 out of 4 days) or occurs frequently enough to interfere with functioning and lifestyle. This may occur due to thickening of the intestinal wall.
- Malabsorption: inability to digest or absorb the nutrients from food. Diagnosed with specific tests measuring fecal fat, xylose uptake, or vitamin level.
- Abdominal pain or cramping.

**Liver:** Record all types of liver abnormalities either clinical or histological.

- Liver involvement may be manifested by elevation of any of the liver function tests (bilirubin, particularly the direct component; alkaline phosphatase; GGT; SGOT [AST]; SGPT [ALT]).
- A liver biopsy may show obliteration of bile ducts (canaliculi) or cirrhosis.
**Genitourinary tract:** Includes, but is not limited to:

- Vaginitis / stricture: pain, ulceration, inflammation, eventually scarring/narrowing of the vaginal opening

**Musculoskeletal:** Refers to pain, contractures, and / or joint deformities.

- Arthritis: inflammation of joints
- Myositis: inflammation of muscles
- Myasthenia: weakness of muscles

**Thrombocytopenia:** Decreased platelet count (<100,000).

**Eosinophilia:** Elevation in eosinophils in the peripheral blood (> 500 cells / µL)

**Serositis:** Inflammation of a serous membrane, includes but is not limited to:

- Pleural effusion: Buildup of fluid between the chest and the tissues which line the lungs
- Ascites: Accumulation of fluid in the peritoneal cavity
- Pericardial effusion: Accumulation of fluid in the pericardial cavity

**Other:**

- Weight loss
- Other organ involvement from chronic GVHD: specify the additional site

**Question 324: Were corticosteroids (topical GI) given for chronic GVHD?**

Report if corticosteroids (topical GI) were given for chronic GVHD. Examples include beclomethasone and budesonide. Do not report corticosteroids (topical GI) given as a GVHD prophylaxis.

**Question 325: Was systemic therapy given to treat chronic GVHD?**

Indicate whether systemic therapy was given to treat chronic GVHD during the reporting period. If systemic therapy was given as treatment for chronic GVHD, report “yes” and continue with question 326. If systemic therapy was not given for treatment of chronic GVHD, report “no” and continue with question 399. See questions 328-399 for Chronic GVHD Treatment Reporting Scenarios.

**Question 326: Was the date therapy was first started previously reported?**

Indicate whether the date therapy was first started for chronic GVHD was previously reported. If the therapy
start date was previously reported, select “yes” and continue with question 328. If the therapy start date for chronic GVHD has not been reported, select “no” and report the start date in question 327.

If treatment is started for a flare of chronic GVHD (see question 234 for definition of flare), report “no” for question 326 and report the date treatment was started for the flare in question 327.

**Question 327: Date therapy was first started:**

Report the first date when therapy was started for chronic GVHD if the date has not been previously reported. If the recipient continued GVHD prophylaxis drugs after the onset of chronic GVHD, report the date of diagnosis of chronic GVHD as the treatment start date. If the recipient starts treatment multiple times during the same reporting period, report the earliest treatment start date.

For more information regarding reporting partial or unknown dates, see General Instructions, *General Guidelines for Completing Forms*.

**Question 328-399: Specify systemic therapy started or escalated for chronic GVHD since the date of last report:**

*Fecal Microbiota Transplant*

Fecal microbiota transplant (FMT) is under investigation as a viable therapy to treat acute or chronic steroid-refractory gastrointestinal GVHD. This procedure involves collecting fecal matter from a pre-screened donor and transferring it to a recipient by the oral or rectal route (for example by nasogastric tube or enema) in order to restore intestinal microbial flora. If an FMT was performed to treat chronic GVHD, report “Yes” for “Other agent” and specify “Fecal Microbiota Transplant.” The date started will be the date of the FMT. If multiple FMTs were performed during reporting period, report the earliest date.

If a therapy was started or escalated for chronic GVHD, report “yes” and answer any additional questions (if applicable). If a dose is required, report the total ordered dose planned to be given at the time treatment was initiated. This may include doses which are planned to be given after the date of contact. Report “yes” for prophylactic drugs if they were continued after the onset of chronic GVHD. Report the date of diagnosis of chronic GVHD as the treatment start date for any prophylactic medications which were continued. See Chronic GVHD Treatment Reporting Scenarios below.

If treatment is started and subsequently escalated during the same reporting period, report the earliest date treatment was actually given during the reporting period. If a dose is required, contact your center’s liaison to determine how to complete the data field. Additionally, report the earliest start date if a drug is started multiple times during the same reporting period.
Refer to questions 132-156 for a description of most agents listed. Agents not described under acute GVHD are described below under Additional Agents. “Systemic” refers to drugs given by mouth, intramuscularly (IM), or intravenously (IV). “Topical” refers to drugs applied to the skin, eye drops, or inhalation therapy. An exception to this would be the drug budesonide; it is a drug given by mouth for treatment of gut GVHD, but it is considered a “topical” drug since it is not absorbed.

**Chronic GVHD Treatment Reporting Scenarios:**

A. During the one year reporting period, a recipient on cyclosporine for GVHD prophylaxis was diagnosed with chronic skin GVHD (5/1/2016). This was initially treated with topical steroids in addition to continuing their cyclosporine at the current dose. The chronic skin GVHD worsened shortly thereafter. On 5/15/2016, prednisone was started and the dose of cyclosporine was increased. Symptoms persisted into the two year reporting period, but improved shortly thereafter. Upon resolution of symptoms, prednisone and cyclosporine doses were tapered.

**One Year Post-HCT Data Form**

Question 324: Report “no” to indicate no topical GI corticosteroids were given. Topical steroids applied to the skin should not be reported here.

Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.

Question 326: Report “no” to indicate the therapy start date was not previously reported.

Question 327: Report 5/1/2016 as the treatment start date. This is the date cyclosporine was started as treatment for chronic GVHD. Note, topical steroids should not be considered when completing questions 325-399.

Question 328-399: Corticosteroids will be reported as “yes” with a start date of 5/15/2016. Cyclosporine will be reported as “yes” with a start date of 5/1/2016. All other medications will be reported as “no.”

**Two Year Post-HCT Data Form**

Question 324: Report “no” to indicate no topical GI corticosteroids were given. Topical steroids applied to the skin should not be reported here.

Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.

Question 326: Report “yes” to indicate the therapy start date was previously reported.

Question 327: Leave blank. This question will be skipped when question 326 has been answered “yes.”

Question 328-399: All medications will be reported as “no.” Prednisone and cyclosporine would only be reported on this form if a dose increase was given to treat chronic GVHD during the reporting period.

B. During the one year reporting period, a recipient on sirolimus for GVHD prophylaxis was diagnosed with chronic gut GVHD (7/1/2016). This was initially treated with topical steroids (oral budesonide) in addition to continuing sirolimus at the current dose. Prednisone was started 7/30/2016 due to minimal
improvement. The chronic gut GVHD resolved and budesonide as well as prednisone were discontinued. Sirolimus was continued as prophylaxis. Later in the one year reporting period, a severe flare chronic gut GVHD occurred (10/15/2016). This was first treated by restarting prednisone on the date of diagnosis; however, no response was observed. Equine ATG was started on 10/20/2016 with a plan to give 6 total doses of 30 mg / kg. Symptoms resolved following administration of ATG.

One Year Post-HCT Data Form

Question 324: Report “yes” to indicate topical GI corticosteroids were given. Budesonide should be reported here.

Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.

Question 326: Report “no” to indicate the therapy start date was not previously reported.

Question 327: Report 7/1/2016 as the treatment start date. This is the date sirolimus was started as treatment for chronic GVHD. Note, topical steroids, including budesonide, should not be considered when completing questions 325-399.

Question 328-399:

- ATG will be reported as “yes” with a start date of 10/20/2016. The total dose will be reported as 180 mg / kg to reflect the total planned dose at the time treatment was initiated (6 * 30 mg / kg).
- Corticosteroids will be reported as “yes” with a start date of 7/30/2016. Report the earliest start date if a medication is started multiple times during the reporting period.
- Sirolimus will be reported as “yes” with a start date of 7/1/2016.
- All other medications will be reported as “no.”

C. During the six month reporting period, a recipient off all immunosuppression was diagnosed with chronic gut GVHD (9/15/2016). This was initially treated with topical steroids (oral budesonide). Cyclosporine was started on 9/20/2016 due to minimal response. Symptoms resolved by the one year date of contact (10/1/2016) at which time budesonide was discontinued. The recipient remained on cyclosporine. During the one year reporting period, a flare of chronic gut GVHD occurred on 11/15/2016 while attempting to taper cyclosporine. This was treated by increasing the dose of cyclosporine on the date of diagnosis of the flare.

Six Month Post-HCT Data Form

Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.

Question 326: Report “no” to indicate the therapy start date was not previously reported.

Question 327: Report 9/20/2016 as the treatment start date. This is the date cyclosporine was started as treatment for chronic GVHD. Note, topical steroids, including budesonide, should not be considered when completing questions 325-399.
Question 328-399: Cyclosporine will be reported as “yes” with a start date of 9/20/2016. All other medications will be reported as “no.”

One Year Post-HCT Data Form

Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.
Question 326: Report “no” to indicate the therapy start date was not previously reported. See question 326 for further instructions.
Question 327: Report 11/15/2016 as the treatment start date.
Question 328-399: Cyclosporine will be reported as “yes” with a start date of 11/15/2016. All other medications will be reported as “no.”

Additional Agents:

Aldesleukin (Proleukin): Increases production of several white blood cells including regulatory T-cells. This drug is also known as interleukin-2.

Azathioprine (Imuran): Azathioprine inhibits purine synthesis. Usually it is used at low doses in combination with other treatments.

Hydroxychloroquine (Plaquenil): Hydroxychloroquine inhibits transcription of DNA to RNA and is commonly used as an anti-malarial drug.

Interleukin Inhibitor: Interleukin inhibitors suppress production of white blood cells and are grouped according to their target. Examples of IL-2 inhibitors include daclizumab (Zynbryta) and basiliximab (Simulect). Examples of IL-6 inhibitors include tocilizumab (Actemra) and siltuximab (Sylvant).

Janus Kinase 2 Inhibitors: Suppress function of T-effector cells. Examples: ruxolitinib (Jakafi, Jakavi) and tofacitinib (Xeljanz, Jakvinus).

Pentostatin (Nipent): Inhibits adenosine deaminase, which blocks DNA (and some RNA) synthesis.

Tyrosine Kinase Inhibitor (TKI): Suppress function of tyrosine kinases thereby downregulating the function of many other cellular proteins / processes including fibrosis and inflammation. Examples: imatinib (Gleevec, Glivec), nilotinib (Tasigna), and dasatinib (Sprycel).

UV Therapy: UVA or UVB radiation administered to affected areas of the skin in order to suppress proliferation of cells responsible for GVHD.

PUVA (Psoralen and UVA): Psoralen is applied or taken orally to sensitize the skin, and then the skin is
exposed to UVA radiation.

**UVB**: Broadband- or Narrowband-UVB radiation is applied to the affected areas of the skin.

Alternative treatments may be used in combination with drug therapy (example: low dose cyclophosphamide). If alternative treatments were used, report in “other agent” (questions 397-399).

**Question 400**: Are symptoms of GVHD still present on the date of actual contact (or present at the time of death)?

Questions 400-406 refer to any symptoms of GVHD (acute and / or chronic) observed during the reporting period. This section of the form must be completed if the center reported yes for question 157, 159, 234, or 236.

Indicate whether the recipient has *active* clinical signs / symptoms of acute and/or chronic GVHD on the date of contact (question 1). If the recipient has died, indicate whether GVHD symptoms were present at the time of death.

**Question 401**: Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, ≤ 10 mg/day for adults, < 0.1 mg/kg/day for children)

**Corticosteroids**

Corticosteroids are captured differently depending on whether they are used topically or systemically. Use the following guidelines when determining how to report corticosteroids used to treat acute GVHD:

- **Topical Creams for Skin**: Do not report topical ointments or creams used to treat skin GVHD including corticosteroid creams such as Triamcinolone or Hydrocortisone.
- **Other Topical Treatments**: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. Do not consider these medications when answering question 401.
- **Systemic Treatments**: Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in question 401.

Indicate whether the recipient is still taking systemic steroids to treat or prevent GVHD on the date of contact. If the recipient is no longer taking systemic steroids for GVHD, report “no” and continue with question 402. If the recipient is still receiving systemic steroids during the reporting period to treat or prevent GVHD, report “yes” and continue with question 404. Refer to the guidelines included in the question text if the recipient is taking low dose steroids or steroids for adrenal insufficiency.

If the recipient did not received systemic steroids for acute and / or chronic GVHD during the reporting period, report “Not applicable” and continue with question 404.
Indicate “Not applicable” in any of the following scenarios:

- The recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD.
- This form is being completed for a subsequent HCT and the recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen is given).
- The recipient stopped taking systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD in a previous reporting period and did not restart systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) during the current reporting period.

Indicate “unknown” if there is no information to determine if the recipient is still taking systemic steroids and continue with question 404. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD on the date of contact.

If the recipient has died prior to the discontinuation of systemic steroids used to treat or prevent acute and/or chronic GVHD, select “yes.”

**Question 402-403: Date final treatment administered**

- **Previously Reported**
  
  Based on the current reporting instructions for GVHD therapy captured in questions 401-406, there is no scenario when it would be appropriate to report “Previously Reported” for questions 402 or 405. In cases where the recipient stopped systemic steroids or non-steroidal immunosuppression in a prior reporting period and did not restart systemic steroids or non-steroidal immunosuppression during the current reporting period, centers should report “Not Applicable” for questions 401 and/or 404 and skip questions 402 and/or 405. The option choices for questions 402 and 405 will be reviewed and updated the next time this form is revised.

Indicate whether the date when systemic steroids were discontinued is “known” or “unknown.” If the final treatment date is “known,” continue with question 403. If the date is “unknown,” continue with question 404.

For question 403, report the date when the final dose of systemic steroids was administered. For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 404: Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for**
**GVHD?**

Indicate whether the recipient is still taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent acute and/or chronic GVHD on the date of contact. If the recipient is still taking non-steroid immunosuppressive agents, report “yes” and continue with question 407. If the recipient is no longer receiving non-steroid agents for GVHD, report “no” and continue with question 405.

If the recipient did not receive non-steroidal immunosuppressive agents to treat or prevent acute and/or chronic GVHD during the reporting period, report “Not applicable” and continue with question 407.

Indicate “Not applicable” in any of the following scenarios:

- The recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD.
- This form is being completed for a subsequent HCT and the recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen was given).
- The recipient stopped taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD in a previous reporting period and did not restart non-steroidal immunosuppressive agents (including PUVA) during the current reporting period.

Indicate “unknown” if there is no information to determine if the recipient is still taking non-steroidal immunosuppressive agents and continue with question 407. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD in the reporting period.

**Question 405-406: Date final treatment administered**

**Previously Reported**

Based on the current reporting instructions for GVHD therapy captured in questions 401-406, there is no scenario when it would be appropriate to report “Previously Reported” for questions 402 or 405. In cases where the recipient stopped systemic steroids or non-steroidal immunosuppression in a prior reporting period and did not restart systemic steroids or non-steroidal immunosuppression during the current reporting period, centers should report “Not Applicable” for questions 401 and/or 404 and skip questions 402 and/or 405. The option choices for questions 402 and 405 will be reviewed and updated the next time this form is revised.
Indicate whether the final administration date of non-steroidal immunosuppressive agents (including PUVA) is “known” or “unknown.” If the final treatment date is “known,” continue with question 406. If the date is “unknown,” continue with question 407.

For question 405, report the date when the final treatment or prophylaxis dose of non-steroidal immunosuppressive agents was administered.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.
Q407-427: Infection Prophylaxis

**Infection Prophylaxis**

It is important to look at the Medication Administration Record (MAR) throughout the entire reporting period to ensure medications are not missed. Also, the use of some infection prophylactic drugs may not start immediately post-HCT (example: Pentamidine). Do not report agents used as treatment for documented or suspected infections. Report prophylactic immunoglobulins in the Immune Reconstitution section (questions 64-68).

**Questions 407-427 can only be completed on the 100 day follow-up form. These questions will be skipped for all subsequent reporting periods.**

Antimicrobial therapy is generally given to HCT recipients to help prevent infections. Questions 407-427 are intended to obtain information on the infection prophylaxis regimen actually received by the recipient. In general, most centers have a standard cocktail of drugs used which include an antibacterial agent (or agents), antiviral agent, antifungal agent, and an anti-pneumocystis agent. Sometimes, recipients are on one of these medications prior to starting the preparative regimen and therefore it could be treating an infection or is being used as “secondary prophylaxis.” Information regarding primary and secondary prophylaxis can provide insight into the development of resistant infections.

**Questions 407-427: Report the first infection prophylaxis drugs administered during the reporting period.**

Indicate whether any antibacterial, antiviral, antifungal, and anti-pneumocystis (PJP) drug(s) were given for infection prophylaxis during the reporting period. Include infection prophylaxis drugs started prior to day 0.

For each category of infection prophylaxis medications, indicate the drug which was administered closest to the start of the preparative regimen (or infusion if no preparative regimen was given) and started no later than day +45. This may include prophylaxis medications started prior to the start of the preparative regimen as long as they were continued at the start of the preparative regimen. Only one drug may be reported for antiviral, antifungal, and anti-pneumocystis categories; however, multiple drugs may be reported under the **antibacterial** category if the drugs were started on the same date (and were administered closest to the start of the preparative regimen and prior to day +45). For example, if both cefepime and vancomycin were started as prophylaxis on the same day the preparative regimen was started, the center should report both medications under the antibacterial category. However, if cefepime was administered at the start of the preparative regimen and vancomycin was started 2 days later, the center should only report cefepime as the first antibacterial infection prophylaxis drug.
Ensure the start date for any medications reported reflects the first date the drug was administered. Refer to the medication administration record to confirm the start date.
Q428-440: Infection

Infections occur frequently in transplant patients. Questions 428-440 are intended to capture detailed information on clinically significant infections diagnosed during the reporting period. A single infection may be found on multiple cultures or at multiple sites. Infections may recur following resolution of symptoms and negative testing. Use the instructions provided in this section to determine when an infection should be considered clinically significant, and therefore reported, as well as when to report new and/or recurrent infections.

Questions 428-436: Did the recipient develop a clinically significant infection since the date of last report?

Do not report the following scenarios:

- Culture-negative neutropenic fever without clear source;
- Suspected (unconfirmed) viral or bacterial infections;
- Upper respiratory infections which are presumed viral, but no virus has been identified;
- Candida detected in oral or stool samples (includes oral thrush);
- Toe nail fungus;
- Yeast infection in the groin, vagina, or under the breasts;
- Surveillance cultures in which normal flora is present and the recipient is asymptomatic;
- Infections persisting from a prior reporting period (including infections which have progressed to new sites since the last report); or
- Infections recurring within the time frames specified in the Definitions for Same Infection table below.

Systemic inflammatory response syndrome and septic shock may be diagnosed with or without an organism...
identified by relevant testing. In either case, a clinical diagnosis of these complications will be reported in questions 437-440. If an organism is identified by molecular report, laboratory report, or other physician documentation, the infection should be reported in questions 428-436. If no organism is identified, the center should use the following guidelines to determine whether to report an infection:

- If a fungal infection is suspected (per radiology assessments), but no organism is isolated during the reporting period, report the suspected infection in questions 428-436.
- If a bacterial or viral infection is suspected, but not confirmed, do not report an infection in questions 428-436.
- If no particular organism group is identified or suspected, do not report an infection in questions 428-436.

For each infection, report the organism, site, and date of diagnosis.

**Definitions for Same Infection**

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Virus</th>
<th>Fungal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>≤ 7 Days</strong></td>
<td><strong>≤ 14 Days</strong></td>
<td><strong>≤ 14 Days</strong></td>
</tr>
<tr>
<td>Any bacteria</td>
<td>Adenovirus</td>
<td>Any yeasts</td>
</tr>
<tr>
<td><strong>≤ 30 Days</strong></td>
<td>Enterovirus</td>
<td></td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>Herpes zoster</td>
<td><strong>≤ 90 Days</strong></td>
</tr>
<tr>
<td><strong>≤ 365 Days</strong></td>
<td>Influenza</td>
<td>Any molds</td>
</tr>
<tr>
<td>Helicobacter pylori</td>
<td>Parainfluenza</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rhinovirus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Respiratory syncytial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Varicella zoster</td>
<td></td>
</tr>
<tr>
<td><strong>≤ 30 Days</strong></td>
<td>Human Herpes Virus - 6</td>
<td></td>
</tr>
<tr>
<td><strong>≤ 60 Days</strong></td>
<td>Cytomegalovirus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epstein-Barr virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Herpes simplex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polyomavirus</td>
<td></td>
</tr>
</tbody>
</table>

**Organism:**

Select the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. If the specific organism is not listed, use the code “777 – Other organism” and report the name of the organism in the space provided. If a fungal infection is suspected, but not
identified, report using code “503 – Suspected fungal infection.” As noted above, only report infections which are *clinically significant*.

Reporting the following infections, will cause a Fungal Infection Post-HCT Data Form (Form 2146) to come due:

- 211 Aspergillus flavus
- 212 Aspergillus fumigatus
- 213 Aspergillus niger
- 210 Aspergillus, NOS
- 215 Aspergillus terreus
- 214 Aspergillus ustus
- 270 Blastomyces (dermatitidis)
- 201 Candida albicans
- 208 Candida non-albicans
- 222 Cryptococcus gattii
- 221 Cryptococcus neoformans
- 230 Fusarium (all species)
- 261 Histoplasma (capsulatum)
- 241 Mucorales (all species)
- 242 Rhizopus (all species)
- 272 Scedosporium (all species)
- 240 Zygomycetes, NOS
- 503 Suspected fungal infection

Reporting the following infections will cause a Hepatitis Serology Post-HSCT Data Form (Form 2147) to come due:

- 307 Hepatitis B Virus
- 308 Hepatitis C Virus

Reporting the following infections will cause a Human Immunodeficiency Virus Post-HSCT Data Form (Form 2148) to come due:

- 309 Human Immunodeficiency Virus 1 or 2

**Site:**  
Infections can occur virtually anywhere. In order to capture sufficient detail without excess burden, there is a list for the potential sites. An infection may occur in more than one site at the same or at different times.
• If the infection is identified at multiple sites with the same organism and within the recurrence interval to be considered the same infection (Definitions for Same Infection table), please report all sites the organism was identified.
• If the infection is identified at multiple sites with an organism already reported, but is outside of the recurrence interval to be considered the same infection, please report as a new infection.

Select the site(s) of the infection from the options provided on the form. Report all sites of infection which were confirmed by microbiology, laboratory report, or other physician documentation during the reporting period. This includes any new sites identified after the date of diagnosis as well as after treatment has been initiated.

For clarification, the following site definitions are provided:

**Blood**: includes blood or serum obtained from a central IV line, catheter tip, or from a direct needle stick (Peripheral draw). Blood should be the reported site for infections identified in the bone marrow.

**Bone**: an infection in the bone itself (Osteomyelitis)

**CNS**: includes CSF (cerebrospinal fluid) specimens as well as abscesses and/or inflammation noted on brain imaging (encephalitis, meningitis)

**Eyes**: includes infection in any part of the eye (i.e. retinitis)

**Genital**: includes vagina, penis, perineum, ovaries, scrotum, testes, uterus

**GI tract, lower**: includes jejunum, ileum, colon, rectum, and stool

**GI tract, upper**: includes mouth, dentition, esophagus, stomach, and duodenum

**Joints**: includes fibrous connective tissue and cartilage at any site of bone articulation, typically isolated to a single area (i.e., not a diffuse infection) such as the knee, elbow, or shoulder

**Liver/Spleen**: includes the gallbladder and biliary tract

**Lung**: also known as the lower respiratory tract

**Skin, cellulitis**: a spreading bacterial or viral infection of the skin and tissues beneath the skin

**Skin, necrotizing fasciitis**: a severe bacterial infection of the fascia, the tissues that line and separate muscles, that causes extensive tissue death including damage to skin and overlying tissues
**Sinus and/or upper respiratory tract:** all areas from the nose to the throat and sinuses, does not include lungs (report as “Lung”), mouth, or dental infections (report mouth and dental as “GI tract, upper).

**Urinary tract, lower:** includes urinary tract infections and cystitis (bladder inflammation)

**Urinary tract, upper:** includes the kidneys and ureters

**Date of Diagnosis:**
Report the date of diagnosis of the infection as the collection date for the positive microbiology culture or laboratory report. For suspected fungal infections, enter the date of a radiological test or the date treatment was started as the date of diagnosis. If multiple sites of infection are identified during the reporting period, report the collection date of the first positive microbiology culture or laboratory report.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

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**Infection Reporting Scenarios:**

**A.** A recipient’s post-HCT CMV testing was consistently negative until 1/10/2015 when CMV PCR testing found 15,000 copies of the virus in the recipient’s peripheral blood. On 1/20/2015, the CMV PCR detects 2000 copies. The CMV PCR is still positive on 1/30/2015, but is documented as “detected but not quantifiable”. From 2/7/15, all subsequent CMV PCRs are negative until 6/3/2015 when the CMV PCR demonstrates 1300 copies.

The center should report one instance of questions 429-436 to capture the CMV infection first documented on 1/10/2015. A second instance of questions 429-436 should also be reported to capture a recurrent CMV infection documented on 6/3/2015. This is >60 days after PCR testing reverts to negative and is therefore considered a recurrence and not the same infection per the guidelines in the Definitions for the Same Infection table above. The recurrent infection would be reported on a subsequent Post-Infusion Data Form if it is diagnosed after the date of contact for the form being completed.

**B.** A recipient with concerning respiratory symptoms undergoes a bronchiolar lavage on 10/1/2014. A culture performed on the sample collected from the procedure revealed a Streptococcus, Group B infection. The recipient received systemic antibacterial antibiotics, but the infection progressed to their...
blood as demonstrated by a culture performed on sample collected 11/1/2014. The recipient did not have any repeat cultures performed between their initial diagnosis and testing performed on 11/1/2014.

The center should report one instance of questions 429-436 to capture the Streptococcus, Group B infection. The diagnosis date is the date of the first positive culture performed on the sample collected 10/1/2014.

- If the positive culture from 11/1/2014 was collected during the same reporting period, “lung” and “blood” should both be reported as sites of infection.
- If the positive culture from 11/1/2014 was collected after the date of contact for the current reporting period, do not report “blood” as a second site of infection.

C. A recipient is empirically diagnosed with septic shock on 8/15/2013, though cultures and viral tests are consistently negative. The recipient is treated with multiple antimicrobial agents which eventually leads to a resolution of all symptoms / complications. The organism responsible for the suspected infection is never identified.

As no organism was identified, the only scenario in which the center should report this as an infection in questions 428-436 is if there is documentation confirming a suspected fungal infection. In any case, the clinical diagnosis of septic shock will be reported in questions 439-440.

**Question 437-438: Did the recipient develop Systemic Inflammatory Response Syndrome (SIRS) since the date of last report?**

Systemic inflammatory response syndrome refers to unregulated inflammation which may or may not be related to an infection. If SIRS was clinically diagnosed during the reporting period, report “yes” for question 437 and indicate the diagnosis date in question 438.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 439-440: Did the recipient develop septic shock since the date of last report?**

Septic shock refers to the failure to maintain sufficient mean arterial pressure without intervention with vasopressors. It results from vasodilation associated with infection. If septic shock was clinically diagnosed during the reporting period, report “yes” for question 439 and indicate the diagnosis date in question 438.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.
**Q441-615: Organ Function**

Links within section:
- Pulmonary Function
- Liver Toxicity Prophylaxis
- Liver Function
- Thrombotic Microangiopathy
- Other Organ Impairment / Disorder

**Pulmonary Function**

* Bacterial, Viral, and Fungal Pneumonia
  Report pneumonia due to infection in the Infection section (questions 428-440).

**Question 441-485: Indicate any non-infectious pulmonary abnormalities diagnosed since the date of the last report.**

Report any non-infectious pulmonary abnormalities diagnosed since the date of the last report. See below for a description of reportable abnormalities as well as common methods of assessment.

**Non-Infectious Pulmonary Abnormalities:**

**Interstitial pneumonitis / Acute respiratory distress syndrome (IPn/ARDS):** IPn refers to inflammation of the alveolar walls. Acute respiratory distress syndrome typically refers to fluid build-up within the alveoli. In either case, gas exchange is impaired resulting in oxygen deprivation. Both conditions can result from infectious or non-infectious causes. Only report IPn / ARDS resulting from non-infectious causes in questions 441-485.

**Idiopathic pneumonia syndrome (IPS):** all non-infectious lung injuries that occur early after HCT (within 100-120 days) including: peri-engraftment respiratory distress syndrome (PERDS), interstitial pneumonitis without a pathogen, radiation / drug-induced lung injury, or transfusion-associated lung injury (TRALI).

**Bronchiolitis obliterans (BO):** an airway obstruction as a result of inflammation of the bronchioles. This complication typically occurs late after HCT. It is often a manifestation of chronic GVHD. If bronchiolitis obliterans is a result of chronic GVHD, confirm that bronchiolitis obliterans was also reported in the chronic GVHD section of this form (question 311).
Cryptogenic organizing pneumonia (COP) / Bronchiolitis obliterans with organizing pneumonia (BOOP): an idiopathic form of pneumonia which affects different parts of the lungs including the bronchioles and alveoli. This complication typically occurs late after HCT.

Diffuse alveolar hemorrhage (DAH): bleeding into the alveolar space typically resulting from an injury to the pulmonary blood vessels.

Other non-infectious abnormalities: any other non-infectious pulmonary abnormalities not already captured in the above categories. Do not report pleural effusions here.

Diagnostic Methods:

Bronchoalveolar lavage (BAL): a procedure in which a bronchoscope is guided into the lower respiratory system. Fluid is emitted from the bronchoscope and then collected for further examination.

Transbronchial biopsy: a procedure in which forceps on the end of the bronchoscope are used to collect lung tissue samples for further examination.

Open / thorascopic lung biopsy: An open lung biopsy is a procedure in which an incision is made between the ribs to collect a sample of lung tissue for further examination. A thorascopic lung biopsy is a procedure in which an incision is made to the chest and an endoscope is used to collect samples of lung tissue.

Autopsy: a post-mortem procedure used to determine the cause of death and to evaluate other disease present at the time of death.

Other: Specify "other diagnostic test" for IPn / ARDs or IPS in question 449, excluding radiographic assessment.

For any reported abnormalities, report the date of diagnosis and the diagnostic tests performed. If the diagnosis was determined at an outside center and no documentation of a clinical, pathological, or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Documentation of diagnostic tests may be attached to the form. For further instructions on how to attach documents in FormsNet3, refer to the training guide.
**Question 486-487: Did the recipient receive endotracheal intubation or mechanical ventilation post-HCT?**

Endotracheal intubation or mechanical ventilation may be used post-HCT for respiratory failure or for airway protection from severe mucositis.

Invasive positive pressure ventilation is delivered via an endotracheal tube. Do not include non-invasive positive pressure ventilation that is delivered through an alternate interface (e.g., facemask).

Indicate whether the recipient received endotracheal intubation or mechanical ventilation (invasive positive pressure ventilation) post-HCT. If “yes,” report the date when endotracheal intubation or mechanical ventilation was started in question 487. If “no,” continue with question 490. Please report “no” if the patient received endotracheal intubation or mechanical ventilation during surgery.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

**Question 488-489: Was the recipient successfully extubated?**

Indicated if the recipient was successfully extubated during the reporting period. If “yes,” report the date of extubation in question 489. If “no,” continue with question 490.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

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**Liver Toxicity Prophylaxis**

Questions 490-496 can only be completed on the 100 day and 6 month follow-up forms. These questions will be skipped for all subsequent reporting periods.

**Question 490: Was specific therapy used to prevent liver toxicity?**

Liver toxicities in transplant patients may be related to drugs / treatments, infection, GVHD, iron overload, cirrhosis, or sinusoidal obstructive syndrome (SOS) / veno-occlusive disease (VOD). Agents such as ursodiol may be given as prophylaxis against one or more of these transplant-related liver injuries. Agents given to prevent liver toxicity will generally be started prior to or during the conditioning regimen, and may be continued well after transplant.

Indicate whether the recipient received any therapy intended to prevent liver toxicity during the reporting
period, including therapy given during the conditioning regimen. Report only agents given to prevent liver toxicities, not those given to treat a diagnosed liver injury or toxicity. If liver toxicity prophylaxis was given, report “yes” and complete with questions 491-496. If liver toxicity prophylaxis was not given during the reporting period, report “no” and continue with question 497.

Question 491-496: Specify therapy (Defibrotide, N-acetylcysteine, tissue plasminogen activator (TPA), Ursodiol, Other)

Report all agents given during the reporting period to prevent liver toxicity, including therapy given during the conditioning regimen. Only report agents given to prevent liver toxicities, not those given to treat a diagnosed liver injury or toxicity. If “other” therapy is reported in question 495, specify agent in question 496.

Liver Function

Liver Toxicity

Questions 497-505 are designed to collect information on the level of liver dysfunction that is not related to acute or chronic GVHD (e.g., chemotoxicity, cyclosporine toxicity, veno-occlusive disease [VOD]). Liver dysfunction may be determined by biopsy, viral culture, or suspected by clinical evidence.

Question 497: Did the recipient develop non-infectious liver toxicity (excluding GVHD) since the date of last report?

Indicate whether the recipient developed a non-infectious liver toxicity during the reporting period. Include and toxicities which developed between the start of the preparative regimen and the date of last contact (question 1) when completing the 100 day follow-up form. Do not report liver complications due to GVHD in this section. If “yes,” continue with question 498. If “no,” continue with question 507.

Question 498-506: Specify the non-infectious liver toxicity etiology (veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS), cirrhosis, other, and unknown etiology)

Report the etiology of the non-infectious liver toxicity that the recipient developed since the date of the last report in questions 498-506.

Veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS): occurs following injury to the hepatic venous endothelium, resulting in hepatic venous outflow obstruction due to occlusion of the hepatic venules and sinusoids. This typically results in a distinctive triad of clinical signs including hepatomegaly with right upper quadrant tenderness, third space fluid retention (e.g., ascites), and jaundice with a cholestatic picture. For more information on VOD / SOS including diagnostic criteria, refer to the VOD / SOS section of the Forms Instructions Manual.
Question 498-499: Did veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOD) develop since the date of last report?

Indicate whether VOD / SOS was diagnosed during the reporting period. If “yes,” report the date of diagnosis in question 499. If VOD / SOS persisted from the prior reporting period, indicate “no” and continue with question 500.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 500-501: Cirrhosis

Cirrhosis is a degenerative disease in which fibrous tissue forms and the lobes become filled with fat. Cirrhosis may be diagnosed using a liver biopsy, but clinical symptoms (enlarged liver), blood tests, laparoscopy, or radiology imaging are often used to determine the diagnosis of cirrhosis when a liver biopsy is not necessary.

Indicate whether cirrhosis was diagnosed during the reporting period. If “yes,” report the date of diagnosis in question 501. If cirrhosis persisted from a prior reporting period, indicate “no” and continue with question 502.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 502-504: Other etiology

Report liver complications not listed above. Do not include hepatic infections or GVHD. Report infections in the Infection section (questions 428-440); and GVHD in the Acute GVHD section (questions 157-233) and / or in the Chronic GVHD section (questions 234-406).

If reporting “yes” for “other etiology,” specify the documented etiology in question 503 and report the date of diagnosis in question 504. If reporting “no,” continue with question 505.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 505: Unknown etiology

Indicate “unknown” if there is no information about the etiology of the non-infectious liver toxicity. This option should be used sparingly and only when no judgment can be made about the etiology in the reporting period.
Thrombotic Microangiopathy (TMA)

Thrombotic microangiopathy (TMA) is a multifactorial condition where intravascular platelet activation, formation of thrombi, and microangiopathic hemolytic anemia occur due to generalized endothelial dysfunction. Organ injury, specifically the kidney, may occur as a result of these processes. Characteristics of thrombotic microangiopathy includes microangiopathic hemolysis, thrombocytopenia (< $5 \times 10^9$/L), neurological changes, and pulmonary dysfunction. Other laboratory features include:

- LDH greater than the center-specific upper limit of normal
- Serum creatinine > 2 mg/dL or >50% rise over baseline
- Bilirubin greater than twice the center-specific upper limit of normal


Question 506: Did the recipient develop post-transplant thrombotic microangiopathy (TMA) (include microangiopathy, thrombotic thrombocytopenia purpura (TTP), hemolytic uremic syndrome (HUS)), or similar syndrome since the date of last report?

Microangiopathy: Disease of the capillaries where the capillaries bleed and slow the flow of blood due to thickening and weakening of capillary walls.

Thrombotic thrombocytopenia (TTP): Blood disorder where blood clots form in the small blood vessels of the body.

Hemolytic uremic syndrome (HUS): Abnormal destruction of red blood cells which block the kidneys resulting in kidney failure. May be caused by Escherichia coli, other infections, and medications.

Indicate whether the recipient developed post-transplant TMA or a similar syndrome since the date of last report. If “yes,” continue with question 507. If “no,” continue with question 527.

Question 507: Date of diagnosis:

Report the clinical diagnosis date of post-transplant TMA or a similar syndrome, including microangiopathy, TTP, and HUS. For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 508-512: Specify signs and symptoms:

For each option listed, indicate whether the recipient had any signs or symptoms due to post-transplant
TMA or a similar syndrome during the reporting period.

**Question 513-517: Was TMA evaluated by biopsy?**

Indicate whether TMA was evaluated by a biopsy. If “yes,” report if the results were “positive,” “suggestive,” “negative,” “inconclusive / equivocal,” or “not done” for each option listed. If “other site” is reported, specify the biopsy site in question 516.

Indicate whether documentation was submitted to CIBMTR in question 517. For further instructions on how to attach documents in FormsNet3, refer to the training guide.

**Question 518-524: Was therapy given for TMA?**

Indicate whether the recipient received any therapy intended to treat TMA during the reporting period. Report only agents given to treat a diagnosis of TMA. If “yes,” report all therapy given during the reporting period in questions 519-524. If “no,” continue with question 525.

**Question 525: Did the TMA resolve? (Normalization of renal function, LDH, and resolution or improvement in renal and / or neurologic dysfunction)**

Indicate whether TMA resolved. If “yes,” report the first date the recipient met the following criteria:

- Normalization of renal function (per institutional guidelines);
- Normalization of LDH (per institutional guidelines);
- Resolution / improvement of renal and neurologic dysfunction.

If TMA did not resolve during the reporting period, skip question 526 and continue with question 527.

**Other Organ Impairment / Disorder**

**Question 527: Has the recipient developed any other clinically significant organ impairment or disorder since the date of last report?**

The intent of this question is to identify serious conditions or impairments occurring after transplant. For the purposes of this manual, the term “clinically significant” refers to conditions requiring treatment or intervention. Additional guidelines for commonly reported organ impairments and disorders are included below. Do not report complications that are expected for most transplant recipients and do not require treatment (i.e., minor complications resolving without intervention).

Indicate whether the recipient developed any other clinically significant organ impairment or disorder during
the reporting period. If this form is being completed for the 100 day reporting period, include any clinically significant impairments or disorders diagnosed between the start of the preparative regimen and the date of contact (question 1). If “yes,” complete questions 528-610. If “no,” continue with question 611.

Do not report any impairments / disorders which have persisted since the last report. If this form is being completed for the 100 day reporting period, do no report conditions which have persisted since before the start of the preparative regimen.

**Questions 528-610: Specify impairment / disorder:**

Indicate whether any of the organ impairments or disorders listed were diagnosed during the reporting period. If the recipient developed an impairment during the reporting period, report “yes,” enter the date of diagnosis, and answer any additional questions pertaining to the impairment / disorder. If the diagnosis was determined at an outside center and no documentation of a clinical, pathological, or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Renal**

**Acute renal failure requiring dialysis:** report whether dialysis was ordered or recommended for renal failure. Also report whether the recipient received the treatment. Symptoms of renal failure include dehydration, nausea, blood in the urine, and / or swelling of extremities.

**Chronic kidney disease / renal impairment:** report whether there was chronic kidney disease or renal impairment (persistent decrease in glomerular filtration to <60 mL/min.1.73m²). Also report whether the recipient received treatment.

**Cardiac**

**Arrhythmia:** report whether the recipient developed an arrhythmia, including atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmia. Specify the arrhythmia. If “other arrhythmia” is reported, specify in question 542.

**Congestive heart failure (CHF):** inability of the heart to supply oxygenated blood to meet the body’s needs. Ejection fraction < 40%.

**Coronary artery disease:** damage or disease in the major blood vessels of the heart. Also called CAD, atherosclerotic heart disease.
Myocardial infarction (MI): an obstruction in the coronary artery resulting in damage / necrosis to the cardiac muscle.

Hypertension (HTN) requiring therapy: report whether treatment was given for high blood pressure.

Vascular

Deep vein thrombosis (DVT) / Pulmonary embolism (PE): development of a blood clot in a deep vein or development of a blood clot in the arteries of the lung.

Neurological

CNS hemorrhage: bleeding within the central nervous system.

Encephalopathy: damage or disease of the brain. Symptoms of encephalopathy include memory loss, personality changes, and declining ability to concentrate and reason.

Neuropathy: nerve damage, usually in hands and feet, which causes pain, weakness, and numbness.

Seizures: sudden, involuntary muscle contractions due to the hyperexcitation of neurons.

Stroke: loss of brain function due to a disturbance in the blood supply to the brain.

Endocrine

Diabetes / hyperglycemia: high blood glucose levels. Diabetes / hyperglycemia should only be reported if insulin and / or oral medication is required for treatment. Diabetes / hyperglycemia controlled through diet and exercise should not be reported.

Growth hormone deficiency / short stature: a condition in which the body does not produce enough growth hormone / a reduced overall rate of growth.

Hypothyroidism requiring replacement therapy: decreased activity of the thyroid gland. Diagnosis of hypothyroidism includes high levels of thyroid-stimulating hormone (TSH). Symptoms of hypothyroidism include fatigue, depression, weakness, weight gain, musculoskeletal pain, decreased taste, hoarseness, and / or puffy face.

Pancreatitis: inflammation of the pancreas.

Genitourinary
Gonadal dysfunction requiring hormone replacement (testosterone or estrogen): Females may experience early symptoms of menopause including amenorrhea. Males may experience decreased spermatogenesis. Low levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and / or testosterone may require hormone replacement therapy.

Hemorrhagic cystitis / hematuria requiring medical intervention (catheterization of bladder, extra transfusions, urology consult): characterized by bleeding and inflammation of the bladder wall. Hemorrhagic cystitis may result from systemic chemotherapy or radiation therapy and / or some viral infections (e.g., BK virus). Report cases with macroscopic (visible to the naked eye) or gross hematuria (WHO Grade III and IV hemorrhagic cystitis). If the etiology is infectious, also report in the Infection section (questions 291-295). Examples of medical intervention include catheterization of bladder, extra transfusions, or a urology consult.

Musculoskeletal

Avascular necrosis: localized tissue death due to inadequate oxygen to the cells. Also known as coagulation necrosis or ischemic necrosis.

Osteonecrosis of the jaw: bones of the jaw weaken and die due to potent antiresorptive medications such as bisphosphonates or RANKL inhibitors, infection, steroid use, and treatment of cancer, including radiation.

Osteoporosis: bones become weak and brittle due to losing bone mass faster than it is created from aging.

Osteoporotic fracture: fractures due to low bone mineral density.

Psychiatric

Depression requiring therapy: mood disorder resulting in persistent feeling of sadness and loss of interest. Common treatments include antidepressant, anxiolytic, and antipsychotic medications. Common names include Amitriptyline, Bupropion (Wellbutrin), Buspirone, and Abilify.

Anxiety requiring therapy: disorder characterized by feelings of worry, anxiety, or fear which are strong enough to interfere with daily activities. Common medications include Duloxetine (Cymbalta), Diazepam (Valium), Buspirone, Pregabalin (Lyrica).

Post-traumatic stress disorder (PTSD) requiring therapy: condition triggered by seeing or experiencing a traumatic event.
Other

**Cataracts:** loss of transparency in the lens of the eye.

**Hyperlipidemia requiring therapy (high total cholesterol, high LDL cholesterol, and/or high triglyceride levels):** high levels of lipids (fat particles) in blood. Common drugs include Atorvastatin (Lipitor), Simvastatin (Zocor), Ezetimibe (Zetia), and Simvastatin (Vytorin).

**Iron overload requiring therapy:** condition characterized by having too much iron in the body. Therapy includes phlebotomy and iron chelation. Indicate which therapy is required. If “other therapy” is required, specify if in question 605.

*Iron overload cannot be answered on the day 100 form. Iron overload questions will be answered for all subsequent reporting periods.*

**Mucositis requiring therapy:** inflammation and ulceration of mucous membranes that line the digestive tract, usually due to chemotherapy and radiotherapy. Specify the grade as “0 (none),” “I (mild) – oral soreness, erythema,” “II (moderate) – oral erythema, ulcers, solid diet tolerated,” “III (severe) – oral ulcers, liquid diet only,” or “IV (life-threatening – oral ulcers, oral alimentation impossible.” Do not report mucositis which did not require treatment or intervention during the reporting period.

*Mucositis can only be answered on the day 100 form. Mucositis questions will be skipped for all subsequent reporting periods.*

Other impairment or disorder: use this category to report any clinically significant impairment(s) / disorder(s) not listed on the form. Specify the other impairment / disorder in question 610.

Do not report complications that have been reported elsewhere on the form.

**Question 611-613: Has the recipient received a solid organ transplant since the date of last report?**

Indicate whether the recipient received a solid organ transplant since the date of the last report. If “yes,” specify the organ transplanted in question 612. If “other organ” is reported, specify organ in question 613. If the recipient did not receive a solid organ transplant during the reporting period, report “no” for question 611 and continue with question 616.

*Solid organ transplant questions cannot be answered on the day 100 or 6 month forms. These questions will be answered for all subsequent reporting periods.*
**Question 614: Date of transplant:**

If the recipient received a solid organ transplant during the reporting period, report the date of the solid organ transplant.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 615: Specify solid organ donor type:**

Specify if the solid organ donor was a "living related donor," "living unrelated donor," or a "cadaveric donor."
Q616-639: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder

Post-Transplant Lymphoproliferative Disorder Instructions section

Question 616: Did a new malignancy, myelodysplastic, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the HCT or cellular therapy was performed? (Include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders)

Indicate whether a new or secondary malignancy, lymphoproliferative disorder, or myeloproliferative disorder was diagnosed during the reporting period. Do not report recurrence, progression, or transformation of the recipient’s primary disease (disease for which the transplant was performed) or relapse of a prior malignancy.

Report relapse of the recipient’s primary disease on the appropriate post-HCT disease-specific data form. Relapse of a prior malignancy will not be captured by the CIBMTR.

New malignancies, lymphoproliferative disorders, and myeloproliferative disorders include but are not limited to:

- Skin cancers (basal, squamous, melanoma)
- New leukemia
- New myelodysplasia
- Solid tumors
- PTLD (post-transplant lymphoproliferative disorder) report as lymphoma or lymphoproliferative disease

The following should not be reported as new malignancy:

- Recurrence of primary disease (report as relapse or disease progression)
- Relapse of malignancy from recipient’s pre-HCT medical history
- Breast cancer found in other (i.e., opposite) breast (report as relapse)
- Post-HCT cytogenetic abnormalities associated with the pre-HCT diagnosis (report as relapse)
- Transformation of MDS to AML post-HCT (report as disease progression)
If a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was diagnosed during the reporting period, report “yes” and completed questions 617-639. If no new malignancies or disorders were diagnosed during the reporting period, report “no” and continue with question 640.

Copy and complete questions 617-639 to report each new malignancy diagnosed since the date of last report. The submission of a pathology report or other supportive documentation for each reported new malignancy is strongly recommended.

**Questions 617-619: Specify the new malignancy:**

Indicate which new malignancy / disorder was diagnosed during the reporting period and indicate the date of diagnosis in question 619. Report the pathologic diagnosis date. If the original assessment confirming diagnosis is not available, report the date of diagnosis indicated in the progress notes.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 620-621: Was the new malignancy donor / cell product derived?**

Indicate whether the new malignancy originated from the donor / cell product. If “yes,” indicate whether documentation was submitted to CIBMTR (e.g., cell origin evaluation (VNTR, cytogenetics, FISH)) in question 621.

For further instructions on how to attach documents in FormsNet3, refer to the training guide.

**Question 622: Was documentation submitted to the CIBMTR? (e.g., pathology report, autopsy report)**

Indicate whether documentation of the new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was submitted to CIBMTR (e.g., pathology report, autopsy report).
For further instructions on how to attach documents in FormsNet3, refer to the training guide.

**Post-Transplant Lymphoproliferative Disorder**

**Question 623: Was there EBV reactivation in the blood?**

If reactivation in the blood was confirmed during the reporting period, report “yes” and continue with question 624. If reactivation did not occur during the reporting period report “no” and continue with question 629.

Indicate “unknown” if no EBV testing was performed during the reporting period.

**Question 625-628: How was EBV reactivation diagnosed?**

Indicate the method of detection for EBV reactivation.

If reactivation was diagnosed by “qualitative PCR of blood,” continue with question 629.

If the diagnoses was made by “quantitative PCR of blood,” report the number of copies detected in question 626. Also, indicate whether repeat testing was performed during the reporting period in question 627. If repeat testing was performed, report the results of the most recent test performed during the reporting period in question 628.

If the diagnosis was made by “Other method,” specify the method of detection in question 625 and then continue with question 630.

**Question 627: Quantitative EBV viral load of blood (at diagnosis of EBV)**

If EBV reactivation was diagnosed by quantitative PCR of blood, report the EBV viral blood load at diagnosis.

**Question 629: Was there lymphomatous involvement? (e.g., a mass)**

Indicate whether a mass or other lymphomatous involvement was detected during the reporting period. If there was lymphomatous involvement was confirmed during the reporting period, report “yes” and complete questions 630-637. If lymphomatous involvement was not confirmed during the reporting period, report “no” and continue with question 638.
**Question 630-637: Specify sites of PTLD involvement:**

For each site listed, indicate whether there was post-transplant lymphoproliferative disorder (PTLD) involvement. Sites may be identified by radiographic or pathologic methods. If there was PTLD involvement at a site not listed, report “other site” and specify in question 637.

**Question 638-639: Was PTLD confirmed by biopsy?**

Indicate whether PTLD was confirmed by a biopsy. If PTLD was confirmed by a biopsy, report “yes” and indicate whether documentation was submitted to CIBMTR (e.g., pathology report) in question 639. If a biopsy did not confirm the diagnosis of PTLD, report “no” and continue with question 640.

For further instructions on how to attach documents in FormsNet3, refer to the training guide.
Q640-664: Functional Status

**Question 640: Was the intent to complete HCT procedure (conditioning, infusion, and period of recovery from neutropenia) as an outpatient?**

Report “yes” if the plan was to complete all conditioning, infusions, and recovery in the outpatient setting. If the plan was to admit the patient for any part of the transplant, report “no” and continue with question 642.

Report “yes” even if the recipient required an unplanned admission. This admission will be captured in question 641.

**Question 641: Did the recipient require an unplanned admission?**

Report whether the recipient required an unplanned admission during the reporting period. This includes unplanned admissions for the purpose of completing an HCT as well as admissions to address any post-HCT complications. If an unplanned admission was required, report “yes” and continue with question 642. If the recipient did not require and unplanned admission, report “no” and continue with question 644.

**Question 642-643: Was the recipient discharged prior to the date of contact?**

If the recipient was discharged from the hospital during the reporting period, report “yes” for question 642 and report the discharge date in question 643. If the recipient was admitted to the hospital multiple times during the reporting period, report first discharge date. If the recipient was not discharged from the hospital during the reporting period, report “no.”

If the recipient died without ever being discharged from the hospital, report “no.”

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 644: Total number of inpatient days (day 0 to day 100) in first 100 days post-HST**

Enter the total number of inpatient days (including day 0). If the recipient was discharged and readmitted during the first 100 days, the total should include days hospitalized after being readmitted. When counting the total number of inpatient days, count either the day of admission or the day of discharge; do not count...
both.

If the recipient receives a subsequent HCT prior to day 100, do not include the start date of the preparative regimen for the subsequent HCT (or the date of the subsequent infusion if no preparative regimen was given).

**Question 645-647: Recipient height: (most recent)**

*Questions 645-647 will only be enabled / answered for pediatric patients (≤ 16 years old) when the form visit ID is 6 months or greater. These questions will be disabled / not answered for all recipients on the day 100 follow-up form.*

Indicate whether the recipient’s height is known. If “known,” report the recipient’s most recent height and specify the units in question 646. Also, report the date the recipient’s height was last measured in question 647. If the recipient’s height was not measured during the reporting period, report “unknown” and continue with question 648.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 648-650: Recipient weight: (most recent)**

Indicate whether the recipient’s weight is known. If “known,” report the recipient’s most recent weight and specify the units in question 649. Also, report the date the recipient’s weight was last measured in question 650. If the recipient’s weight was not measured during the reporting period, report “unknown” and continue with question 651.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 651-653: Functional status**

The CIBMTR uses the Karnofsky / Lansky scale to determine the functional status of the recipient on the date of contact. The Karnofsky Scale is designed for recipients aged 16 years and older, and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. If the recipient is less than one year old, leave questions 651-653 blank.

Select the appropriate performance scale, Karnofsky or Lansky, based on the recipient’s age. Using this scale, select the score (10-100) that best represents the recipient’s activity status immediately prior to the date of last actual contact. Acceptable performance scores include those recorded within 14 days prior to 100 Day and Six Month contact dates. For the annual reporting periods, performance scores may be
reported if dictated within one month of the contact date. The only valid scores are 10-100; zero is not a valid response for this scale, nor are values not ending in zero, such as “85.” The Karnofsky / Lansky scale can be found in Appendix L.

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. Determination of performance status is ideally performed by a healthcare provider. Centers are encouraged to put tools in place to facilitate this collection. If a Karnofsky / Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician’s clinic note), data professionals are encouraged to discuss a determination with the healthcare provider rather than make an assignment themselves, based on inadequate information.

The CIBMTR recognizes that some transplant centers prefer to assign and use the ECOG performance score as opposed to the Karnofsky / Lansky score. Although the ECOG and Karnofsky / Lansky performance score systems are based on similar principles, the scales are not the same. For example, the Karnofsky / Lansky scale is described in 10 categories, whereas the ECOG performance status is reported in six categories. Due to the overlap between the two systems, an ECOG score of “one” can represent either “80” or “90” on the Karnofsky / Lansky scale; whereas, a Karnofsky / Lansky score of “80” or “90” is converted directly to an ECOG score of “one.” Therefore, the Karnofsky / Lansky scale can be more accurately converted into ECOG.

However, for centers that collect only an ECOG performance score, CIBMTR will make the following accommodations when auditing the source data:

- Centers assigning ECOG scores should do so using standard practices to ensure accuracy.
- For the purposes of CIBMTR reporting, conversion of ECOG to Karnofsky / Lansky should follow a standard and consistent practice to account for the lack of direct mapping. This practice should be clear and reproducible.

**Pregnancy Questions**

Questions 654 and 655 will only be answered for recipients between the ages of 10 and 60.

**Question 654: Was the recipient pregnant at any time in this reporting period? (Female only)**

Indicate whether the recipient was pregnant at any time during the reporting period. Skip this question for male recipients. If “yes,” complete questions 656-657. If “no,” continue with question 658.

**Question 655: Was the recipient’s female partner pregnant at any time in this reporting period (Male only)**

Indicate whether the recipient’s female partner was pregnant at any time during the reporting period. Skip
this question for female recipients. If “yes,” complete questions 656-657. If “no,” continue with question 658.

**Question 656: Was the recipient or recipient’s partner still pregnant at the date of last contact?**

Indicate whether the recipient or recipient’s partner was still pregnant on the date of last contact? If the recipient or recipient’s partner was still pregnant on the date of last contact, report “yes” and continue with question 658. If the recipient or recipient’s partner was not pregnant at the date of last contact, report “no” and indicate the outcome in question 657.

**Question 657: Specify the outcome of pregnancy:**

Specify the outcome of the pregnancy using the options provided on the form.

**Question 658-660: Has the recipient smoked tobacco cigarettes since the date of last report?**

The intent of this question is to determine the recipient’s history of smoking cigarettes only. Do not report the use of cigars, pipe tobacco, chewing tobacco, or other drugs. Indicate whether the recipient has smoked tobacco cigarettes since the date of the last report. If “yes,” complete questions 659-660. If the recipient has not smoked tobacco cigarettes since the date of the last report, or their smoking history is not known, report “no” or “unknown” respectively and continue with question 661.

**Question 661: Specify the category which best describes the recipient’s current occupation.**

Select the category that best describes the recipient’s current occupation. If the recipient is a student, check “student.” If the recipient is younger than school-aged, check “under school age” and continue with question 665. If “other” is selected, report the recipient’s occupation in question 662.

Only one work status may be reported. If a recipient has multiple possible occupations, report the highest level of work being performed. For example, full time work would be reported over part time work and part time work would be reported over being a student.

If the recipient is not currently employed, check the box that best describes his/her last job.

**Questions 663-664: What is the recipient’s current or most recent work status during this reporting period?**

Select the work status that best describes the recipient’s current or most recent employment during this reporting period. If the recipient is retired, specify their retirement status in question 664.
**Q665-672: Subsequent HCT**

**Subsequent Transplant**
Complete this section if the recipient received a subsequent HCT (question 3, answered “yes”).
In addition to this section, a new Pre-TED Form (Form 2400) and Recipient Baseline Data Form (Form 2000) must be completed for the subsequent HCT. The exception to this is an autologous HCT (question 666) performed for graft failure / insufficient hematopoietic recovery (question 664). The cells used for this subsequent autologous HCT would have been collected prior to the previous transplant. For information on how to distinguish infusion types (e.g., HCT versus DCI), see Appendix D.

**Question 665: Date of subsequent HCT**
Report the date when the recipient received the subsequent HCT.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 666: Was the subsequent HCT performed at a different institution?**
Indicate whether the subsequent HCT was performed at another institution. If the subsequent HCT was performed at a different institution, report “yes” and continue with question 667. If the subsequent HCT was not performed at a different institution, report “no” and continue with question 668.

**Question 667: Specify the institution that performed the subsequent HCT**
Report the name, city, state, and country of the institution where the recipient’s subsequent HCT was performed. These data are used to identify and link the recipient’s information in the database.

**Questions 668-669: What was the indication for subsequent HCT?**
Indicate the reason for the subsequent HCT (check only one).

- **Graft failure / insufficient hematopoietic recovery**: Additional hematopoietic stem cells are required because the hematopoietic recovery indefinitely declined after the initial hematopoietic recovery (ANC was greater than or equal to $0.5 \times 10^9/L$ for three consecutive days, and then declined to below $0.5 \times 10^9/L$ for at least three consecutive days). This option also includes primary graft
failure (no ANC recovery following HCT).

- **Persistent primary disease:** Additional hematopoietic stem cells are required because of the persistent presence of disease pre and post-transplant (i.e., complete remission was never achieved following the previous transplant).

- **Recurrent primary disease:** Additional hematopoietic stem cells are required because of relapsed primary disease (i.e., complete remission was achieved pre or post-transplant, but the disease relapsed following the previous transplant).

- **Planned second HCT, per protocol:** Additional hematopoietic stem cells are given as defined by the protocol for a subsequent transplant/infusion. This transplant is not based upon recovery, disease status, or any other assessment.

- **New malignancy (including PTLD and EBV lymphoma):** Additional hematopoietic stem cells are required because the recipient has developed a new malignancy. This does not include a transformation or progression of the original malignancy for which the recipient was transplanted (refer to question 617 for more information). If “new malignancy” is selected, also complete questions 617-640.

- **Insufficient chimerism:** In the case of a stable, mixed donor chimerism, the infusion of additional cells (usually lymphocytes and not mobilized hematopoietic stem cells) is typically classified as a DCI. Verify with the transplant physician that the cells given should be reported as a subsequent transplant and that stable, mixed chimerism is the reason for the transplant. In the case of declining chimerism—when the percentage of donor cells is sequentially decreasing on several studies, indicating possible impending graft failure—additional stem cells are required. Usually the donor chimerism has fallen below 30-50%.

- **Other:** If additional hematopoietic stem cells are given for a reason other than the options listed, select “other” and complete question 669.

### Question 670-672: Source of HSCs

Report the hematopoietic stem cell source of the recipient’s subsequent HCT.

If “allogeneic, related” is selected, indicate whether the same donor was used in question 671 and submit the form.

If “allogeneic, unrelated” is selected, indicate whether the same donor was used in question 671 and specify the product/donor type in question 672. Submit the form after completing questions 670-672.

If “autologous” is selected, skip questions 671-672 and submit the form.

If more than one product is infused, copy and complete questions 670-672 for each product.
2900: Recipient Death

The Recipient Death Data (Form 2900) captures cause of death data fields for recipients on the Comprehensive Report Form follow-up track and the cellular therapy track. The leading cause of post-infusion mortality is persistent, recurrent, or relapsed primary disease. Other common causes of death include graft-versus-host disease, infection, and organ failure. As hematopoietic cell transplant and cellular therapies evolve, reporting accurate cause of death data is important to investigating the variables that are associated with post-infusion outcomes.

If “dead” is reported as the current survival status at the date of last contact on the Post-HCT Data (Form 2100) or the Cellular Therapy Essential Data Follow-Up (Form 4100) at the 100 day, six month and yearly time points, complete the Recipient Death Data (Form 2900) as soon as possible after the recipient has died.

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**Do not complete the Recipient Death Data (Form 2900) for:**
- **Recipients on the TED track.** Death data is reported on the Post-TED form. Review the Post-TED Manual section for additional instructions for completing cause of death data fields on the Post-TED forms.
- **Autologous recipients who did not consent to be a part of the research database.**

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**Lost to Follow-Up**

Occasionally, centers may lose contact with recipients for a variety of reasons, including the recipient’s moving, changing physicians, or death. After attempts to contact the recipient or referring physician have failed, the recipient may be declared lost to follow-up. If your center later receives documentation that a recipient is dead, report this on the appropriate follow-up form for the time period in which the recipient died. This may require contacting your CRC to open a form for completion. For example, a center may only become aware of the death after it has reported that the recipient is lost to follow-up. If a recipient dies a year and a half after transplant with no contact at your center, and a lost to follow-up form is reported for the two-year time point, your CRC should be contacted to make the two-year follow-up form due.

**Q1-4: Recipient Death Data**

**Cause of Death Codes**

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.
If you need to reference the historical Manual Change History for this form, you can reference the retired manual section on the [Retired Forms Manuals](#) webpage.

<table>
<thead>
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<th>Date</th>
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<th>Add/ Remove/ Modify</th>
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Q1-4: Recipient Death Data

Question 1: Date of Death:

Report the date the recipient died. Confirm that the date matches the last date of actual contact reported on the Form 2100 or Form 4100.

If the death occurred at an outside location and records of death are not available, the dictated date of death within a physician note may be reported. If the progress notes detailing the circumstances of death are available, request these records. These records are useful for completing required follow-up data fields on the Form 2100 or Form 4100 and the cause of death data fields on this form.

If the exact date of death is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 2: Was cause of death confirmed by autopsy?

Indicate if the cause of death was confirmed by autopsy.

- If “yes,” continue with question 3.
- If “autopsy pending,” continue with question 4. Report the cause of death as determined by a physician. A second Form 2900 will become due six months from the date of death to report any additional cause of death information found during autopsy. All pertinent causes of death should be reported on the second Form 2900.
- If “no,” continue with question 4.
- If “unknown,” continue with question 4.

Question 3: Is an autopsy report attached?

Indicate if a copy of the autopsy report is attached. Use the “Add Attachment” feature to attach a copy of the autopsy report in FormsNet. Attaching a copy of the report may prevent additional queries.

Questions 4-5: Primary cause of death:

Report the underlying cause of death. According to the Centers for Disease Control and Prevention, National Center for Health Statistics, the underlying cause of death is “the disease or injury that initiated the chain of events that led directly or inevitably to death.”

Report only one primary cause of death. Options which require additional specification include “Other”
infection”, “Other pulmonary syndrome”, “Multiple organ failure”, “Other organ failure”, “Other hemorrhage”, “Other vascular”, and “Other cause”. Information reported in the specify field (Question 5) must pertain to the option selected (e.g., an infectious cause of death should be specified for “Other infection”).

If the recipient has recurrent/persistent/progressive disease at the time of death, consider if the disease was the primary cause of death or a contributing cause of death. It should not be assumed that the presence of disease indicates that the disease was the primary cause of death.

If a cause of death has related questions on the follow up form, report the appropriate data in both locations. For example, if a primary cause of death was infection, complete the infection data fields on the follow up form.

If the primary cause of death is unclear, consult with a physician for their best medical opinion.

**Questions 6-7: Contributing cause of death:**

Report any additional causes of death. All contributing causes of death are important for analysis of transplant outcomes.

Options which require additional specification include “Other infection”, “Other pulmonary syndrome”, “Multiple organ failure”, “Other organ failure”, “Other hemorrhage”, “Other vascular”, and “Other cause”. Information reported in the specify field (Question 5) must pertain to the option selected (e.g., an infectious cause of death should be specified for “Other infection”).

If a cause of death has related questions on the follow up form, report the appropriate data in both locations. For example, if a contributing cause of death was acute graft-versus-host disease (GVHD), complete the acute GVHD data fields on the follow up form.

If there were multiple contributing causes of death, check all that apply.
Cause of Death Codes

Recurrence / persistence / progression of disease for which the HCT or cellular therapy was performed.

If the disease is present at death, but not the underlying cause of death, “Recurrence/persistence/progression of disease for which the HCT or cellular therapy was performed” should be reported as a contributing cause of death. For example, if a recipient’s disease had been stable for months and the recipient died by accidental means, this option should be used as a contributing cause of death (not the primary cause of death).

Acute versus Chronic GVHD

In the past, GVHD was classified as acute or chronic based on when it was diagnosed following transplant, as well as other clinical and histological (biopsy or post-mortem) features. Today, there is increased recognition that acute and chronic GVHD are not dependent upon the time since HCT, so determination of acute versus chronic should rest on clinical and histological features identified by the clinician.

Acute GVHD

If reported as a primary or contributing cause of death, acute GVHD should also be reported on the appropriate Post-HCT Data Form.

Chronic GVHD

If reported as a primary or contributing cause of death, chronic GVHD should also be reported on the appropriate Post-HCT Data Form.

Graft rejection or failure

The recipient had no hematopoietic recovery or had graft failure following initial hematopoietic recovery. If secondary graft failure is due to GVHD or infection, also report GVHD or infection as causes of death.

Cytokine release syndrome (CRS)

CRS occurs when there is a systemic inflammatory response as the result of immunotherapy (i.e. CAR T-cell therapy). In severe cases, it’s also known as “Cytokine storm.”

Infection

Report the etiology of the infection as Bacterial, Fungal, Viral, Protozoal, or Other infection, specify. If the
organism was not identified, but evidence of infection was present based on clinical opinion, select “Infection organism not identified.” Also report infections in the “Infection” section on the 2100 form.

Do not report interstitial pneumonitis (IPn) using this cause of death code. IPn is collected in the “pulmonary” section.

**Pulmonary**

_Idiopathic pneumonia syndrome (IPS)_ describes non-infectious lung injuries that occur early after HCT (within 100-120 days). Also report idiopathic pneumonia syndrome in the “Pulmonary Function” section on the 2100 form.

_Interstitial pneumonitis (IPn)_ can result from infection by cytomegalovirus, adenovirus, respiratory syncytial virus, influenza, or _Pneumocystis jirovecii_ (PCP). Interstitial pneumonitis resulting from cytomegalovirus should be reported using “pneumonitis due to cytomegalovirus.” Pneumonitis caused by other virii should be reported as “pneumonitis due to other virus.” Pneumonitis due to any other organism can be reported as “other pulmonary syndrome (excluding pulmonary hemorrhage)” and specifying IPn and the virus in question 5 or 7. Also report interstitial pneumonitis in the “Pulmonary Function” section on the appropriate Post-HCT Data Form.

_Diffuse alveolar damage (without hemorrhage)_ describes histological changes found in lung disease. It’s associated with acute respiratory distress syndrome (ARDS) and transfusion related acute lung injury (TRALI).

_Adult Respiratory Distress Syndrome (ARDS)_ , also called acute respiratory distress syndrome, has acute onset, infiltrative respiratory distress. It is considered to be adult respiratory distress syndrome, rather than IPS/IPn. Also report adult respiratory distress syndrome in the “Pulmonary Function” section on the appropriate Post-HCT Data Form.

_Organ failure (not due to GVHD or infection)._ If the recipient died with organ failure (not due to GVHD or infection), it should be reported as a cause of death. If the organ system that has failed is not specified, but present at death based on clinical opinion, use “Other organ failure” and specify the organ involved in question 5 or 7.

_Liver._ If a cause of death was liver failure, except for veno-occlusive disease/sinusoidal obstruction syndrome (use VOD/SOS) or GVHD (use Acute GVHD or Chronic GVHD). Liver abnormalities should also be reported in the “Liver Function” sections of the appropriate Post-HCT Data Form.

_Veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS)._ If a cause of death was VOD or
SOS. Pulmonary veno-occlusive disease should be reported using this cause of death code. Do not report other types of liver failure using this cause of death code. Liver VOD/SOS should also be reported in the “Liver Function” sections of the appropriate Post-HCT Data Form.

Cardiac. If a cause of death was cardiac failure. Congestive heart failure and myocardial infarctions should also be reported on the appropriate Post-HCT Data Form.

Pulmonary. If a cause of death was pulmonary failure from non-infectious causes such as bronchiolitis obliterans (BO) or cryptogenic organizing pneumonia (COP). BO and COP should also be reported in the “Pulmonary Function” section of the appropriate Post-HCT Data Form.

Do not report pulmonary hemorrhage using this cause of death code (use “Pulmonary hemorrhage”).

Central nervous system (CNS). If a cause of death was due to central nervous system failure. CNS failure may include radiation-induced atrophy, brain stem dysfunction, or encephalitis of unknown origin.

Do not report death due to brain infection (e.g., meningitis) using this cause of death code (use “Infection”).

Do not report hemorrhagic stroke using this cause of death code (use “Intracranial hemorrhage”).

Renal. If a cause of death was due to renal failure. Renal failure that was severe enough to warrant dialysis (or the recommendation of dialysis) should also be reported on the appropriate Post-HCT Data Form.

Gastrointestinal (GI) (not liver). If the cause of death was due to gastrointestinal failure (such as intestinal obstruction or perforation).

Do not report gastrointestinal hemorrhage using this cause of death code (use “Gastrointestinal hemorrhage”).

Do not report liver failure using this cause of death code (use “Liver failure (not VOD)”).

Do not report graft-versus-host disease (GVHD) using this cause of death code (use “Acute GVHD” or “Chronic GVHD”).

Multiple organ failure, specify. If the cause of death is due to failure of more than one organ, please provide additional detail. Each failed organ system should be reported in the “specify” field (question 5 or 7).

If multiple organ failure was due to sepsis, report the infection as a cause of death. The infectious organism should be also reported in the “Infection” section of the 2100 form.
Other organ failure, specify. If a cause of death was not due to a specific organ or organ system listed above. Specify the organ or organ system involved.

**Malignancy**

The recipient died with evidence of a new malignancy post-HCT. If the recipient develops a new malignancy after transplant, it should also be reported in the “New Malignancy” section of the appropriate Post-HCT Data Form.

If there was a history of malignancy prior to transplant (i.e., not the primary disease for which the recipient was transplanted) and the recipient died with evidence of recurrence, persistence, or progression of the previous malignancy, it should be reported by selecting "Prior malignancy (malignancy initially diagnosed prior to HCT or cellular therapy, other than the malignancy for which the HCT or cellular therapy was performed)."

**Hemorrhage.**

If the recipient died with evidence of hemorrhage, use the cause of death options to report its location. If the hemorrhage was in an organ system that does not have a cause of death option, use "Other hemorrhage, specify." and report the organ or location of the hemorrhage.

Pulmonary hemorrhages should also be reported in the “Pulmonary Function” sections on the appropriate Post-HCT Data Form.

Stroke should also be reported in the "Other Organ Impairment/Disorder" section on the appropriate Post-HCT Data Form.

Hemorrhagic cystitis should also be reported in the “Other Organ Impairment/Disorder” section on the appropriate Post-HCT Data Form.

**Vascular**

If the recipient died with evidence of vascular dysfunction, use the cause of death options to report the specific disorders. If the vascular disorder does not have a cause of death code, use “Other vascular, specify” and report the vascular abnormality.

**Other**

**Accidental Death.** The recipient’s death was caused by accidental or unintentional means.

**Suicide.** The recipient intentionally caused their own death.
In states where physician-assisted suicide is used to hasten death in terminally ill recipients, the cause of death should be reported as the underlying condition and suicide as a contributing cause of death.

Other cause, specify. If the recipient has a cause of death that is not captured using any of the above categories, please provide detailed information on the cause of death.
Comprehensive Disease-Specific Manuals

The sections below provide explanatory text for disease specific forms. For many disease inserts, subsections include disease response criteria which are linked to/from within the disease insert itself, or from other forms which reference the disease criteria (i.e., Pre-TED). Additional disease inserts are in development.

- 2010/2110: Acute Myelogenous Leukemia
- 2011/2111: Acute Lymphoblastic Leukemia
- 2012/2112: Chronic Myeloid Leukemia
- 2013/2113: Chronic Lymphocytic Leukemia
- 2014/2114: Myelodysplastic Syndrome/Myeloproliferative Neoplasms
- 2015/2115: Juvenile Myelomonocytic Leukemia
- 2016/2116: Plasma Cell Disorders
- 2019/2119: Waldenström’s Macroglobulinemia
- 2028/2128: Aplastic Anemia
- 2031/2131: Immune Deficiencies
- 2034/2134: X-Linked Lymphoproliferative Syndrome
- 2039/2139: Hemophagocytic Lymphohistiocytosis
2010/2110: Acute Myelogenous Leukemia (AML)

Acute Myelogenous Leukemia (AML) is a cancer of the white blood cells. It is characterized by the rapid proliferation of abnormal, immature myelocytes, known as myeloblasts, in the bone marrow. This accumulation of blasts in the marrow prevents the formation of healthy red blood cells, white blood cells, and/or platelets. Normal myeloblasts develop into neutrophils, basophils, and eosinophils, which are all white blood cells that fight infection. In AML, the leukemic myeloblasts do not fully develop and are unable to fight infection. The symptoms of AML result from a drop in red blood cell, platelet, and normal white blood cell counts caused by the replacement of normal bone marrow with leukemic cells.

Certain prognostic indicators are associated with poorer outcomes. These include advanced age (50+ years of age), AML arising from MDS or secondary/therapy-related AML, and certain genetic mutations that are described in greater detail later in this manual.

AML Response Criteria
2010: AML Pre-HCT
2110: AML Post-HCT
AML Response Criteria

Complete Remission (CR)

Hematologic complete remission is defined as meeting all of the following response criteria for at least four weeks.

- < 5% blasts in the bone marrow
- No blasts with Auer rods
- Normal maturation of all cellular components in the bone marrow
- No extramedullary disease (e.g., CNS, soft tissue disease)
- Neutrophils ≥ 1,000/µL
- Platelets ≥ 100,000/µL
- Transfusion independent

Alternative post-transplant CR criteria are accepted in the setting of pediatric AML when the center does not routinely perform bone marrow biopsies post-transplant and the patient was in CR pre-transplant. These criteria are not used for pre-transplant AML disease status. The criteria are as follows:

- Complete donor chimerism (≥ 95% donor chimerism without recipient cells detected)
- No extramedullary disease (e.g., CNS, soft tissue disease)
- Neutrophils ≥ 1,000/µL
- Platelets ≥ 100,000/µL
- Transfusion independent

In some cases, there may not be a four-week interval between completion of therapy and the pre-transplant disease assessment. In this case, CR should still be reported as the status at transplant since it represents the “best assessment” prior to HCT. This is an exception to the criteria that CR be durable beyond four weeks; the pre-transplant disease status should not be changed based on early relapse or disease assessment post-transplant.
Include recipients with persistent cytogenetic or molecular abnormalities who meet the above CR criteria for hematologic CR.

Include recipients meeting the above CR criteria regardless of how many courses of therapy were required to achieve CR.

The number of this complete remission can be determined by using the following guidelines:

- 1st CR: no prior relapse
- 2nd CR: one prior relapse
- 3rd or higher: two or more prior relapses

**Complete Remission with Incomplete Hematologic Recovery (CRi)**

Hematologic complete remission with incomplete hematologic recovery is defined as meeting all of the following response criteria for at least four weeks:

- < 5% blasts in the bone marrow
- No blasts with Auer rods
- Normal maturation of all cellular components in the bone marrow
- No extramedullary disease (e.g., CNS, soft tissue disease)
- Transfusion independent (Please note, if the physician documents transfusion dependence related to treatment and not the patient’s underlying AML, CRi can be reported)

**Primary Induction Failure (PIF)**

The patient received treatment for AML but never achieved CR or CRi at anytime. PIF is not limited by the number of unsuccessful treatments; this disease status only applies to recipients who have never been in CR or CRi.

**Relapse (REL)**

Relapse is defined as the recurrence of disease after CR, meeting one or more of the following criteria:

- ≥ 5% blasts in the marrow or peripheral blood
- Extramedullary disease
- Disease presence determined by a physician upon clinical assessment

The number of this relapse can be determined by using the following guidelines:
• 1st relapse: one prior CR
• 2nd relapse: two prior CRs
• 3rd or higher: three or more CRs

Do not include a partial response (PR) when determining number of relapse. Recipients who achieve a PR to treatment should be classified as either PIF or relapse; PR in AML is generally of short duration and is unlikely to predict clinical benefit.

**No Treatment**

The recipient was diagnosed with acute leukemia and never received therapeutic agents; include patients who have received only supportive therapy, including growth factors and/or blood transfusions.

**Manual Updates:**

Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

Reference the retired manual section on the [Retired Forms Manuals](#) webpage for the historical manual change history.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/1/18</td>
<td>AML Response Criteria</td>
<td>Add</td>
<td>Added (in red below) further instruction on reporting the CRi response criteria: <em>Transfusion independent (Please note, if the physician documents transfusion dependence related to treatment and not the patient’s underlying AML, CRi can be reported)</em></td>
</tr>
</tbody>
</table>
2010: AML Pre-Infusion

The Acute Myelogenous Leukemia Pre-Infusion Data Form (Form 2010) is one of the Comprehensive Report Forms. This form captures AML-specific pre-infusion data such as: the recipient's hematologic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HCT treatments administered and the best response to each line of therapy.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on Disease Classification Form (Form 2402), as Acute Myelogenous Leukemia (AML or ANLL). Additional disease insert forms will be required if the recipient had Myelodysplastic / Myeloproliferative Syndrome (MDS / MPS), Aplastic Anemia, Fanconi Anemia, or Juvenile Myelomonocytic Leukemia (JMML) prior to their diagnosis of Acute Myelogenous Leukemia. This form must also be completed if the recipient received a cellular therapy to treat AML as reported on the Pre-CTED Form (Form 4000).

Is this the report of a second or subsequent transplant or cellular therapy for the same disease? Report “no” and go to question 1 in any of the following scenarios:

- this is the first infusion reported to the CIBMTR;
- this is a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than AML); or
- this is a second or subsequent infusion for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior infusion, prior infusion was autologous with no consent, etc.).

If this is a report of a second or subsequent infusion for the same disease and this baseline AML disease insert was completed previously, report “yes” and go to question 69.

Links to Sections of Form
Q1-13: Disease Assessment at Diagnosis
Q14-31: Laboratory Studies at Diagnosis
Q32-68: Pre-HCT or Pre-Infusion Therapy
Q69-96: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional
information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please [click here](#) or reference the retired manual section on the [Retired Forms Manuals](#) webpage.

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<thead>
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</thead>
<tbody>
<tr>
<td>8/10/18</td>
<td>2010: AML Pre-Infusion</td>
<td>Add</td>
<td>Added the following instruction for questions 72 – 74: If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be reported on the form.</td>
</tr>
<tr>
<td>11/21/17</td>
<td>2010: AML Pre-Infusion Data</td>
<td>Modify</td>
<td>Corrected incorrect instruction provided for questions 6-9. The form asks for cytotoxic therapy; however, the manual incorrectly instructed centers to report any systemic therapies. <strong>Systemic Cytotoxic Therapy:</strong> chemotherapy, immunotherapy, or targeted therapies delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally.</td>
</tr>
</tbody>
</table>
Q1-13: Disease Assessment at Diagnosis

Question 1: Is the disease (AML) therapy related? (not MDS / MPN)

Agents such as radiation or systemic therapy used to treat other diseases (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, and breast cancer) can damage the marrow and lead to a secondary malignancy such as AML. If the diagnosis of AML is therapy-related, report “Yes” and go to question 2.

Report “No” and go to question 10 in any of the following scenarios:

- the diagnosis of AML was not therapy related; or
- AML was preceded by therapy-related MDS; or
- the recipient developed AML after an environmental exposure (e.g., exposure to benzene), check “no.”

If it is not known whether the diagnosis of AML was therapy-related, check “Unknown” and go to question 10.

Question 2-3: Specify prior disease

Indicate the disease for which the recipient received therapy prior to the diagnosis of therapy-related AML. If the patient’s prior disease is best classified as “Other disease (malignant or non-malignant),” specify in question 3.

Question 4-5: Date of diagnosis of prior disease

Report “Known” if the exact date or an estimated date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) has been documented. Enter the date the sample was collected for examination. Do not report the date symptoms first appeared. This date must be prior to the AML diagnosis date reported on the Disease Classification Form (Form 2402). If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

If the date is “Unknown,” continue with question 6.

Question 6-9: Specify therapy for prior disease

Indicate whether each type of therapy was given to treat the recipient’s prior disease. Report “Yes” for any therapies known to have been given to treat the disease reported in questions 2-3. Report “No” for any therapies which were not given to treat the disease reported in questions 2-3. Report “Unknown” if no information is available to determine whether the therapy was given to treat the disease reported in...
questions 2-3.

See below for descriptions of each type of therapy captured on the form. Do not report surgery or intrathecal chemotherapy in questions 6-9.

**Cytotoxic Therapy:** chemotherapy injected into a vein or given orally.

**Radiation:** high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. Radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes.

**Other Therapy:** cellular therapy, therapeutic vaccines, hormone therapy, or other treatments which would not be considered systemic or radiation therapy.

**Questions 10-11: Did the recipient have an antecedent hematologic disorder (preleukemia or myelodysplastic syndrome)?**

AML often evolves from MDS or MPN, but may also transform from other diseases including juvenile myelomonocytic leukemia (JMML), chronic myelomonocytic leukemia (CMMoL), and aplastic anemia. AML which transforms from MDS or MPN has a lower survival prognosis because of the association with unfavorable cytogenetic abnormalities. Only report antecedent disorders which were diagnosed prior to the diagnosis of AML. Do not report suspected or concurrent diagnoses of antecedent disorders in questions 10-13. See reporting Antecedent Disorder Reporting Scenarios below.

If AML transformed from an antecedent hematologic disorder, report “yes” and indicated the date of diagnosis in question 11. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. Also report the specific antecedent hematologic disorder in questions 12-13.

If the recipient did not have an antecedent hematologic disorder or it is not known, report “No” or “Unknown” respectively and go to question 14. Unknown should only be reported if there is no documentation available summarizing the recipient’s medical history.

**Antecedent Disorder Reporting Scenarios:**

**A.** Patient presents with fatigue; initial work-up reveals anemia. Subsequent bone marrow biopsy with specimen taken on May 14, 2015 shows MDS, refractory anemia with excess blasts at 7%, or RAEB-1. The patient chooses supportive therapy and their disease progresses to AML, which is shown in a bone marrow biopsy with 28% blasts on September 7, 2015 of the same year.

**AML Pre-Infusion Data Form:**
**Question 10:** Report “Yes” to confirm an antecedent hematologic disorder was diagnosed prior to the diagnosis of AML.

**Question 11:** Report 5/14/2015 as the date of diagnosis of the antecedent hematologic disorder.

**Questions 12-13:** Report RAEB-1 as the disorder identified.

**B.** Patient presents with severe fatigue and chronic upper respiratory infections; initial work-up reveals anemia. Subsequent bone marrow biopsy with specimen taken June 17 shows 26% blasts and myelodysplasia-related features; an aspirate sample was sent for cytogenetic testing, which reveals monosomy 7. The physician states this recipient has AML arising from MDS.

*AML Pre-Infusion Data Form:*

**Question 10:** Report “No.” This would be considered as concurrent diagnosis which should not be reported in questions 10-13. Only report antecedent hematologic disorders diagnosed prior to the diagnosis of AML.

**Question 12-13: What was the classification of the hematologic disorder at diagnosis?**

Indicate the classification of the antecedent hematologic disorder at diagnosis. Do not report any transformations or progressions of an antecedent hematologic disorder. See Antecedent Disorders Reporting Scenarios below for examples. For a list of MDS / MPN subtypes and their diagnostic criteria, see Appendix H, MDS / MPN Subtypes.

If the antecedent hematologic disorder is not listed as an option choice in question 12, report “Other hematologic disorder” and specify the disorder in question 13.

An additional pre-infusion disease insert must be completed if any of the following have been reported in questions 12-13:

- **MDS / MPN subtype:** complete the Myelodysplasia / Myeloproliferative Disorders Pre-HCT Data Form (Form 2014).
- **JMML:** complete the Juvenile Myelomoncytic Leukemia Pre-HCT Data Form (Form 2015).
- **Aplastic anemia:** Complete the Aplastic Anemia Pre-HCT Data Form (Form 2028).
- **Fanconi anemia:** Complete the Fanconi Anemia Pre-HCT Data Form (Form 2029).

Any additional required forms should appear automatically in FormsNet3SM after the AML Pre-Infusion Data Form (Form 2010) has been successfully submitted. If the appropriate forms do not appear, contact your assigned CRC (Clinical Research Coordinator).
Q14-31: Laboratory Studies at Diagnosis

All values reported in questions 14-31 must reflect testing performed prior to any treatment of AML. If testing was not performed near the time of diagnosis (within approximately 30 days) and prior to the initiation of treatment, the center should report “Unknown” for that value.

**Question 14-16: WBC**

Indicate whether the white blood count (WBC) in the peripheral blood is “Known” or “Unknown” at the time of diagnosis. If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the WBC at diagnosis is not known, report “Unknown” and go to question 17.

**Question 17-19: Blasts in blood**

Indicate whether the percent blasts in the peripheral blood is “Known” or “Unknown” at the time of diagnosis. This may be determined by an automated differential, a manual count, or flow cytometry. Testing by any of these methods may be reported in questions 17-19. If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the percent blasts in blood at diagnosis is not known, report “Unknown” and go to question 20.

**Question 20-22: Blasts in bone marrow**

Indicate whether the percent blasts in the bone marrow is “Known” or “Unknown” at the time of diagnosis. The percent blasts may be assessed by manual differential or flow cytometry. If available, report the manual differential performed on the bone marrow aspirate sample. If a manual differential was not performed on an aspirate sample, other methods / sample types may be reported (such as flow cytometry on an aspirate sample, or testing on a core biopsy) may be reported.

If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the percent blasts in bone marrow at diagnosis is not known, report “Unknown” and go to question 23.

**Question 23-31: Extramedullary disease**

Extramedullary disease refers to any confirmed site of AML other than the peripheral blood and bone...
marrow. Examples include detection of leukemic blasts in the cerebrospinal fluid and skin (leukemia cutis) as well as detection of soft tissue masses (myeloid sarcoma). If the recipient had extramedullary disease at the time of diagnosis, report “Yes” for question 23 and report all extramedullary sites of involvement in questions 24-31. If the recipient did not have any extramedullary disease at diagnosis, report “No” for question 23 and go to question 32. If extramedullary disease at diagnosis is not known, report “Unknown” and go to question 32.
Q32-68: Pre-HCT or Pre-Infusion Therapy

The FormsNet3℠ application allows questions 33-68 to be reported multiple times. Complete these questions for each line of therapy administered on or after the date of diagnosis of AML and prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given). When submitting the paper version of the form for more than one line of therapy, copy the “Pre-HCT or Pre-Infusion Therapy” section and complete a copy of the section for each line of therapy administered.

A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.). If a recipient’s disease status changes resulting in a change to treatment, a new line of therapy should be reported. Additionally, if therapy is changed because a favorable disease response was not achieved, a new line of therapy should be reported.

Question 32: Was therapy given?

Indicate if the recipient received treatment for their primary disease between diagnosis and the start of the preparative regimen. This includes systemic chemotherapy, intrathecal therapy, radiation therapy, and cellular therapies. Do not report a prior HCT or any surgery in questions 32-68. If therapy was given to treat AML during the time frame indicated above, report “Yes” and go to question 33. If reporting “No” or “Unknown,” go to question 69.

Question 33: Purpose of therapy

The purpose of each line of therapy depends on the disease status at the time of administration. See below for general definitions of each option choice. Indicate the purpose of the line of therapy being reported and go to question 34.

**Induction:** The first line(s) of therapy given following diagnosis to achieve a complete remission (CR). If the first line of therapy (induction) fails to produce a CR, the recipient may undergo another cycle or a different line of therapy (re-induction) in order to achieve their first CR. Report “Induction” as the purpose for all lines of therapy given to achieve the first CR.

**Consolidation:** Once a recipient has achieved a hematologic CR (1st, 2nd, 3rd or greater), they may receive several additional lines of therapy as part of a protocol or to eliminate known minimal residual disease. In either case, report “Consolidation” as the purpose for these lines of therapy.

**Maintenance:** Following induction and consolidation, a recipient may receive low dose chemotherapy over an extended period of time to maintain a CR. Maintenance therapy is usually given as a single drug
taken in the outpatient setting when the recipient has no known evidence of disease. Report “Maintenance” as the purpose for these lines of therapy.

**Treatment for disease relapse:** Once the recipient has achieved their first CR, their disease may relapse and require further treatment to produce another CR (2nd or greater). The intent is the same as induction, but setting is different as the recipient has already achieved at least one prior CR. Report “Treatment for disease relapse” as the purpose for all lines of therapy given to induce a CR following relapse.

**Question 34: Intrathecal Therapy**

Intrathecal therapy refers to chemotherapy administered via lumbar puncture to treat or prevent leukemic blasts in the central nervous system. Report “Yes” if intrathecal therapy was given as part of the line of therapy being reported. Report “No” if intrathecal therapy was not given as part of the line of therapy being reported.

**Question 35: Systemic therapy**

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein / central line or given orally. Do not report intrathecal therapy as systemic therapy. If systemic therapy was administered as part of the line of therapy being reported, report “Yes” and continue with question 36. If not, report “No” and go to question 47.

**Question 36-37: Date therapy started**

Indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 37. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If the date therapy started is “Unknown,” go to question 38.

**Question 38-39: Date therapy stopped**

Indicate if therapy stop date is “Known” or “Unknown.” If the therapy is being given in cycles, report the date the recipient started the last cycle for this line of therapy in question 39. Otherwise, report the final administration date for the therapy being reported. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If the date therapy stopped is “Unknown,” go to question 40.
Question 40-41: Number of cycles

Systemic therapy is usually administered in cycles with rest periods in-between. This enables cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from the damage sustained during therapy. A cycle can last one or more days and can repeat weekly, bi-weekly, or monthly. A single systemic therapy course may consist of multiple cycles.

Indicate whether the number of cycles is “Known” or “Unknown.” If “Known,” enter the number of cycles the recipient received in question 41. If “Unknown,” go to question 42.

If therapy is not being administered in cycles (e.g., daily chemotherapy), report “Not Applicable” for question 40 and go to question 42.

Question 42: Specify therapy given

Treatments vary based on protocol. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. Select all chemotherapy drugs administered as part of the line of therapy being reported. If the recipient received a systemic therapy which is not listed, select “Other systemic therapy” and specify the treatment in question 46. Report the generic name of the agent, not the name brand.

Question 43-45: Specify months of therapy

Azacytidine, decitabine, and sorafenib may be given daily rather than in cycles. In order to capture the duration for which these medications are given, centers are asked to report the number of months these drugs were given whenever they have been reported in question 42. Question 43 will only be answered if azacytidine has been reported. Question 44 will only be answered if decitabine has been reported. Question 45 will only be answered if sorafenib has been reported. If more than one of these drugs was reported as part of a single line of therapy, ensure questions 43-45 are completed for the correct drug.

Question 46: Specify other systemic therapy

If “Other systemic therapy” has been selected in question 42, question 46 must be answered. Complete question 46 by reporting any / all chemotherapy drugs which were given as part of the line of therapy being reported and have not been selected in question 42.

Question 47: Radiation therapy

Radiation therapy utilizes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. Radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes. Radiation therapy may be given in conjunction with systemic chemotherapy or as a separate line of therapy.
If radiation therapy was given during or adjacent to administration of systemic therapy, report them together as single line of therapy on the form (i.e., one copy of questions 33-68). Otherwise, capture the radiation treatment as a separate line of therapy.

If the recipient received radiation therapy as part of the line of therapy being reported, report “Yes” and go to question 48. If not, report “No” and go to question 55.

**Question 48-49: Date therapy started**

Indicate whether the start date for radiation therapy is “Known” or “Unknown.” If “Known,” enter the date radiation therapy began in question 49. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

**Question 50-51: Date therapy stopped**

Indicate if the stop date for radiation therapy is “Known” or “Unknown.” If “Known,” enter the final date radiation was administered in question 50. If the stop date is partially known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 52-54: Specify site(s) of radiation therapy**

Report all sites of radiation therapy administered between the start and stop dates reported in questions 48-51. If “Yes” is reported for “Other site,” specify all other sites in question 54.

**Question 55: Cellular Therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “Yes” if the recipient received cellular therapy as part of the line of therapy being reported. If not, report “No.”

**Question 56: Best response to line of therapy**

Indicate the best response to the line of therapy using the international working group criteria provided in AML Response Criteria section of the Forms Instructions Manual. The best response is determined by a disease assessment, such as hematologic testing, pathology study, and / or physician assessment.
**Question 57: Date assessed**

Report the date the best response to the line of therapy was established. This should be the earliest date all international working group criteria were met for the response reported in question 56. Enter the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically evaluated the recipient's response.

If the best response was achieved prior to starting the line of therapy being reported, indicate the date of the first assessment which was performed after initiating the current line of therapy and confirms the sustained response.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 58: Was the recipient MRD negative following this line of therapy?**

Minimal residual disease (MRD) can be assessed by different methods including, but not limited to, the following:

- Next generation sequencing
- Sanger sequencing
- Polymerase chain reaction (PCR) testing
- Chromosomal / genomic microarray analysis
- Fluorescence in situ hybridization (FISH)
- Karyotyping
- Flow cytometry

If any MRD testing was performed following the line of therapy being reported, answer question 58 based on the results of the testing performed within 30 days after the date therapy was stopped and prior to any new therapy being initiated. If any MRD testing during this timeframe was positive for markers of AML, report “No” for question 58. If all MRD testing during this timeframe was negative for markers of AML, report “Yes” for question 58. If no MRD testing was performed during this timeframe, leave question 58 blank and override the error in FormsNetSM using the code “Unknown.”

**Question 59: Did the recipient relapse following this line of therapy?**

Refer to the international working group criteria provided in AML Response Criteria section of the Forms Instructions Manual for more information on how to determine recurrence of disease. Report “Yes” if the
recipient met the criteria for relapse after starting this line of therapy and prior to starting a subsequent line of therapy. If “Yes” is reported, also completed questions 60-68.

Report “No” if the recipient never relapsed following this line of therapy. Also, report “No” if the recipient relapsed after beginning a subsequent line of therapy. This episode of relapse will be captured in the instance (i.e., copy) of questions 33-68 completed for the subsequent line of therapy. If “No” is reported, go to question 69.

If this is the last line of therapy administered prior to infusion, only report “Yes” if relapse occurred prior to infusion. Relapse occurring after the infusion date will be reported on the AML Post-Infusion Data Form (Form 2110).

**Question 60: Date of relapse**

Enter the assessment date relapse was established following initiation of this line of therapy. Report the date of the pathologic evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathologic and laboratory evaluations. If extranodal disease is detected upon radiographic examination (e.g., X-rays, CT scans, MRI scans, PET scans), enter the date the imaging took place. If the physician determines evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 61-68: Sites of Relapse**

Report all known sites of active disease at the time of relapse in questions 61-68. This includes any sites identified between the date of relapse reported in question 60 and the time treatment for relapse is initiated. If “Yes” has been reported for “Other site” in question 67, use question 68 to specify all sites of active disease not already reported in questions 61-66.
Q69-96: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

All values reported in questions 69-96 must reflect the most recent testing prior to the start of the preparative regimen (or infusion if not preparative regimen was given). Do not report testing performed during a line of therapy reported in questions 33-68. If testing was not performed near the start of the start of the preparative regimen / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable), the center should report “Unknown” for that value.

Questions 69-71: WBC

Indicate whether the white blood count (WBC) in the peripheral blood is “Known” or “Unknown” at the last evaluation prior to the start of the preparative regimen / infusion. If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the WBC at the last evaluation prior to the start of the preparative regimen / infusion is not known, report “Unknown” and go to question 72.

Questions 72-74: Blasts in blood

If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be reported on the form.

Indicate whether the percent blasts in the peripheral blood is “Known” or “Unknown” at the last evaluation prior to the start of the preparative regimen / infusion. This may be determined by an automated differential, a manual count, or flow cytometry. Testing by any of these methods may be reported in questions 72-74. If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the percent blasts in blood at the last evaluation prior to the start of the preparative regimen / infusion is not known, report “Unknown” and go to question 75.

Questions 75-77: Blasts in bone marrow

Indicate whether the percent blasts in the bone marrow is “Known” or “Unknown” at the last evaluation prior
to the start of the preparative regimen / infusion. The percent blast may be assessed by manual differential or flow cytometry. If available, report the manual differential performed on the bone marrow aspirate sample. If a manual differential was not performed on an aspirate sample, other methods / sample types may be reported (such as flow cytometry on an aspirate sample, or testing on a core biopsy) may be reported.

If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the percent blasts in bone marrow at the last evaluation prior to the start of the preparative regimen / infusion is not known, report “Unknown” and go to question 79.

Questions 78: Specify method of assessment

The percent blasts in the bone marrow may be assessed by a manual differential (morphology) or flow cytometry. Report the method used to determine the value reported in question 76.

Question 79: Was flow cytometry performed?

Indicate whether flow cytometry (immunophenotyping) was performed on the blood and / or bone marrow at the last evaluation prior to the start of the preparative regimen / infusion. If “Yes,” go to question 80. If “No” or “Unknown,” go to question 88.

Question 80-83: Flow cytometry testing on blood

Indicate whether flow cytometry was performed on the blood at the last evaluation prior to the start of the preparative regimen / infusion. If “Yes,” report the date the sample was collected and whether disease was detected in questions 81 and 82 respectively. If disease was detected, report the percent disease detected (i.e., percent leukemic blasts) in question 83. Otherwise, go to question 84.

If flow cytometry was not performed on the blood at the last evaluation prior to the start of the preparative regimen / infusion, report “No” for question 80 and go to question 84.

Question 84-87: Flow cytometry testing on bone marrow

Indicate whether flow cytometry was performed on the bone marrow at the last evaluation prior to the start of the preparative regimen / infusion. If “Yes,” report the date the sample was collected and whether disease was detected in questions 85 and 86 respectively. If disease was detected, report the percent disease detected (i.e., percent leukemic blasts) in question 87. Otherwise, go to question 88.

If flow cytometry was not performed on the bone marrow at the last evaluation prior to the start of the preparative regimen / infusion, report “No” for question 84 and go to question 88.
Questions 88-96: Was extramedullary disease present?

Refer to the instructions for questions 23-31 for a description of extramedullary disease. If the recipient had extramedullary disease at the last evaluation prior to the start of the preparative regimen / infusion, report “Yes” for question 88 and report all extramedullary sites of involvement in questions 89-96. If the recipient did not have any extramedullary disease at this time point or it is not known whether extramedullary disease is present, report “No” or “Unknown” respectively for question 88 and submit the form.
2110: AML Post-Infusion

The Acute Myelogenous Leukemia Post-Infusion Data Form (Form 2110) is one of the Comprehensive Report Forms. This form captures AML-specific post-infusion data such as: the recipient's best response to HCT or cellular therapy, cytogenetic and molecular findings at the time of best response, post-infusion therapy for AML, assessment and treatment of relapse, and current disease assessments.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on Disease Classification Form (Form 2402), as Acute Myelogenous Leukemia (AML or ANLL). This form must also be completed if the recipient received a cellular therapy to treat AML as reported on the Pre-CTED Form (Form 4000).

Links to Sections of Form
Q1-40: Disease Assessment at the Time of Best Response to HCT or Cellular Therapy
Q41-50: Post-HCT / Post-Infusion Therapy
Q51-103: Disease Detection Since the Date of Last Report
Q104-144: Disease Status at the Time of Evaluation for This Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/19/18</td>
<td>Comprehensive Disease Specific Manuals</td>
<td>Add</td>
<td>Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119). The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.</td>
</tr>
<tr>
<td>2/22/</td>
<td>2110: AML Post-Infusion</td>
<td>Modify</td>
<td>Added (in red) and removed (struck out) text from instructions for questions 51-52.</td>
</tr>
<tr>
<td>Date</td>
<td>Data Section</td>
<td>Action</td>
<td>Notes</td>
</tr>
<tr>
<td>------------</td>
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<td>------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>18</td>
<td>Data</td>
<td></td>
<td>If any testing for molecular markers occurred and detected the recipient’s primary disease during the reporting period, report “Yes” for question 51 and report the date the sample was collected in question 52. If molecular marker testing did not detect disease at any time during the reporting period, report “No” for question 51 and go to question 63. If molecular marker testing was not performed during the reporting period, report “No Unknown” go to question 63.</td>
</tr>
<tr>
<td>2/22/18</td>
<td>2110: AML Post-Infusion Data</td>
<td>Modify</td>
<td>Added (in red) and removed (struck out) text from the beginning of section Q51-103: Disease Detection Since Date of Last Report. If testing by a particular method for molecular or cytogenetic markers / abnormalities was not done during the reporting period or it is not known whether testing was performed, report “Unknown” for that method those methods (question 51 and 70). If testing by flow cytometry, clinical / hematologic assessment, or other assessment was not done during the reporting period or it is not known whether testing was performed, report “No” for those methods (questions 63, 80, and 87).</td>
</tr>
<tr>
<td>2/22/18</td>
<td>2110: AML Post-Infusion Data</td>
<td>Add</td>
<td>Added text (in red) to the Questions 51-103 warning box. For questions 51, 63, 70, 80, and 87, report “No” or “Unknown” (see instructions below) if the recipient did not relapse, have persistent or minimal residual disease even if testing was performed.</td>
</tr>
</tbody>
</table>
Q1-40: Disease Assessment at the Time of Best Response to HCT or Cellular Therapy

Question 1: What was the best response to HCT or cellular therapy since the date of the last report? (Include response to any therapy given for post-HCT / post-infusion maintenance or consolidation, but exclude any therapy given for relapsed, persistent or progressive disease.)

The intent of this question is to determine the best overall response to HCT or cellular therapy. This is assessed in each reporting period. For any recipients in complete remission (CR) or complete remission with incomplete hematologic recovery (CRi) at the time of infusion, report “Continued Complete Remission” for question 1 and go to question 41.

When evaluating the best response, determine the disease status within the reporting period using the international working group criteria provided in the in AML Response Criteria section of the Forms Instructions Manual. Compare this response to all previous post-infusion reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status. See question 2 to indicate that this disease status was previously reported.

Include response to any post-infusion treatment planned as of Day 0. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR or as preemptive therapy for recipients with minimal residual disease, consider this “planned therapy,” even if this was not documented prior to the transplant. Do not include response any treatment for relapse, progression, or persistent disease. If a recipient started treatment for relapse, progression, or persistent disease, report the best response prior to the initiation of treatment (even if this was confirmed in a prior reporting period).

Best Response to HCT Reporting Scenarios:

A. A recipient in complete remission at the time of infusion has a disease relapse detected on their first bone marrow biopsy post-HCT. They do not achieve a sustained recovery of their absolute neutrophil count by day 100.

100 Day Follow-Up Form:

Question 1: Report “Continued complete remission.” This option should be used for all recipients in CR at the time of infusion regardless of post-infusion disease assessments.

B. A recipient in primary induction failure at the time of infusion achieves a CRi on 6/1/2016. Their platelets are persistently low through their day 100 contact date (6/15/2016); however, they do rise /
remain above $100 \times 10^9$/L beginning 6/30/2016 at which time the recipient’s disease status was CR.

100 Day Follow-Up Form:

**Question 1:** Report “Complete Remission.” Use this option to indicate CR or CRi was achieved post-infusion for recipients not in CR / CRi at the time of infusion.

**Question 2:** Report “No.” The date of best response has not been previously reported. Never report “Yes” for question 2 on the day 100 follow-up form.

**Question 3:** Report 6/1/2016 as indicated in the report scenario.

Six Month Follow-Up Form:

**Question 1:** Report “Complete Remission.” Use this option to indicate CR or CRi was achieved post-infusion for recipients not in CR / CRi at the time of infusion.

**Question 2:** Report “Yes.” The date of best response was previously reported on the 100 day follow-up form.

**Question 3:** Leave blank. This question will not be answered when question 2 has been answered “Yes.”

C. A recipient in primary induction failure at the time of infusion achieves a CR during the 100 day reporting period on 5/1/2014. The recipient has a disease relapse during the 6 month reporting period and their disease status remains “Relapse” on the 6 month date of contact despite multiple treatments.

100 Day Follow-Up Form:

**Question 1:** Report “Complete Remission.” Use this option to indicate CR or CRi was achieved post-infusion for recipients not in CR / CRi at the time of infusion.

**Question 2:** Report “No.” The date of best response has not been previously reported. Never report “Yes” for question 2 on the day 100 follow-up form.

**Question 3:** Report 5/1/2014 as indicated in the report scenario.

Six Month Follow-Up Form:

**Question 1:** Report “Complete Remission.” Use this option to indicate CR or CRi was achieved post-infusion for recipients not in CR / CRi at the time of infusion.

**Question 2:** Report “Yes.” The date of best response was previously reported on the 100 day follow-up form.

**Question 3:** Leave blank. This question will not be answered when question 2 has been answered “Yes.”

Note, once a CR / CRi is achieved post-infusion, the best response will always be reported as CR for question 1. Changes to disease status after CR / CRi is achieved are not reported in question 1.

**Question 2: Was the date of best response previously reported?**

If the best response to HCT / cellular therapy was first documented during the current reporting period,
report “no” and go to question 3. If the best response was achieved during a previous reporting period (and therefore reported on a previous AML Post-Infusion Data Form), report “Yes” and go to question 41.

Do not report “Yes” if completing this form for the 100 day reporting period.

**Question 3: Date assessed**

Report the date the best response to HCT / cellular therapy was established. This should be the earliest date when all international working group criteria for the response reported in question 1 were met. Report the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessments were performed to establish the best response, report the office visit in which the physician clinically evaluated the response.

If the exact date is not known, use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](#).

**Disease Assessments at Time of Best Response**

For reporting purposes, the definition of “at the time of best response” depends on the reporting period. See Disease Assessment Time Windows below. Only consider assessments with samples collected within the time window which corresponds to the follow-up form being completed. If assessments were performed during the reporting period, but the samples were not collected within the indicated time window, consider them “Not done” when completing questions 4-40.

**Table 1. Disease Assessment Time Windows**

<table>
<thead>
<tr>
<th>Follow-Up Form</th>
<th>Approximate Time Window</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 Day</td>
<td>+ / – 15 days of date of best response (Question 3)</td>
</tr>
<tr>
<td>6 Month</td>
<td>+ / – 15 days of date of best response (Question 3)</td>
</tr>
<tr>
<td>Annual</td>
<td>+ / – 30 days of date of best response (Question 3)</td>
</tr>
</tbody>
</table>

**Question 4: Were tests for molecular markers performed (e.g. PCR, NGS)?**

**Negative Disease Assessments**

Prior versions of the AML Post-Infusion Data Form have only permitted reporting of testing for molecular abnormalities known to be associated with the recipient’s AML (i.e., only report testing that has been positive least once between diagnosis and the date of the assessment being reported). The wording of this question has been updated to include any
Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient’s primary disease. Testing for these sequences is often performed using PCR based methods; however, lower sensitivity testing, including FISH, may also be used to detect molecular markers. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include chromosomal microarray / chromosomal genomic array, Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

If testing for molecular markers was performed at the time of best response (see Table 1), report “Yes” and go to question 5.

If molecular marker testing was not performed at the time of best response or it is unknown if testing was done, report “No” or “Unknown” respectively and go to question 15.

**Question 5-14: Specify results**

For each molecular marker in questions 5-14, report whether testing was “Positive,” “Negative,” or “Not done.” If tests identified a molecular marker other than those listed in questions 5-12, report the result in question 13 and specify the marker in question 14.

If multiple “Other molecular marker[s]” were tested at the time of best response, report one instance (i.e., copy) of question 13-14 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” were tested, do the following:

- report one instance of question 13-14; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 14; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”

If CEBPA is reported as “Positive” (question 5) question 6 must be completed. If the lab report does not specify whether the detected marker was biallelic / homozygous or monoallelic / heterozygous, confirm with
the laboratory whether this information can be determined prior to reporting “Unknown.”

**Question 15: Was the disease status assessed via flow cytometry?**

Flow cytometry (immunophenotyping) is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be detected on cellular material. Only testing performed on the blood or bone marrow may be reported in questions 15-23.

If flow cytometry was performed at the time of best response (see Table 1), report “Yes” and go to question 16.

If flow cytometry was not performed at the time of best response, report “no” and go to question 24.

**Question 16-19: Flow cytometry testing on blood**

Indicate whether flow cytometry was performed on peripheral blood at the time of best response (refer to Table 1). If “Yes,” report the date the sample was collected and whether disease was detected in questions 17 and 18 respectively. If disease was detected, report the percent disease detected (i.e., percent leukemic blasts) in question 19. Otherwise, go to question 20.

If flow cytometry was not performed on the blood at the time of best response, report “No” for question 16 and go to question 20.

**Question 20-23: Flow cytometry testing on bone marrow**

Indicate whether flow cytometry was performed on bone marrow at the time of best response. If “Yes,” report the date the sample was collected and whether disease was detected in questions 21 and 22 respectively. If disease was detected, report the percent disease detected (i.e., percent leukemic blasts) in question 23. Otherwise, go to question 24.

If flow cytometry was not performed on the bone marrow at the time of best response, report “No” for question 20 and go to question 24.

**Question 24: Were cytogenetics tested (karyotyping or FISH)?**

*Negative Disease Assessments*

Prior versions of the AML Post-Infusion Data Form have only permitted reporting of cytogenetic testing if it has been positive least once between diagnosis and the date of the assessment being reported. The wording of this question has been updated to include any cytogenetic testing regardless of previous or current test results. When completing questions 24-34, consider all cytogenetic testing performed at the time of best response.
Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality which reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C, Cytogenetic Assessments.

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

FISH is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA. These probes are mixed with cells from the recipient’s blood or bone marrow. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells. Additionally, the FISH probe panel should reflect the patient’s current disease; FISH may be used as surveillance for changes associated with post-therapy malignancy.

FISH testing for sex chromosomes after sex-mismatched allogeneic HCT should not be considered a disease assessment as the purpose is to determine donor chimerism. Additionally, the FISH probe panel should reflect the patient’s current disease; FISH may be used as surveillance for changes associated with post-therapy malignancy.

If cytogenetic (karyotyping or FISH) studies were obtained at the time of best response (see Table 1) report “Yes” and go to question 24.

If cytogenetic studies were attempted at the time of best response, but there were not adequate cells (metaphases), report “No,” and go to question 36.

If no cytogenetic studies were obtained at the time of best response, indicate “No” and go to question 36.

If it is not known whether any cytogenetic studies were obtained at the time of best response, indicate “Unknown” and go to question 36.

**Question 25-26: Were cytogenetics tested via FISH?**

If FISH studies were performed at the time of best response (see Table 1), report “Yes” for question 25 and
indicate whether clonal abnormalities were detected in question 26. If FISH studies were not performed, report “No” for question 25 and go to question 30. Examples of this include: no FISH study performed or FISH sample was inadequate.

**Question 27-29: Specify cytogenetic abnormalities (FISH)**

Report the number of abnormalities detected by FISH at the time of best response in question 27. After indicating the number of abnormalities in question 27, select all abnormalities detected in questions 28-29.

If a clonal abnormality is detected, but not listed as an option in question 28, select “Other abnormality” and specify the abnormality in question 29. If multiple “Other abnormalities” were detected, report “see attachment” in question 29 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 30-31: Were cytogenetics tested via karyotyping?**

If karyotyping was performed at the time of best response (see Table 1), report “Yes” for question 30 and indicate whether clonal abnormalities were detected in question 31. If karyotyping was not performed, indicate “No” and go to question 35. Examples of this include: karyotyping was not performed or karyotyping sample was inadequate.

**Question 32-34: Specify cytogenetic abnormalities (karyotyping)**

Report the number of abnormalities detected by karyotyping at the time of best response in question 32. After indicating the number of abnormalities in question 32, select all abnormalities detected in questions 33-34.

If a clonal abnormality is detected, but not listed as an option in question 33, select “Other abnormality” and specify the abnormality in question 34. If multiple “Other abnormalities” were detected, report “see attachment” in question 34 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 35: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 24-34. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 36-40: Was the disease status assessed by other assessment?**

Indicate whether AML was assessed by any method other than those included in questions 4-35 at the time
of best response (see Table 1). If “Yes,” report the date assessed and specify the type of assessment in questions 37 and 38 respectively. Also indicate whether the reported assessment detected disease (question 38) and, if so, whether this was considered a disease relapse (question 40). If the exact date of assessment is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. If AML was not assessed by any methods other than those included in questions 4-35, report “No” for question 36 and go to question 41.
Q41-50: Post-HCT / Post-Infusion Therapy

Question 41: Was therapy given since the date of last report for reasons other than relapse or persistent disease?

Indicate if the recipient received treatment post-infusion for reasons other than relapse or persistent disease during the current reporting period. Recipients generally receive a HCT / cellular therapy under a specific protocol which defines radiation and / or systemic therapy to be given prior to infusion; prophylactic medications to be administered pre- and / or post-infusion; as well as any systemic therapy, radiation, and / or other treatments to be administered post-infusion as planned (or maintenance) therapy. Planned (maintenance) therapy is given to assist in prolonging a remission. Planned therapy may be described in a research protocol or standard of care protocol. Refer to these documents (if available) when completing this section. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR, report the therapy in questions 41-50. Do not include any treatment administered as a result of relapse or persistent disease (including treatment for minimal residual disease).

If therapy was given for reasons other than relapse or persistent disease during the reporting period, report “Yes” and go to question 42. If “No” or “Unknown,” go to question 51.

Question 42: Central nervous system irradiation

Radiation therapy includes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. Radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes. If the recipient received radiation targeting part or all of the central nervous system (excluding total body irradiation) during the reporting period for reasons other than relapse or persistent disease, report “Yes." If not, report “No.”

Question 43: Systemic therapy

**Intrathecal Therapy**

Intrathecal therapy given for reasons other than minimal residual disease, persistent disease, or relapse must be reported as “Systemic therapy” in questions 43-47. Specifically, if a recipient receives intrathecal therapy during the reporting period for reasons other than minimal residual disease, persistent disease, or relapse, answer question 43 “Yes” and select “Intrathecal therapy” under question 46.

Systemic therapy includes chemotherapy, immunotherapy, or targeted therapies delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally. Do not
report total body irradiation or subsequent HCT / cellular therapies in questions 43-47. If the recipient received systemic therapy during the reporting period for reasons other than relapse or persistent disease, report “Yes” and go to question 44. If not, report “No” and go to question 48.

**Question 44-45: Date therapy (maintenance) was first started post-HCT / post-infusion**

*Form Revision Change*

If maintenance therapy was started during a prior reporting period, for which, an AML Post-HCT Data Form Revision 3 was completed, the start date will not have been reported on that form. In this case, report the date maintenance therapy was started on the current form (AML Post-Infusion Data Form, Revision 4) and override the validation error using the code “Verified Correct.” If the reported maintenance therapy continues into the next reporting period, the site will indicate “Previously reported” in question 44.

If the recipient **started** systemic therapy for reasons other than relapse or persistent disease during the reporting period, report “Known” for question 44 and indicate the date started in question 45. If the exact date is not known, use the process for reporting partial or unknown dates as described in the [General Instructions, Guidelines for Completing Forms](#).

If the recipient started therapy for reasons other than relapse or persistent disease in a prior reporting period and continued the therapy into the current reporting period, report “Previously reported” and go to question 46.

For recipients who start and stop therapy multiple times post-infusion, first determine whether the recipient stopped therapy for at least 30 days. If not, consider the therapy continuous. Only report a new therapy start date if all three of the below conditions are met.

1. The recipient stopped all therapy given for reasons other than relapse or persistent disease during a prior reporting period; and
2. The recipient restarted therapy for reasons other than relapse or persistent disease during the current reporting period; and
3. Therapy was restarted at least 30 days after the therapy stop date.

**Question 46-47: Specify systemic therapy given**

Select all systemic therapy (see question 43 for definition) given for reasons other than relapse or persistent disease during the reporting period. If a therapy is given, but not listed as an option in question 46, select “Other systemic therapy” and specify the drug in question 47.
**Question 48: Cellular therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells). Do not report a HCT as a cellular therapy in question 48.

Report “Yes” if the recipient received cellular therapy for reasons other than relapse or persistent disease during the reporting period. If not, report “No.”

**Question 49-50: Other therapy**

Indicate if the recipient received any other therapy (not already reported in questions 42-48) given for reasons other than relapse or persistent disease during the reporting period. Do not report HCT in questions 49-50. If “Yes,” specify all other therapies given in question 50. If “No,” go to question 51.
Questions 51-103: Disease Detection Since Date of Last Report

This section is intended to capture information only on recipients who relapse, have persistent or minimal residual disease in this reporting period. For questions 51, 63, 70, 80, and 87, report “No” or “Unknown” (see instructions below) if the recipient did not relapse, have persistent or minimal residual disease even if testing was performed. These results will be reported in questions 104-142.

Questions 51-88 are intended to capture the earliest instance of disease detection by each method of assessment performed during the reporting period. For each method of assessment, report “Yes” if that method detected the recipient’s AML (or markers of AML) during the reporting period. If testing by a particular method (e.g., molecular makers, cytogenetic, flow cytometry, etc.) was done, but did not shown evidence of disease during the reporting period, report “No” for that method. If testing for molecular or cytogenetic markers / abnormalities was not done during the reporting period or it is not known whether testing was performed, report “Unknown” for those methods (question 51 and 70). If testing by flow cytometry, clinical / hematologic assessment, or other assessment was not done during the reporting period or it is not known whether testing was performed, report “No” for those methods (questions 63, 80, and 87).

If multiple tests by a particular method have demonstrated evidence of disease during the reporting period, report the date / result of the earliest positive assessment(s) performed during the reporting period.

Question 51-52: Were tests for molecular markers performed (e.g. PCR, NGS)?

See question 4 for a description of molecular testing. If any testing for molecular markers detected the recipient’s primary disease during the reporting period, report “Yes” for question 51 and report the date the sample was collected in question 52. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If molecular marker testing did not detect disease at any time during the reporting period, report “No” for question 51 and go to question 63.

If molecular marker testing was not performed during the reporting period, report “Unknown” go to question 63. If it is not known whether testing for molecular markers was performed during the reporting period, or the test results are not known, report “Unknown” and go to question 63.
**Question 52-61: Specify results**

For each molecular marker in questions 53-62, report whether testing was “Positive,” “Negative,” or “Not done.” If tests identified a molecular marker other than those listed in questions 53-60, report the result in question 61 and specify the marker in question 62. If multiple “Other molecular markers” were tested at the time of best response, report one instance (i.e., copy) of question 61-62 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” are tested, do the following:

- report one instance of question 61-62; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 62; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”

If CEBPA is reported as “Positive” (question 53) question 54 must be completed. If the lab report does not specify whether the detected marker was biallelic / homozygous or monoallelic / heterozygous, confirm with the laboratory whether this information can be determined prior to reporting “Unknown.”

**Question 63: Was the disease detected via flow cytometry?**

See question 15 for a description of flow cytometry. If flow cytometry detected the recipient’s primary disease at any time during the reporting period, report “Yes” and go to question 64. Report “No” and go to question 70 in either of the following cases:

- all flow cytometry assessments performed on the blood and marrow were negative for evidence of the recipient’s primary disease during the current reporting period; or
- flow cytometry testing was not performed on the blood or bone marrow during the reporting period.

**Question 64-66: Flow cytometry testing on blood**

Indicate whether flow cytometry detected disease in a blood sample at any time during the reporting period. If “Yes,” report the date the sample was collected and the percent disease detected (i.e., percent leukemic blasts) in questions 65 and 66 respectively. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. Report “No” for question 64 and go to question 67 in either of the following cases:

- all flow cytometry assessments performed on the blood were negative for evidence of the recipient’s primary disease during the current reporting period; or
- flow cytometry testing was not performed on the blood during the reporting period.
If multiple flow cytometry assessments performed on blood samples were positive for disease, report the date / results of the earliest positive assessment performed during the reporting period.

**Question 67-69: Flow cytometry testing on bone marrow**

Indicate whether flow cytometry detected disease in a bone marrow sample at any time during the reporting period. If “Yes,” report the date the sample was collected and the percent disease detected (i.e., percent leukemic blasts) in questions 68 and 69 respectively. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. Report “No” for question 67 and go to question 70 in either of the following cases:

- all flow cytometry assessments performed on the marrow were negative for evidence of the recipient’s primary disease during the current reporting period; or
- flow cytometry testing was not performed on the marrow during the reporting period.

If multiple flow cytometry assessments performed on bone marrow samples were positive for disease, report the date and results of the earliest positive assessment performed during the reporting period.

**Question 70: Was disease detected by cytogenetic testing (karyotyping or FISH)?**

Refer to question 24 for a description of cytogenetic studies. If cytogenetic testing detected the recipient’s primary disease at any time during the reporting period, report “Yes” and go to question 71. If all cytogenetic testing was negative for evidence of the recipient’s primary disease during the current reporting period, report “No” and go to question 79. Report “Unknown” for question 70 and go to question 79 in any of the following cases:

- cytogenetic testing was not performed during the reporting period; or
- cytogenetic testing was attempted, but no assessments could be performed during the reporting period (e.g., insufficient sample); or
- it cannot be determined whether cytogenetic testing was performed during the reporting period.

**Question 71-72: Were cytogenetic abnormalities identified via FISH?**

Indicate whether FISH studies detected disease at any time during the reporting period. If “Yes,” report the date the sample was collected in question 72 and go to question 73. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. Report “No” for question 71 and go to question 75 in any of the following cases:
• FISH testing was not performed during the reporting period; or
• FISH testing was attempted, but no assessments could be performed during the reporting period (e.g., insufficient sample); or
• it cannot be determined whether FISH testing was performed during the reporting period.

If multiple FISH assessments were positive for disease, report the date / results of the earliest positive assessment performed during the reporting period.

**Question 73-74: Specify cytogenetic abnormalities (FISH)**

Select all clonal cytogenetic abnormalities detected by FISH on the date reported in question 72. If an abnormality is detected, but not listed as an option in question 73, select “Other abnormality” and specify the abnormality in question 74. If multiple “Other abnormalities” were detected by FISH at the time of best response, report “see attachment” in question 74 and attach a copy of the FISH report. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 75-76: Were cytogenetic abnormalities identified via karyotyping?**

Indicate whether karyotyping studies detected disease at any time during the reporting period. If “Yes,” report the date the sample was collected in question 76 and go to question 77. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. Report “No” for question 75 and go to question 79 if:

• karyotyping was not performed during the reporting period; or
• karyotyping was attempted, but no assessments could be performed during the reporting period (e.g., insufficient sample); or
• it cannot be determined whether karyotyping was performed during the reporting period.

If multiple karyotypes were positive for disease, report the date / results of the earliest positive assessment performed during the reporting period.

**Question 77-78: Specify cytogenetic abnormalities (karyotyping)**

Select all clonal cytogenetic abnormalities detected by karyotyping on the date reported in question 76. If an abnormality is detected, but not listed as an option in question 77, select “Other abnormality” and specify the abnormality in question 78. If multiple “Other abnormalities” were detected by karyotyping at the time of best response, report “see attachment” in question 74 and attach a copy of the karyotype report. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.
Question 79: Was documentation submitted to the CIBMTR?

Indicate if a karyotyping or FISH testing report is attached to support the reported cytogenetic findings in question 70-78. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 80-81: Was disease detected by clinical / hematologic assessment?

Clinical / hematologic assessments include, but are not limited to, biopsies, imaging assessments, complete blood counts, and physical exams. If clinical / hematologic testing detected disease during the reporting period, report “Yes” for question 81 and report the date of the positive assessment in question 81. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If multiple clinical / hematologic assessments detected disease, report the date of the earliest positive assessment performed during the reporting period.

Question 82-86: Specify Sites of Disease

Report “Yes” for each site where disease was detected by clinical / hematologic methods on the date reported in question 81. If clinical / hematologic assessments detected disease at a site not specified in questions 82-86, report “Yes” for question 85 and specify all other sites where disease was detected on the date reported in question 81.

Report “No” if a site:

• was not tested during the reporting period; or
• was tested during the reporting period, but disease was not detected.

Question 87-89: Was the disease status assessed by other assessment?

Indicate whether the recipient’s primary disease was assessed by any method other than those included in questions 51-86 during the reporting period. If “Yes,” report the date assessed and specify the type of assessment in questions 88 and 89 respectively. If the exact date of assessment is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. If AML was not assessed by any methods other than those included in questions 51-86, report “No” for question 87 and go to question 90.
Question 90: Was intervention given for relapsed disease or progressive disease, or minimal residual disease? (since the date of last report)

Indicate if the recipient received treatment post-infusion for minimal residual disease, persistent disease, or relapse since the date of last report. If “Yes,” go to question 90. If “No,” go to question 103. See question 91 for definitions each of these indications for treatment.

Question 91: Specify reason for which intervention was given

Select all indications for which treatment was administered during the reporting period. See below for definitions of each indication.

**Minimal Residual Disease:** Recipient is in hematologic CR, but has evidence of disease by more sensitive assessments including molecular, flow cytometry or cytogenetic methods.

**Persistent Disease:** The recipient was in primary induction failure or relapse at the time of infusion and has not achieved a hematologic CR post-infusion.

**Relapsed Disease:** The recipient was in CR at the time of infusion or the recipient achieved a CR post-infusion. In either case, treatment is administered for a relapse which occurred post-infusion.

Question 92: Central nervous system irradiation

See question 42 for a description of central nervous system (CNS) irradiation. If the recipient received CNS irradiation to treat minimal residual disease, persistent disease, or relapse during the reporting period, report “Yes.” If not, report “No.”

Question 93: Intrathecal Therapy

Intrathecal therapy is chemotherapy administered to the CNS via a lumbar puncture. It may be given to treat or prevent leukemic blasts in the cerebrospinal fluid or other CNS tissues. If intrathecal therapy was given as part of treatment for minimal residual disease, persistent disease, or relapse, report “Yes.” If not, report “No.”

Question 94: Systemic therapy

**Intrathecal Therapy**

Intrathecal therapy given for minimal residual disease, persistent disease, or relapse must be reported in question 93. Do not report intrathecal therapy given for minimal residual disease, persistent disease, or relapse in questions 94-98.
See question 43 for a description of systemic therapy. Do not report total body irradiation or subsequent HCT / cellular therapies in questions 94-98. If the recipient received systemic therapy during the reporting period for minimal residual disease, persistent disease, or relapse, report “Yes” and go to question 95. If not, report “No” and go to question 98.

**Question 95-96: Date therapy was first started post-HCT / post-infusion**

If the recipient started systemic therapy for minimal residual disease, persistent disease, or relapse during the reporting period, report “Known” for question 95 and indicate the date started in question 96. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If the recipient started therapy for minimal residual disease, persistent disease, or relapse in a prior reporting period and continued the therapy into the current reporting period, report “Previously reported” and go to question 97.

For recipients who start and stop therapy multiple times post-infusion, first determine whether the recipient stopped therapy for at least 30 days. If not, consider the therapy continuous. Only report a new therapy start date if all three of the below conditions are met:

1. The recipient stopped all therapy given for minimal residual disease, persistent disease, or relapse during a prior reporting period; and
2. The recipient restarted therapy for minimal residual disease, persistent disease, or relapse during the current reporting period; and
3. Therapy was restarted at least 30 days after the therapy stop date.

**Question 97-98: Specify systemic therapy given**

Select all systemic therapy (see question 43 for definition) given for minimal residual disease, persistent disease, or relapse during the reporting period. If a therapy is given, but not listed as an option in question 97, select “Other systemic therapy” and specify the drug in question 98.
**Question 99: Cellular therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “Yes” if the recipient received cellular therapy as treatment for minimal residual disease, persistent disease, or relapse during the reporting period. If not, report “No.”

**Question 100: Subsequent HCT**

Indicate whether the recipient received a HCT since the date of the last report (or since infusion if completing this is the 100 day follow-up form). Hematopoietic stem cells (HSC) are defined as mobilized peripheral blood stem cells, bone marrow, or cord blood. The source of HSC may be allogeneic unrelated, allogeneic related, or autologous. For more information on how to distinguish infusion types (example: HCT versus DCI), see Appendix D.

**Question 101: Accelerated withdrawal of immunosuppression**

Immunosuppressive medications may be tapered or entirely withdrawn in order to promote a graft vs leukemia effect in the setting of relapsed, progressive, or persistent disease. For reporting purposes, accelerated withdrawal is defined as any decrease in immunosuppression to promote graft versus leukemia effect.

If the recipient undergoes an accelerated withdrawal immunosuppression during the reporting period in order to treat disease, report “yes.” If not, report “no.”

**Question 102-103: Other therapy**

Indicate if the recipient received any other treatment for minimal residual disease, persistent disease, or relapse during the reporting period. If “Yes,” specify the type of treatment administered in question 103. If “No,” go to question 104.
Q104-144: Disease Status at the Time of Evaluation for This Reporting Period

Question 104: Does the current disease status reflect the disease detected in this reporting period section (as captured in questions 51-89), without subsequent therapy?

This section of the form is intended to capture the most recent disease assessment. The most recent disease assessments may have already been reported in questions 51-89 and, if that is the case, it is not necessary to report those same disease assessments in questions 105-143. Refer to the instructions below to determine how to complete this section of the form. Reporting scenarios have also been provided below.

Report “Yes” for question 104 and go to question 144 if the most recent disease assessments have already been reported in questions 51-59. Also, report “Yes” for question 104 and go to question 144 if assessments were reported in questions 51-59 and no therapy was given to treat disease between the date(s) of the reported assessments and the date of contact for this reporting period.

Report “No” for question 104 and go to question 105 in any of the following scenarios:

- disease was not detected by any method of assessment during the reporting period; or
- disease was detected by at least one method of assessment during the reporting period (reported in questions 51-89), but the most recent assessments have not yet been reported on the form.

Report “Not applicable” for question 104 and submit the form if the disease was not assessed during the reporting period. Only report this option if the recipient did not have any disease evaluations, including a physical exam by their primary care provider, performed during the reporting period. Obtain clarification from your center’s liaison if there are questions regarding whether a visit or test should be reported as a disease assessment.

Disease Status Evaluation Reporting Scenarios:

A. A recipient has a bone marrow assessment on D+30 (1/15/2016) including morphology review, flow cytometry, and PCR testing for FLT3-ITD (FLT3-ITD was detected at diagnosis). Disease was not detected by any of these three assessments. Subsequently, on D+95 (3/20/2016), a repeat bone marrow assessment is performed including morphology and flow cytometry. Testing for molecular markers is not done. Both assessments (morphology and flow) are negative. The date of contact for the 100 Day Follow-Up Form is 3/20/2016.
100 Day Follow-Up Form:

Questions 51-89: No assessments will be reported here since the recipient's disease did not relapse, did not persist or have evidence of minimal residual disease. In this scenario, questions 51, 63, 70, 80, and 87 must be answered “No”.

Question 104: Report “No” for question 104. Disease was not detected by any method of assessment during the reporting period.

Questions 105-143: Report the results of the most recent assessment by each method including:

- PCR testing for FLT3-ITD performed on 1/15/2016.
- Flow cytometry testing performed on the bone marrow on 3/20/2016.
- Morphology review performed on the bone marrow on 3/20/2016.

B. A recipient has a bone marrow assessment on D+30 (1/15/2016) including morphology review, flow cytometry, and PCR testing for FLT3-ITD (FLT3-ITD was detected at diagnosis). Disease was not detected by any of these three assessments. Subsequently, on D+95 (3/20/2016), all three tests are repeated and are positive indicating disease relapse. The date of contact for the 100 Day Follow-Up Form is 3/20/2016.

100 Day Follow-Up Form:

Questions 51-89: All three disease assessments performed on 3/20/2016 (PCR test for FLT3-ITD as well as morphology and flow cytometry on the bone marrow) will be reported because they were the earliest positive assessments of disease during the reporting period.

Question 104: Report “Yes” for question 103. The most recent assessments have already been reported in questions 51-59.

Questions 105-143: These questions will be left blank.

C. A recipient has a bone marrow assessment on D+30 (1/15/2016) including morphology review, flow cytometry, and PCR testing for FLT3-ITD (FLT3-ITD was detected at diagnosis). Disease was not detected by any of these three assessments. Subsequently, on D+95 (3/20/2016), a repeat bone marrow assessment is performed including morphology and flow cytometry. Testing for molecular markers is not done. Both assessments (morphology and flow) are positive indicating disease relapse. The date of contact for the 100 Day Follow-Up Form is 3/20/2016.

100 Day Follow-Up Form:

Questions 51-89: Morphology and flow cytometry assessments of the bone marrow on 3/20/2016 will be reported because they were the earliest positive assessments of disease during the reporting period. Testing for molecular markers was not done at the time of relapse and should not be reported here.

Question 104: Report “Yes” for question 103 since the most recent test results were reported in Q51-88.

Questions 105-143: These questions will be left blank.
D. A recipient has a bone marrow assessment on D+30 (1/15/2016) including morphology review, flow cytometry, and PCR testing for FLT3-ITD. All three assessments detect disease. Subsequently, on D+95 (3/20/2016), a repeat bone marrow assessment is performed including morphology and flow cytometry. Testing for molecular markers is not done. Both assessments (morphology and flow) are again positive for disease. The date of contact for the 100 Day Follow-Up Form is 3/20/2016.

100 Day Follow-Up Form:

Questions 51-89: All three disease assessments performed on 1/15/2016 (PCR test for FLT3-ITD as well as morphology and flow cytometry on the bone marrow) will be reported because they were the earliest positive assessments of disease during the reporting period.

Question 104-143: Report “Yes” for question 103 and leave questions 105-143 blank if no therapy was given to treat the disease between 1/15/2016 and 3/20/2016. If therapy was used to treat the disease during this time frame, “No” and report the most recent test results in questions 105-143.

Question 105: Were tests for molecular markers performed (e.g. PCR, NGS)?

Negative Disease Assessments
Prior versions of the AML Post-Infusion Data Form have only permitted reporting of testing for molecular abnormalities known to be associated with the recipient’s AML (i.e., only report testing that has been positive least once between diagnosis and the date of the assessment being reported). The wording of this question has been updated to include any testing for molecular markers of AML regardless of previous or current test results. When completing questions 105-115, consider all testing for molecular markers performed during the reporting period. Testing may be reported in these fields even if it has never been positive.

Refer to question 4 for a description of testing for molecular markers. If molecular testing was performed during the reporting period, report “Yes” and go to question 106. If testing was not performed during the reporting period or it is not known whether testing was performed, report “No” or “Unknown” respectively and go to question 116.

Question 106-115: Specify results

For each molecular marker in questions 106-115, report whether testing was “Positive,” “Negative,” or “Not done” at the time of the most recent assessment during the reporting period. If the most recent testing performed during the reporting period identified a molecular marker other than those listed in questions 106-113, report the result in question 114 and specify the marker in question 115.

If multiple “Other molecular marker[s]” were tested at the time of best response, report one instance (i.e., copy) of question 114-115 for each “Other molecular marker” tested. If greater than 3 “Other molecular
marker[s]” were tested, do the following:

- report one instance of question 114-115; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 115; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”

If CEBPA is reported as “Positive” (question 106) question 107 must be completed. If the lab report does not specify whether the detected marker was biallelic / homozygous or monoallelic / heterozygous, confirm with the laboratory whether this information can be determined prior to reporting “Unknown.”

**Question 116: Was the disease status assessed via flow cytometry?**

Refer to question 15 for a description of flow cytometry. Only testing performed on the blood or bone marrow may be reported in questions 116-124. If flow cytometry was performed on the blood and / or bone marrow during the reporting period, report “Yes” and go to question 117. If testing was not performed during the reporting period, report “No” and go to question 125.

**Question 117-120: Flow cytometry testing on blood**

If flow cytometry was performed on the blood during the reporting period, report “Yes” for question 117 and go to question 118. If testing was not performed during the reporting period, report “No” and go to question 121.

If “Yes” has been reported for question 117, report the date of collection and results for the most recent assessment performed during reporting period in questions 118 and 119 respectively. If disease was detected by the most recent assessment, report the percent disease detected (i.e., percent leukemic blasts) in question 120. Otherwise, go to question 121.

**Question 121-124: Flow cytometry testing on bone marrow**

If flow cytometry was performed on the bone marrow during the reporting period, report “Yes” for question 121 and go to question 122. If testing was not performed during the reporting period, report “No” and go to question 125. If it is not known whether testing was performed, leave question 121 blank and override the validation error using the code “Unknown.”

If “Yes” has been reported for question 121, report the date of collection and results for the most recent assessment performed during reporting period in questions 122 and 123 respectively. If disease was detected by the most recent assessment, report the percent disease detected (i.e., percent leukemic blasts)
in question 124. Otherwise, go to question 125.

**Question 125: Were cytogenetics tested (karyotyping or FISH)?**

Refer to question 24 for a description of cytogenetic testing. If cytogenetic testing was performed during the reporting period, report “Yes” and go to question 126. If testing was not performed during the reporting period or it is not known whether testing was performed, report “No” or “Unknown” respectively and go to question 137.

If cytogenetic studies were attempted during the reporting period, but there were not adequate cells (metaphases) for any cytogenetic assessments, report “No,” and go to question 137.

**Question 126-127: Were cytogenetics tested via FISH?**

If FISH studies were performed during the reporting period, report “Yes” and indicate whether clonal abnormalities were detected on the most recent assessment in the reporting period in question 127. If FISH studies were not performed, report “No” for question 126 and go to question 131. Examples of this include: no FISH study performed or FISH sample was inadequate.

**Question 128-130: Specify cytogenetic abnormalities (FISH)**

Report the number of clonal abnormalities detected by the most recent FISH assessment in the reporting period in question 128. After indicating the number of abnormalities in question 128, select all clonal abnormalities detected in questions 129-130.

If a clonal abnormality is detected on the most recent FISH assessment in the reporting period, but not listed as an option in question 129, select “Other abnormality” and specify the abnormality in question 130. If multiple “Other abnormalities” were detected, report “see attachment” in question 130 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.
**Question 131-132: Were cytogenetics tested via karyotyping?**

If karyotyping was performed during the reporting period, report “Yes” for question 131 and indicate whether clonal abnormalities were detected in question 132. If karyotyping was not performed, indicate “No” for question 131 and go to question 136. Examples of this include: karyotyping was not performed or karyotyping sample was inadequate.

**Question 133-135: Specify cytogenetic abnormalities (karyotyping)**

Report the number of clonal abnormalities detected by the most recent karyotype in the reporting period in question 133. After indicating the number of clonal abnormalities in question 133, select all abnormalities detected in questions 134-135.

If a clonal abnormality is detected on the most recent karyotype during the reporting period, but not listed as an option in question 134, select “Other abnormality” and specify the abnormality in question 135. If multiple “Other abnormalities” were detected, report “see attachment” in question 135 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 136: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 125-135. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 137-139: Was disease detected by clinical / hematologic assessment?**

Clinical / hematologic assessments include, but are not limited to, biopsies, imaging assessments, complete blood counts, radiographic studies and physical exams. If clinical / hematologic testing was performed during the reporting period, report “Yes” for question 137 and report the date and result in questions 138 and 139 respectively. The date and results reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). Indicate the date the sample was collected for examination for pathological and laboratory evaluations; enter the date of physical examination. If no disease assessments were performed within approximately 30 days prior to the date of contact, report the results and date of the most recent assessment performed during the reporting period. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If no clinical / hematologic assessments (including a physical exam by the recipient’s primary care provider) were performed during the reporting period, report “No” for question 137 and go to question 140.
**Question 140-143: Was the disease status assessed by other assessment?**

Indicate in question 140 whether AML was assessed by any method other than those included in questions 105-139 during the reporting period. If “Yes,” report the date of assessment and specify the type of assessment in questions 141 and 142 respectively. Also report the results of the assessment in question 143. If the exact date of assessment is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. If AML was not assessed by any methods other than those included in questions 105-139, report “No” for question 140 and go to question 144.

**Question 144: What is the current disease status?**

Indicate the hematologic disease status of AML as of the last evaluation during the reporting period. Determine the current disease status using the international working group criteria provided in the in AML Response Criteria of the Forms Instructions Manual. Report “Complete Remission” for recipients who meet the criteria for complete remission (CR). Do not consider testing for molecular markers, testing for cytogenetic abnormalities, or testing by flow cytometry when reporting the hematologic disease status in question 144.

Some clinical judgment is required for evaluating whether a recipient meets the CR criteria, specifically neutrophil, platelet, and transfusion parameters. If a recipient does not meet these specifications, the underlying cause should be assessed; if the cause for not meeting one of these parameters is felt to be due to a reason other than underlying leukemia, such as renal insufficiency, hemolysis, or drug-related causes, the disease status may be reported as “complete remission.” If the cause for not meeting the parameters is judged to be leukemia-related, the disease status should be reported as “not in complete remission.”

If the recipient did not meet the criteria for CR report “Not in complete remission.”

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

**Question 145: Date assessed**

Enter the date of the most recent assessment establishing disease status within the reporting period. The date reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). In addition to clinician evaluation and physical examination, clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory analysis (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluation; the date
the imaging took place for radiographic assessments, or the date of physical examination.
Acute Lymphoblastic Leukemia (ALL) is a cancer of the white blood cells. It is characterized by the rapid proliferation of abnormal, immature lymphocytes, or lymphoblasts, in the bone marrow. This accumulation of blasts in the marrow prevents the formation of healthy red blood cells, white blood cells, and/or platelets. Normal lymphoblasts develop into B and T lymphocytes that fight infection. In ALL, the leukemic lymphoblasts do not fully develop and therefore cannot fight infection. The symptoms of ALL are caused by the replacement of normal bone marrow with lymphoblasts, resulting in lower numbers of red blood cells, platelets, and normal white blood cells. It is estimated that 80-85% of ALL cases occur in children, with peak incidence of pediatric ALL at age 5. Biologically, adult and pediatric ALL are very different. Pediatric cases are more often characterized by favorable prognostic indicators including a precursor B-cell population, TEL/AML1 fusion gene, and/or hyperdiploidy; adult cases are more often characterized by poor prognostic indicators including a precursor T-cell population and/or BCR/ABL fusion gene.¹


ALL Response Criteria
2011: ALL Pre-HCT
2111: ALL Post-HCT
ALL Response Criteria

Complete Remission (CR)

Hematologic complete remission is defined as meeting all of the following response criteria for at least four weeks.

- < 5% blasts in the bone marrow
- Normal maturation of all cellular components in the bone marrow
- No extramedullary disease (e.g., CNS, soft tissue disease)
- ANC (absolute neutrophil count) ≥ 1,000/µL
- Platelets ≥ 100,000/µL
- Transfusion independent

Alternative post-transplant CR criteria are accepted in the setting of pediatric ALL when the center does not routinely perform bone marrow biopsies post-transplant and the patient was in CR pre-transplant. These criteria are not used for pre-transplant ALL disease status. The criteria are as follows:

- Complete donor chimerism (≥ 95% donor chimerism without recipient cells detected)
- No extramedullary disease (e.g., CNS, soft tissue disease)
- Neutrophils ≥ 1,000/µL
- Platelets ≥ 100,000/µL
- Transfusion independent

In some cases, there may not be a four-week interval between completion of therapy and the pre-transplant disease assessment; in this case, CR should still be reported as the status at transplant, since it represents the “best assessment” prior to HCT. This is an exception to the criteria that CR be durable beyond four weeks. The pre-transplant disease status should not be changed based on early relapse or disease assessment post-transplant.

Include recipients with persistent cytogenetic or molecular abnormalities who meet the above CR criteria for hematologic CR.

Include recipients meeting the above CR criteria regardless of how many courses of therapy were required to achieve CR.

The number of this complete remission can be determined by using the following guidelines:
• 1st CR: no prior relapse
• 2nd CR: one prior relapse
• 3rd or higher: two or more prior relapses

**Complete Remission with Incomplete Hematologic Recovery (CRi)**

Hematologic complete remission with incomplete hematologic recovery is defined as meeting all of the following response criteria for at least four weeks:

• < 5% blasts in the bone marrow
• Normal maturation of all cellular components in the bone marrow
• No extramedullary disease (e.g., CNS, soft tissue disease)
• Transfusion independent (Please note, if the physician documents transfusion dependence related to treatment and not the patient’s underlying ALL, CRi can be reported)

**Primary Induction Failure (PIF)**

The patient received treatment for ALL but **never achieved CR or CRi at anytime**. PIF is not limited by the number of unsuccessful treatments; this disease status only applies to recipients who have **never been in CR or CRi**.

**Relapse (REL)**

Relapse is defined as the recurrence of disease after CR, meeting at least one of the following criteria:

• ≥ 5% blasts in the marrow or peripheral blood
• Extramedullary disease
• Disease presence determined by a physician upon clinical assessment

The number of this relapse can be determined by using the following guidelines:

• 1st relapse: one prior CR
• 2nd relapse: two prior CRs
• 3rd or higher: three or more CRs

Do not include a partial response (PR) when determining number of relapse. Recipients who achieve a PR to treatment should be classified as either PIF or relapse; PR in ALL is generally of short duration and is unlikely to predict clinical benefit.
No Treatment

The recipient was diagnosed with acute leukemia and never received therapeutic agents. Include patients who have received only supportive therapy, including growth factors and/or blood transfusions.

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

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<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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<tbody>
<tr>
<td>6/1/18</td>
<td>ALL Response Criteria</td>
<td>Add</td>
<td>Added (in red below) further instruction on reporting the CRi response criteria: <strong>Transfusion independent</strong> <em>(Please note, if the physician documents transfusion dependence related to treatment and not the patient's underlying ALL, CRi can be reported)</em></td>
</tr>
</tbody>
</table>
| 3/2/18 | ALL Response Criteria   | Remove            | Removed the following bullet from the CRi criteria.  
• **No blasts with Auer rods**                                                                                                                                                                                                                                                                                                           |
2011: ALL Pre-Infusion

The Acute Lymphoblastic Leukemia Pre-Infusion Data Form (Form 2011) is one of the Comprehensive Report Forms. This form captures ALL-specific pre-infusion data such as: the recipient’s hematologic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HCT treatments administered and the best response to each line of therapy.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on Disease Classification Form (Form 2402), as Acute Lymphoblastic Leukemia (ALL). This form must also be completed if the recipient received a cellular therapy to treat ALL as reported on the Pre-CTED Form (Form 4000).

Is this the report of a second or subsequent transplant or cellular therapy for the same disease?
Report “no” and go to question 1 in any of the following scenarios:

- this is the first infusion reported to the CIBMTR;
- this is a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than ALL); or
- this is a second or subsequent infusion for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior infusion, prior infusion was autologous with no consent, etc.).

If this is a report of a second or subsequent infusion for the same disease and this baseline ALL disease insert was completed previously, report “yes” and go to question 64.

Links to Section of Form
Q1-19: Laboratory Studies at Diagnosis
Q20-63: Pre-HCT or Pre-Infusion Therapy
Q64-91: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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<td>10/17/18</td>
<td>2011: ALL Pre-Infusion Data</td>
<td>Modify</td>
<td>Modified (red text was added, struck out text was deleted) the instructional text for questions 37-38: Treatments vary based on protocol. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. If chemotherapy drugs were administered as part of the line of therapy, select the box for ‘chemotherapy’. You do not need to specify each drug. Select all chemotherapy drugs administered as part of the line of therapy being reported. If the recipient received a systemic therapy which is not listed, select “Other systemic therapy” and specify the treatment in question 38. Report the generic name of the agent, not the name brand.</td>
</tr>
<tr>
<td>8/31/17</td>
<td>2011: ALL Pre-Infusion Data</td>
<td>Add</td>
<td>Added CNS Prophylaxis Reporting Scenarios A and B located below the instructions for questions 20-26.</td>
</tr>
</tbody>
</table>
Q1-19: Laboratory Studies at Diagnosis

All values reported in questions 1-19 must reflect testing performed prior to any treatment of ALL. If testing was not performed near the time of diagnosis (within approximately 30 days) and prior to the initiation of treatment, the center should report “Unknown” for that value.

Questions 1-3: WBC

Indicate whether the white blood count (WBC) in the peripheral blood is “Known” or “Unknown” at the time of diagnosis. If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the WBC at diagnosis is not known, report “Unknown” and go to question 4.

Questions 4-6: Blasts in blood

Indicate whether the percent blasts in the peripheral blood is “Known” or “Unknown” at the time of diagnosis. This may be determined by an automated differential, a manual count, or flow cytometry. Testing by any of these methods may be reported in questions 4-6. If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the percent blasts in blood at diagnosis is not known, report “Unknown” and go to question 7.

Questions 7-9: Blasts in bone marrow

Indicate whether the percent blasts in the bone marrow is “Known” or “Unknown” at the time of diagnosis. The percent blasts may be assessed by manual differential or flow cytometry. If available, report the manual differential performed on the bone marrow aspirate sample. If a manual differential was not performed on an aspirate sample, other methods / sample types may be reported (such as flow cytometry on an aspirate sample, or testing on a core biopsy) may be reported.

If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the percent blasts in bone marrow at diagnosis is not known, report “Unknown” and go to question 10.

Questions 10-19: Extramedullary disease

Extramedullary disease refers to any confirmed site of ALL other than the peripheral blood and bone
marrow. Examples include detection of leukemic blasts in the cerebrospinal fluid and skin (leukemia cutis) as well as detection of soft tissue masses (myeloid sarcoma). If the recipient had extramedullary disease at the time of diagnosis, report “Yes” for question 10 and report all extramedullary sites of involvement in questions 11-19. If the recipient did not have any extramedullary disease at diagnosis, report “No” for question 10 and go to question 20. If extramedullary disease at diagnosis is not known, report “Unknown” and go to question 20.
Q20-63: Pre-HCT or Pre-Infusion Therapy

The FormsNet3℠ application allows questions 28-63 to be reported multiple times. Complete these questions for each line of therapy administered on or after the date of diagnosis of ALL and prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given). When submitting the paper version of the form for more than one line of therapy, copy the “Pre-HCT or Pre-Infusion Therapy” section and complete a copy of the section for each line of therapy administered.

A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.). If a recipient’s disease status changes resulting in a change to treatment, a new line of therapy should be reported. Additionally, if therapy is changed because a favorable disease response was not achieved, a new line of therapy should be reported.

Question 20-26: Was central nervous system prophylaxis given?

Central nervous system (CNS) prophylaxis may be administered as irradiation, chemotherapy, or other agents. Report therapy administered to the CNS as prophylaxis only if the recipient did not have any evidence of ALL in the CNS prior to the initiation of therapy. See the reporting scenarios below for further clarification.

If the recipient received CNS prophylaxis during the time frame indicated above, report “Yes” for question 20 and then report “Yes” for any prophylactic therapies included in questions 21-24 which were administered. If a prophylactic therapy was given, but is not included in questions 21-24, report “Yes” for question 25 and specify the therapy in question 26. If the recipient did not receive CNS prophylaxis during the time frame indicated above or it is not known whether CNS prophylaxis was given, report “No” or “Unknown” respectively for question 20 and go to question 27.

CNS Prophylaxis Reporting Scenarios

A. A recipient is diagnosed with ALL from a bone marrow biopsy. There is no indication of CNS disease involvement based on the available testing. Treatment is commenced with combination systemic chemotherapy followed by several doses of intrathecal chemotherapy. The recipient achieves a complete remission and proceeds to HCT.

   Question 20: Report “Yes” to indicate CNS prophylaxis was given between diagnosis and HCT / cellular therapy.

   Questions 21-26: Report “Yes” for intrathecal therapy and report “No” for all other questions.
B. A recipient is diagnosed with ALL from a bone marrow biopsy and a positive sample from their cerebrospinal fluid (CSF). Treatment is commenced with combination systemic chemotherapy and intrathecal therapy. The recipient achieves a morphologic complete remission. The CSF is tested and found to be negative and the patient commences consolidation therapy including several intrathecal treatments to prevent relapse in the CNS.

**Question 20:** Report “No” to indicate no CNS prophylaxis was given between diagnosis and HCT / cellular therapy. All intrathecal therapy was given after CNS involvement was discovered.

**Question 21-26:** These questions will be left blank.

**Question 27: Was therapy given?**

Indicate if the recipient received treatment for their primary disease between diagnosis and the start of the preparative regimen. This includes systemic chemotherapy, intrathecal therapy, radiation therapy, and cellular therapies. Do not report a prior HCT or any surgery in questions 27-49. If therapy was given to treat ALL during the time frame indicated above, report “Yes” and go to question 28. If reporting “No,” go to question 64.

**Question 28: Purpose of therapy**

The purpose of each line of therapy depends on the disease status at the time of administration. See below for general definitions of each option choice. Indicate the purpose of the line of therapy being reported and go to question 29.

**Induction:** The first line(s) of therapy given following diagnosis to achieve a complete remission (CR). If the first line of therapy (induction) fails to produce a CR, the recipient may undergo another cycle or a different line of therapy (re-induction) in order to achieve their first CR. Report “Induction” as the purpose for all lines of therapy given to achieve the first CR.

**Consolidation:** Once a recipient has achieved a hematologic CR (1st, 2nd, 3rd or greater), they may receive several additional lines of therapy as part of a protocol or to eliminate known minimal residual disease. In either case, report “Consolidation” as the purpose for these lines of therapy.

**Maintenance:** Following induction and consolidation, a recipient may receive low dose chemotherapy over an extended period of time to maintain a CR. Maintenance therapy is usually given as a single drug taken in the outpatient setting when the recipient has no known evidence of disease. Report “Maintenance” as the purpose for these lines of therapy.

**Treatment for disease relapse:** Once the recipient has achieved their first CR, their disease may relapse and require further treatment to produce another CR (2nd or greater). The intent is the same as induction,
but setting is different as the recipient has already achieved at least one prior CR. Report “Treatment for disease relapse” as the purpose for all lines of therapy given to induce a CR following relapse.

**Question 29: Intrathecal Therapy**

Intrathecal therapy refers to chemotherapy administered via lumbar puncture to treat or prevent leukemic blasts in the central nervous system. Report “Yes” if intrathecal therapy was given as part of the line of therapy being reported. Report “No” if intrathecal therapy was not given as part of the line of therapy being reported.

**Question 30: Systemic therapy**

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein / central line or given orally. Do not report intrathecal therapy as systemic therapy. If systemic therapy was administered as part of the line of therapy being reported, report “Yes” and continue with question 31. If not, report “No” and go to question 39.

**Question 31-32: Date therapy started**

Indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 32. If the start date is partially known (e.g., the recipient started in mid-July 2011), use the process for reporting partial or unknown dates as described in the [General Instructions, Guidelines for Completing Forms](https://CIBMTR.org).

If the date therapy started is “Unknown,” go to question 33.

**Question 33-34: Date therapy stopped**

Indicate if therapy stop date is “Known” or “Unknown.” If the therapy is being given in cycles, report the date the recipient started the last cycle for this line of therapy in question 34. Otherwise, report the final administration date for the therapy being reported. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the [General Instructions, Guidelines for Completing Forms](https://CIBMTR.org).

If the date therapy stopped is “Unknown,” go to question 35.

**Question 35-36: Number of cycles**

Systemic therapy is usually administered in cycles with rest periods in-between. This enables cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from the damage sustained during therapy. A cycle can last one or more days and can repeat weekly, bi-weekly, or monthly. A single systemic therapy course may consist of multiple cycles.
Indicate whether the number of cycles is “Known” or “Unknown.” If “Known,” enter the number of cycles the recipient received in question 36. If “Unknown,” go to question 37.

If therapy is not being administered in cycles (e.g., daily chemotherapy), report “Unknown” for question 35 and go to question 37.

**Question 37-38: Specify systemic therapy**

Treatments vary based on protocol. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. If chemotherapy drugs were administered as part of the line of therapy, select the box for ‘chemotherapy’. You do not need to specify each drug. If the recipient received a systemic therapy which is not listed, select “Other systemic therapy” and specify the treatment in question 38. Report the generic name of the agent, not the name brand.

**Question 39: Radiation therapy**

Radiation therapy utilizes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. Radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes. Radiation therapy may be given in conjunction with systemic chemotherapy or as a separate line of therapy.

If radiation therapy was given during or adjacent to administration of systemic therapy, report them together as single line of therapy on the form (i.e., one copy of questions 28-63). Otherwise, capture the radiation treatment as a separate line of therapy.

If the recipient received radiation therapy as part of the line of therapy being reported, report “Yes” and go to question 39. If not, report “No” and go to question 49.

**Question 40-41: Date therapy started**

Indicate whether the start date for radiation therapy is “Known” or “Unknown.” If “Known,” enter the date radiation therapy began in question 41. If the start date is partially known (e.g., the recipient started in mid-July 2011), use the process for reporting partial or unknown dates as described in the [General Instructions, Guidelines for Completing Forms](#).

If the date therapy started is “Unknown,” go to question 42.

**Question 42-43: Date therapy stopped**

Indicate if the stop date for radiation therapy is “Known” or “Unknown.” If “Known,” enter the final date radiation was administered in question 43. If the stop date is partially known, use the process described for
reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

If the date therapy stopped is “Unknown,” go to question 44.

**Question 44-48: Specify site(s) of radiation therapy**

Report all sites of radiation therapy administered between the start and stop dates reported in questions 40-43. If “Yes” is reported for “Other site,” specify all other sites in question 48.

**Question 49: Cellular Therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “Yes” if the recipient received cellular therapy as part of the line of therapy being reported. If not, report “No.”

**Question 50: Best response to line of therapy**

Indicate the best response to the line of therapy using the international working group criteria provided in ALL Response Criteria section of the Forms Instructions Manual. The best response is determined by a disease assessment, such as hematologic testing, pathology study, and / or physician assessment.

**Question 51: Date assessed**

Report the date the best response to the line of therapy was established. This should be the earliest date all international working group criteria were met for the response reported in question 50. Enter the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically evaluated the recipient's response.

If the best response was achieved prior to starting the line of therapy being reported, indicate the date of the first assessment which was performed after initiating the current line of therapy and confirms the sustained response.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.
Question 52: Was the recipient MRD negative following this line of therapy?

Minimal residual disease (MRD) can be assessed by different methods including, but not limited to, the following:

- Next generation sequencing
- Sanger sequencing
- Polymerase chain reaction (PCR) testing
- Chromosomal / genomic microarray analysis
- Fluorescence in situ hybridization (FISH)
- Karyotyping
- Flow cytometry

If any MRD testing was performed following the line of therapy being reported, answer question 52 based on the results of the testing performed within 30 days after the date therapy was stopped and prior to any new therapy being initiated. If any MRD testing during this timeframe was positive for markers of ALL, report “No” for question 52. If all MRD testing during this time frame was negative for markers of ALL, report “Yes” for question 52. If no MRD testing was performed during this timeframe, leave question 52 blank and override the error in FormsNetSM using the code “Unknown.”

Question 53: Did the recipient relapse following this line of therapy?

Refer to the international working group criteria provided in ALL Response Criteria section of the Forms Instructions Manual for more information on how to determine recurrence of disease. Report “Yes” if the recipient met the criteria for relapse after starting this line of therapy and prior to starting a subsequent line of therapy. If “Yes” is reported, also completed questions 54-63.

Report “No” if the recipient never relapsed following this line of therapy. Also, report “No” if the recipient relapsed after beginning a subsequent line of therapy. This episode of relapse will be captured in the instance (i.e., copy) of questions 28-63 completed for the subsequent line of therapy. If “No” is reported, go to question 64.

If this is the last line of therapy administered prior to infusion, only report “Yes” if relapse occurred prior to infusion. Relapse occurring after the infusion date will be reported on the ALL Post-Infusion Data Form (Form 2111).

Question 54: Date of relapse

Enter the assessment date relapse was established following initiation of this line of therapy. Report the date of the pathologic evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral
blood smear). Enter the date the sample was collected for pathologic and laboratory evaluations. If extranodal disease is detected upon radiographic examination (e.g., X-rays, CT scans, MRI scans, PET scans), enter the date the imaging took place. If the physician determines evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 55-63: Sites of Relapse**

Report all known sites of active disease at the time of relapse in questions 55-63. This includes any sites identified between the date of relapse reported in question 54 and the time treatment for relapse is initiated. If “Yes” has been reported for “Other site” in question 62, use question 63 to specify all sites of active disease not already reported in questions 55-61.
Q64-91: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

All values reported in questions 64-91 must reflect the most recent testing prior to the start of the preparative regimen (or infusion if no preparative regimen was given). Do not report testing performed during a line of therapy reported in questions 20-68. If testing was not performed near the start of the preparative regimen / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable), the center should report “Unknown” for that value.

Question 64-66: WBC

Indicate whether the white blood count (WBC) in the peripheral blood is “Known” or “Unknown” at the last evaluation prior to the start of the preparative regimen / infusion. If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the WBC at the last evaluation prior to the start of the preparative regimen / infusion is not known, report “Unknown” and go to question 67.

Question 67-69: Blasts in blood

Indicate whether the percent blasts in the peripheral blood is “Known” or “Unknown” at the last evaluation prior to the start of the preparative regimen / infusion. This may be determined by an automated differential, a manual count, or flow cytometry. Testing by any of these methods may be reported in questions 67-69. If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the percent blasts in blood at the last evaluation prior to the start of the preparative regimen / infusion is not known, report “Unknown” and go to question 70.

Question 70-72: Blasts in bone marrow

Indicate whether the percent blasts in the bone marrow is “Known” or “Unknown” at the last evaluation prior to the start of the preparative regimen / infusion. The percent blast may be assessed by manual differential or flow cytometry. If available, report the manual differential performed on the bone marrow aspirate sample. If a manual differential was not performed on an aspirate sample, other methods / sample types may be reported (such as flow cytometry on an aspirate sample, or testing on a core biopsy) may be reported.
If “Known,” report the laboratory value, unit of measure, and date sample collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms. If the percent blasts in bone marrow at the last evaluation prior to the start of the preparative regimen / infusion is not known, report “Unknown” and go to question 73.

**Question 73: Was flow cytometry performed?**

Indicate whether flow cytometry (immunophenotyping) was performed on the blood and/or bone marrow at the last evaluation prior to the start of the preparative regimen / infusion. If “Yes,” go to question 74. If “No” or “Unknown,” go to question 82.

**Question 74-77: Flow cytometry testing on blood**

Indicate whether flow cytometry was performed on the blood at the last evaluation prior to the start of the preparative regimen / infusion. If “Yes,” report the date the sample was collected and whether disease was detected in questions 75 and 76 respectively. If disease was detected, report the percent disease detected (i.e., percent leukemic blasts) in question 77. Otherwise, go to question 78.

If flow cytometry was not performed on the blood at the last evaluation prior to the start of the preparative regimen / infusion, report “No” for question 74 and go to question 78.

**Question 78-81: Flow cytometry testing on bone marrow**

Indicate whether flow cytometry was performed on the bone marrow at the last evaluation prior to the start of the preparative regimen / infusion. If “Yes,” report the date the sample was collected and whether disease was detected in questions 79 and 80 respectively. If disease was detected, report the percent disease detected (i.e., percent leukemic blasts) in question 81. Otherwise, go to question 82.

If flow cytometry was not performed on the bone marrow at the last evaluation prior to the start of the preparative regimen / infusion, report “No” for question 78 and go to question 82.

**Question 82-91: Was extramedullary disease present?**

Refer to the instructions for questions 10-19 a description of extramedullary disease. If the recipient had extramedullary disease at the last evaluation prior to the start of the preparative regimen / infusion, report “Yes” for question 82 and report all extramedullary sites of involvement in questions 83-91. If the recipient did not have any extramedullary disease at this time point or it is not known whether extramedullary disease is present, report “No” or “Unknown” respectively for question 82 and submit the form.
2111: ALL Post-Infusion

The Acute Lymphoblastic Leukemia Post-Infusion Data Form (Form 2111) is one of the Comprehensive Report Forms. This form captures ALL-specific post-infusion data such as: the recipient’s best response to HCT or cellular therapy, cytogenetic and molecular findings at the time of best response, post-infusion therapy for ALL, assessment and treatment of relapse, and current disease assessments.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on Disease Classification Form (Form 2402), as Acute Lymphoblastic Leukemia (ALL). This form must also be completed if the recipient received a cellular therapy to treat ALL as reported on the Pre-CTED Form (Form 4000).

Links to Sections of Form
Q1-34: Disease Assessment at the Time of Best Response to HCT or Cellular Therapy
Q35-47: Post-HCT / Post-Infusion Therapy
Q48-94: Disease Detection Since the Date of Last Report
Q95-130: Disease Status at the Time of Evaluation for This Reporting Period

Manual Updates:
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<td>Add</td>
<td>Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119). The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.</td>
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<tr>
<td>2/22/18</td>
<td>2111: ALL Post-Infusion Data</td>
<td>Modify</td>
<td>Added (in red) and removed (struck out) text from instructions for questions 48-49. If any testing for molecular markers occurred detected the recipient’s primary disease during the reporting period, report “Yes” for question 48 and report the date the sample was collected in question 49.</td>
</tr>
</tbody>
</table>
If molecular marker testing did not detect disease at any time during the reporting period, report “No” for question 48 and go to question 49. If molecular marker testing was not performed during the reporting period, report “No Unknown” go to question 53.

<table>
<thead>
<tr>
<th>Date</th>
<th>Code</th>
<th>Description</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/22/18</td>
<td>2111: ALL Post-Infusion Data</td>
<td>Added (in red) and removed (struck out) text from the beginning of section Q48-94: Disease Detection Since Date of Last Report. If testing by a particular method for molecular or cytogenetic markers / abnormalities was not done during the reporting period or it is not known whether testing was performed, report “Unknown” for that method those methods (question 48 and 61). If testing by flow cytometry, clinical / hematologic assessment, or other assessment was not done during the reporting period or it is not known whether testing was performed, report “No” for those methods (questions 54, 71, and 78).</td>
<td>Modify</td>
</tr>
<tr>
<td>2/22/18</td>
<td>2111: ALL Post-Infusion Data</td>
<td>Added text (in red) to the Questions 48-94 warning box. For questions 48, 54, 61, and 78, report “No” or “Unknown” (see instructions below) if the recipient did not relapse, have persistent or minimal residual disease even if testing was performed.</td>
<td>Add</td>
</tr>
<tr>
<td>7/25/17</td>
<td>2111: ALL Post-Infusion Data</td>
<td>Version 3 of the 2111: ALL Post-Infusion Data section of the Forms Instructions Manual released. Version 3 corresponds to revision 4 of the Form 2111.</td>
<td>Modify</td>
</tr>
</tbody>
</table>
Q1-34: Disease Assessment at the Time of Best Response to HCT

Question 1: What was the best response to HCT or cellular therapy since the date of the last report?  
(Include response to any therapy given for post-HCT / post-infusion maintenance or consolidation, but exclude any therapy given for relapsed, persistent or progressive disease.)

The intent of this question is to determine the best overall response to HCT or cellular therapy. This is assessed in each reporting period. For any recipients in complete remission (CR) or complete remission with incomplete hematologic recovery (CRi) at the time of infusion, report “Continued Complete Remission” for question 1 and go to question 35.  

When evaluating the best response, determine the disease status within the reporting period using the international working group criteria provided in the in ALL Response Criteria section of the Forms Instructions Manual. Compare this response to all previous post-infusion reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status. See question 2 to indicate that this disease status was previously reported.

Include response to any post-infusion treatment planned as of Day 0. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR or as preemptive therapy for recipients with minimal residual disease, consider this “planned therapy,” even if this was not documented prior to the transplant. Do not include response any treatment for relapse, progression, or persistent disease. If a recipient started treatment for relapse, progression, or persistent disease, report the best response prior to the initiation of treatment (even if this was confirmed in a prior reporting period).

Best Response to HCT Reporting Scenarios:

A. A recipient in complete remission at the time of infusion has a disease relapse detected on their first bone marrow biopsy post-HCT. They do not achieve a sustained recovery of their absolute neutrophil count by day 100.

100 Day Follow-Up Form:
Question 1: Report “Continued complete remission.” This option should be used for all recipients in CR at the time of infusion regardless of post-infusion disease assessments.

B. A recipient in primary induction failure at the time of infusion achieves a CRi on 6/1/2016. Their platelets are persistently low through their day 100 contact date (6/15/2016); however, they do rise /
remain above 100 × 10^9/L beginning 6/30/2016 at which time the recipient’s disease status was CR.

100 Day Follow-Up Form:
**Question 1:** Report “Complete Remission.” Use this option to indicate CR or CRi was achieved post-infusion for recipients not in CR / CRi at the time of infusion.

**Question 2:** Report “No.” The date of best response has not been previously reported. Never report “Yes” for question 2 on the day 100 follow-up form.

**Question 3:** Report 6/1/2016 as indicated in the report scenario.

Six Month Follow-Up Form:
**Question 1:** Report “Complete Remission.” Use this option to indicate CR or CRi was achieved post-infusion for recipients not in CR / CRi at the time of infusion.

**Question 2:** Report “Yes.” The date of best response was previously reported on the 100 day follow-up form.

**Question 3:** Leave blank. This question will not be answered when question 2 has been answered “Yes.”

C. A recipient in primary induction failure at the time of infusion achieves a CR during the 100 day reporting period on 5/1/2014. The recipient has a disease relapse during the 6 month reporting period and their disease status remains “Relapse” on the 6 month date of contact despite multiple treatments.

100 Day Follow-Up Form:
**Question 1:** Report “Complete Remission.” Use this option to indicate CR or CRi was achieved post-infusion for recipients not in CR / CRi at the time of infusion.

**Question 2:** Report “No.” The date of best response has not been previously reported. Never report “Yes” for question 2 on the day 100 follow-up form.

**Question 3:** Report 5/1/2014 as indicated in the report scenario.

Six Month Follow-Up Form:
**Question 1:** Report “Complete Remission.” Use this option to indicate CR or CRi was achieved post-infusion for recipients not in CR / CRi at the time of infusion.

**Question 2:** Report “Yes.” The date of best response was previously reported on the 100 day follow-up form.

**Question 3:** Leave blank. This question will not be answered when question 2 has been answered “Yes.”

*Note, once a CR / CRi is achieved post-infusion, the best response will always be reported as CR for question 1. Changes to disease status after CR / CRi is achieved are not reported in question 1.*

**Question 2: Was the date of best response previously reported?**

If the best response to HCT / cellular therapy was first documented during the current reporting period,
report “no” and go to question 3. If the best response was achieved during a previous reporting period (and therefore reported on a previous ALL Post-Infusion Data Form), report “Yes” and go to question 35.

Do not report “Yes” if completing this form for the 100 day reporting period.

**Question 3: Date assessed**

Report the date the best response to HCT / cellular therapy was established. This should be the earliest date when all international working group criteria for the response reported in question 1 were met. Report the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessments were performed to establish the best response, report the office visit in which the physician clinically evaluated the response.

If the exact date is not known, use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](https://CIBMTR.org).

### Disease Assessments at Time of Best Response

For reporting purposes, the definition of “at the time of best response” depends on the reporting period. See Disease Assessment Time Windows below. Only consider assessments with samples collected within the time window which corresponds to the follow-up form being completed. If assessments were performed during the reporting period, but the samples were not collected within the indicated time window, consider them “Not done” when completing questions 4-34.

**Table 1. Disease Assessment Time Windows**

<table>
<thead>
<tr>
<th>Follow-Up Form</th>
<th>Approximate Time Window</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 Day</td>
<td>+ / – 15 days of date of best response (Question 3)</td>
</tr>
<tr>
<td>6 Month</td>
<td>+ / – 15 days of date of best response (Question 3)</td>
</tr>
<tr>
<td>Annual</td>
<td>+ / – 30 days of date of best response (Question 3)</td>
</tr>
</tbody>
</table>

**Question 4: Were tests for molecular markers performed (e.g. PCR, NGS)?**

**Negative Disease Assessments**

Prior versions of the ALL Post-Infusion Data Form have only permitted reporting of testing for molecular abnormalities known to be associated with the recipient’s ALL (i.e., only report testing that has been positive least once between diagnosis and the date of the assessment being reported). The wording of this question has been updated to include any testing for...
Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient’s primary disease. Testing for these sequences is often performed using PCR based methods; however, lower sensitivity testing, including FISH, may also be used to detect molecular markers. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include chromosomal microarray / chromosomal genomic array, Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

If testing for molecular markers was performed at the time of best response (see Table 1), report “Yes” and go to question 5.

If molecular marker testing was not performed at the time of best response or it is unknown if testing was done, report “No” or “Unknown” respectively and go to question 9.

**Question 5-8: Specify results**

For each molecular marker in questions 5-8, report whether testing was “Positive,” “Negative,” or “Not done.” If tests identified a molecular marker other than those listed in questions 5-6, report the result in question 7 and specify the marker in question 8.

If multiple “Other molecular marker[s]” were tested at the time of best response, report one instance (i.e., copy) of question 7-8 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” were tested, do the following:

- report one instance of question 7-8; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 8; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”

**Question 9: Was the disease status assessed via flow cytometry?**

Flow cytometry (immunophenotyping) is a technique that can be performed on blood, bone marrow, or
tissue preparations where cell surface markers can be detected on cellular material. Only testing performed on the blood or bone marrow may be reported in questions 10-17.

If flow cytometry was performed at the time of best response (see Table 1), report “Yes” and go to question 10.

If flow cytometry was not performed at the time of best response, report “no” and go to question 18.

**Question 10-13: Flow cytometry testing on blood**

Indicate whether flow cytometry was performed on peripheral blood at the time of best response (refer to Table 1). If “Yes,” report the date the sample was collected and whether disease was detected in questions 11 and 12 respectively. If disease was detected, report the percent disease detected (i.e., percent leukemic blasts) in question 13. Otherwise, go to question 14.

If flow cytometry was not performed on the blood at the time of best response, report “No” for question 10 and go to question 14.

**Question 14-17: Flow cytometry testing on bone marrow**

Indicate whether flow cytometry was performed on bone marrow at the time of best response. If “Yes,” report the date the sample was collected and whether disease was detected in questions 15 and 16 respectively. If disease was detected, report the percent disease detected (i.e., percent leukemic blasts) in question 17. Otherwise, go to question 18.

If flow cytometry was not performed on the bone marrow at the time of best response, report “No” for question 14 and go to question 18.

**Question 18: Were cytogenetics tested (karyotyping or FISH)?**

Prior versions of the ALL Post-Infusion Data Form have only permitted reporting of cytogenetic testing if it has been positive least once between diagnosis and the date of the assessment being reported. The wording of this question has been updated to include any cytogenetic testing regardless of previous or current test results. When completing questions 18-28, consider all cytogenetic testing performed at the time of best response (see Table 1 above). Testing may be reported in these fields even if it has never been positive.

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality which reflects the recipient’s disease.
Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C, Cytogenetic Assessments.

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

FISH is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA. These probes are mixed with cells from the recipient's blood or bone marrow. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells. Additionally, the FISH probe panel should reflect the patient’s current disease; FISH may be used as surveillance for changes associated with post-therapy malignancy.

FISH testing for sex chromosomes after sex-mismatched allogeneic HCT should not be considered a disease assessment as the purpose is to determine donor chimerism. Additionally, the FISH probe panel should reflect the patient’s current disease; FISH may be used as surveillance for changes associated with post-therapy malignancy.

If cytogenetic (karyotyping or FISH) studies were obtained at the time of best response (see Table 1), report “Yes” and go to question 19.

If cytogenetic studies were attempted at the time of best response, but there were not adequate cells (metaphases), report “No,” and go to question 30.

If no cytogenetic studies were obtained at the time of best response, indicate “No” and go to question 30.

If it is not known whether any cytogenetic studies were obtained at the time of best response, indicate “Unknown” and go to question 30.

**Question 19-20: Were cytogenetics tested via FISH?**

If FISH studies were performed at the time of best response (see Table 1), report “Yes” for question 19 and indicate whether clonal abnormalities were detected in question 20. If FISH studies were not performed, report “No” for question 19 and go to question 24. Examples of this include: no FISH study performed or FISH sample was inadequate.

**Question 21-23: Specify cytogenetic abnormalities (FISH)**

Report the number of abnormalities detected by FISH at the time of best response in question 21. After
indicating the number of abnormalities in question 21, select all abnormalities detected in questions 22-23. If a clonal abnormality is detected, but not listed as an option in question 22, select “Other abnormality” and specify the abnormality in question 23. If multiple “Other abnormalities” were detected, report “see attachment” in question 23 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 24-25: Were cytogenetics tested via karyotyping?**

If karyotyping was performed at the time of best response (see Table 1), report “Yes” for question 24 and indicate whether clonal abnormalities were detected in question 32. If karyotyping was not performed, indicate “No” and go to question 29. Examples of this include: karyotyping was not performed or karyotyping sample was inadequate.

**Question 26-28: Specify cytogenetic abnormalities (karyotyping)**

Report the number of abnormalities detected by karyotyping at the time of best response in question. After indicating the number of abnormalities in question 26, select all abnormalities detected in questions 27-28. If a clonal abnormality is detected, but not listed as an option in question 27, select “Other abnormality” and specify the abnormality in question 28. If multiple “Other abnormalities” were detected, report “see attachment” in question 28 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 29: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 18-28. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 30-34: Was the disease status assessed by other assessment?**

Indicate whether ALL was assessed by any method other than those included in questions 4-29 at the time of best response (see Table 1). If “Yes,” report the date assessed and specify the type of assessment in questions 31 and 32 respectively. Also indicate whether the reported assessment detected disease (question 33) and, if so, whether this was considered a disease relapse (question 34). If the exact date of assessment is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. If ALL was not assessed by any methods other than those included in questions 4-29, report “No” for question 30 and go to question 35.
Q35-47: Post-HCT / Post-Infusion Therapy

Question 35: Was therapy given since the date of last report for reasons other than relapse or persistent disease?

Indicate if the recipient received treatment post-infusion for reasons other than relapse or persistent disease during the current reporting period. Recipients generally receive a HCT / cellular therapy under a specific protocol which defines radiation and/or systemic therapy to be given prior to infusion; prophylactic medications to be administered pre- and/or post-infusion; as well as any systemic therapy, radiation, and/or other treatments to be administered post-infusion as planned (or maintenance) therapy. Planned (maintenance) therapy is given to assist in prolonging a remission. Planned therapy may be described in a research protocol or standard of care protocol. Refer to these documents (if available) when completing this section. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR, report the therapy in questions 35-47. Do not include any treatment administered as a result of relapse or persistent disease (including treatment for minimal residual disease).

If therapy was given for reasons other than relapse or persistent disease during the reporting period, report “Yes” and go to question 36. If “No” or “Unknown,” go to question 48.

Question 36-38: Central nervous system irradiation

Radiation therapy includes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. Radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes. If the recipient received radiation targeting part or all of the central nervous system (CNS), excluding total body irradiation, during the reporting period for reasons other than relapse or persistent disease, report “Yes” and report all CNS sites to which radiation therapy was administered since the date of the last report. If no radiation therapy was administered to the CNS, report “No” for question 36 and go to question 39.

Question 39: Intrathecal Therapy

Report “Yes” if the recipient received intrathecal therapy given for reasons other than minimal residual disease, persistent disease, or relapse during the reporting period. Otherwise, report “No.”

Question 40: Systemic therapy

Systemic therapy includes chemotherapy, immunotherapy, or targeted therapies delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally. Do not report total body irradiation or subsequent HCT / cellular therapies in questions 40-44. If the recipient received systemic therapy during the reporting period for reasons other than relapse or persistent disease,
report “Yes” and go to question 41. If not, report “No” and go to question 45.

Question 41-42: Date therapy (maintenance) was first started post-HCT / post-infusion

Form Revision Change
If maintenance therapy was started during a prior reporting period, for which, an ALL Post-HCT Data Form Revision 3 was completed, the start date will not have been reported on that form. In this case, report the date maintenance therapy was started on the current form (ALL Post-Infusion Data Form, Revision 4) and override the validation error using the code “Verified Correct.” If the reported maintenance therapy continues into the next reporting period, the site will indicate “Previously reported” in question 41.

If the recipient started systemic therapy for reasons other than relapse or persistent disease during the reporting period, report “Known” for question 41 and indicate the date started in question 42. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If the recipient started therapy for reasons other than relapse or persistent disease in a prior reporting period and continued the therapy into the current reporting period, report “Previously reported” and go to question 43.

For recipients who start and stop therapy multiple times post-infusion, first determine whether the recipient stopped therapy for at least 30 days. If not, consider the therapy continuous. Only report a new therapy start date if all three of the below conditions are met.

1. The recipient stopped all therapy given for reasons other than relapse or persistent disease during a prior reporting period; and
2. The recipient restarted therapy for reasons other than relapse or persistent disease during the current reporting period; and
3. Therapy was restarted at least 30 days after the therapy stop date.

Question 43-44: Specify systemic therapy given

Select all systemic therapy (see question 40 for definition) given for reasons other than relapse or persistent disease during the reporting period. If a therapy is given, but not listed as an option in question 43, select “Other systemic therapy” and specify the drug in question 44.

Question 45: Cellular therapy

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations,
administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells). Do not report a HCT as a cellular therapy in question 45.

Report “Yes” if the recipient received cellular therapy for reasons other than relapse or persistent disease during the reporting period. If not, report “No.”

**Question 46-47 Other therapy**

Indicate if the recipient received any other therapy (not already reported in questions 42-48) given for reasons other than relapse or persistent disease during the reporting period. Do not report HCT in questions 46-47. If “Yes,” specify all other therapies given in question 47. If “No,” go to question 48.
**Q48-94: Disease Detection Since Date of Last Report**

**Questions 48-94**

This section is intended to capture information only on recipients who relapse, have persistent or minimal residual disease in this reporting period. For questions 48, 54, 61, 71, and 78, report “No” or “Unknown” (see instructions below) if the recipient did not relapse, have persistent or minimal residual disease even if testing was performed. These results will be reported in questions 95-120.

Questions 48-94 are intended to capture the earliest instance of disease detection by each method of assessment performed during the reporting period. For each method of assessment, report “Yes” if that method detected the recipient’s ALL (or markers of ALL) during the reporting period. If testing by a particular method (e.g., molecular markers, cytogenetic, flow cytometry, etc.) was done, but did not show evidence of disease during the reporting period, report “No” for that method. If testing for molecular or cytogenetic markers / abnormalities was not done during the reporting period or it is not known whether testing was performed, report “Unknown” for those methods (question 48 and 61). If testing by flow cytometry, clinical / hematologic assessment, or other assessment was not done during the reporting period or it is not known whether testing was performed, report “No” for those methods (questions 54, 71, and 78).

If multiple tests by a particular method have demonstrated evidence of disease during the reporting period, report the date / result of the earliest positive assessment(s) performed during the reporting period.

**Question 48-49: Were tests for molecular markers performed (e.g. PCR, NGS)?**

See question 4 for a description of molecular testing. If any testing for molecular markers detected the recipient’s primary disease during the reporting period, report “Yes” for question 48 and report the date the sample was collected in question 49. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If molecular marker testing did not detect disease at any time during the reporting period, report “No” for question 48 and go to question 54.

If molecular marker testing was not performed during the reporting period, report “Unknown” go to question 53. If it is not known whether testing for molecular markers was performed during the reporting period, or the test results are not known, report “Unknown” and go to question 53.
**Question 50-53: Specify results**

For each molecular marker in questions 50-53, report whether testing was “Positive,” “Negative,” or “Not done.” If tests identified a molecular marker other than those listed in questions 50-51, report the result in question 52 and specify the marker in question 53. If multiple “Other molecular markers” were tested at the time of best response, report one instance (i.e., copy) of question 52-53 for each “Other molecular marker” tested. If greater than 3 “Other molecular marker[s]” are tested, do the following:

- report one instance of question 52-53; and
- report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
- report “see attachment” in question 53; and
- attach any / all reports documenting the results of testing for “Other molecular marker[s].”

**Question 54: Was the disease detected via flow cytometry?**

See question 9 for a description of flow cytometry. If flow cytometry detected the recipient’s primary disease at any time during the reporting period, report “Yes” and go to question 55. Report “No” and go to question 61 in either of the following cases:

- all flow cytometry assessments performed on the blood and marrow were negative for evidence of the recipient’s primary disease during the current reporting period; or
- flow cytometry testing was not performed on the blood or bone marrow during the reporting period.

**Question 55-57: Flow cytometry testing on blood**

Indicate whether flow cytometry detected disease in a blood sample at any time during the reporting period. If “Yes,” report the date the sample was collected and the percent disease detected (i.e., percent leukemic blasts) in questions 56 and 57 respectively. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. Report “No” for question 55 and go to question 58 in either of the following cases:

- all flow cytometry assessments performed on the blood were negative for evidence of the recipient’s primary disease during the current reporting period; or
- flow cytometry testing was not performed on the blood during the reporting period.

If multiple flow cytometry assessments performed on blood samples were positive for disease, report the date / results of the earliest positive assessment performed during the reporting period.
**Question 58-60: Flow cytometry testing on bone marrow**

Indicate whether flow cytometry detected disease in a bone marrow sample at any time during the reporting period. If “Yes,” report the date the sample was collected and the percent disease detected (i.e., percent leukemic blasts) in questions 59 and 60 respectively. If the exact date is not known, use the process for reporting partial or unknown dates as described in the [General Instructions, Guidelines for Completing Forms](https://www.cibmtr.org/forms-instruction-manual). Report “No” for question 58 and go to question 61 in either of the following cases:

- all flow cytometry assessments performed on the marrow were negative for evidence of the recipient’s primary disease during the current reporting period; or
- flow cytometry testing was not performed on the marrow during the reporting period.

If multiple flow cytometry assessments performed on bone marrow samples were positive for disease, report the date and results of the earliest positive assessment performed during the reporting period.

**Question 61: Was disease detected by cytogenetic testing (karyotyping or FISH)?**

Refer to [question 18](https://www.cibmtr.org/forms-instruction-manual) for a description of cytogenetic studies. If cytogenetic testing detected the recipient’s primary disease at any time during the reporting period, report “Yes” and go to question 62. If all cytogenetic testing was negative for evidence of the recipient’s primary disease during the current reporting period, report “No” and go to question 71. Report “Unknown” for question 70 and go to question 71 in any of the following cases:

- cytogenetic testing was not performed during the reporting period; or
- cytogenetic testing was attempted, but no assessments could be performed during the reporting period (e.g., insufficient sample); or
- it cannot be determined whether cytogenetic testing was performed during the reporting period.

**Question 62-63: Were cytogenetic abnormalities identified via FISH?**

Indicate whether FISH studies detected disease at any time during the reporting period. If “Yes,” report the date the sample was collected in question 63 and go to question 64. If the exact date is not known, use the process for reporting partial or unknown dates as described in the [General Instructions, Guidelines for Completing Forms](https://www.cibmtr.org/forms-instruction-manual). Report “No” for question 62 and go to question 66 in any of the following cases:

- FISH testing was not performed during the reporting period; or
- FISH testing was attempted, but no assessments could be performed during the reporting period (e.g., insufficient sample); or
- it cannot be determined whether FISH testing was performed during the reporting period.
If multiple FISH assessments were positive for disease, report the date / results of the earliest positive assessment performed during the reporting period.

**Question 64-65: Specify cytogenetic abnormalities (FISH)**

Select all clonal cytogenetic abnormalities detected by FISH on the date reported in question 63. If an abnormality is detected, but not listed as an option in question 64, select “Other abnormality” and specify the abnormality in question 65. If multiple “Other abnormalities” were detected by FISH at the time of best response, report “see attachment” in question 65 and attach a copy of the FISH report. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 66-67: Were cytogenetic abnormalities identified via karyotyping?**

Indicate whether karyotyping studies detected disease at any time during the reporting period. If “Yes,” report the date the sample was collected in question 67 and go to question 68. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. Report “No” for question 66 and go to question 70 in any of the following cases:

- karyotyping was not performed during the reporting period; or
- karyotyping was attempted, but no assessments could be performed during the reporting period (e.g., insufficient sample); or
- it cannot be determined whether karyotyping was performed during the reporting period.

If multiple karotypes were positive for disease, report the date / results of the earliest positive assessment performed during the reporting period.

**Question 68-69: Specify cytogenetic abnormalities (karyotyping)**

Select all clonal cytogenetic abnormalities detected by karyotyping on the date reported in question 68. If an abnormality is detected, but not listed as an option in question 68, select “Other abnormality” and specify the abnormality in question 69. If multiple “Other abnormalities” were detected by karyotyping at the time of best response, report “see attachment” in question 69 and attach a copy of the karyotype report. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 70: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the reported cytogenetic findings in
question 61-69. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 71-72: Was disease detected by clinical / hematologic assessment?**

Clinical / hematologic assessments include, but are not limited to, biopsies, imaging assessments, complete blood counts, and physical exams. If clinical / hematologic testing detected disease during the reporting period, report “Yes” for question 71 and report the date of the positive assessment in question 72. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If multiple clinical / hematologic assessments detected disease, report the date of the earliest positive assessment performed during the reporting period.

**Question 73-77: Specify Sites of Disease**

Report “Yes” for each site where disease was detected by clinical / hematologic methods on the date reported in question 72. If clinical / hematologic assessments detected disease at a site not specified in questions 73-75, report “Yes” for question 76 and specify all other sites where disease was detected on the date reported in question 77.

Report “No” if a site:

- was not tested during the reporting period; or
- was tested during the reporting period, but disease was not detected.

**Question 78-80: Was the disease status assessed by other assessment?**

Indicate whether the recipient’s primary disease was assessed by any method other than those included in questions 48-77 during the reporting period. If “Yes,” report the date assessed and specify the type of assessment in questions 79 and 80 respectively. If the exact date of assessment is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. If ALL was not assessed by any methods other than those included in questions 48-77, report “No” for question 88 and go to question 81.

**Question 81: Was intervention given for relapsed disease or progressive disease, or minimal residual disease? (since the date of last report)**

Indicate if the recipient received treatment post-infusion for minimal residual disease, persistent disease, or relapse since the date of last report. If “Yes,” go to question 82. If “No,” go to question 95. See question 82...
for definitions each of these indications for treatment.

**Question 82: Specify reason for which intervention was given**

Select the indication for which treatment was administered during the reporting period. See below for definitions of each indication.

**Minimal Residual Disease:** Recipient is in hematologic CR, but has evidence of disease by more sensitive assessments including molecular, flow cytometry or cytogenetic methods.

** Persistent Disease:** The recipient was in primary induction failure or relapse at the time of infusion and has not achieved a hematologic CR post-infusion.

**Relapsed Disease:** The recipient was in CR at the time of infusion or the recipient achieved a CR post-infusion. In either case, treatment is administered for a relapse which occurred post-infusion.

**Question 83: Central nervous system irradiation**

See question 36 for a description of central nervous system (CNS) irradiation. If the recipient received CNS irradiation to treat minimal residual disease, persistent disease, or relapse during the reporting period, report “Yes.” If not, report “No.”

**Question 84: Intrathecal Therapy**

See question 39 for a description of intrathecal therapy. If intrathecal therapy was given as part of treatment for minimal residual disease, persistent disease, or relapse, report “Yes.” If not, report “No.”

**Question 85: Systemic therapy**

See question 40 for a description of systemic therapy. Do not report total body irradiation or subsequent HCT / cellular therapies in questions 85-89. If the recipient received systemic therapy during the reporting period for minimal residual disease, persistent disease, or relapse, report “Yes” and go to question 86. If not, report “No” and go to question 90.

**Question 86-87: Date therapy was first started post-HCT / post-infusion**

*Form Revision Change*

If maintenance therapy was started during a prior reporting period, for which, an ALL Post-HCT Data Form Revision 3 was completed, the start date will not have been reported on that form. In this case, report the date maintenance therapy was started on the current form (ALL Post-Infusion Data Form, Revision 4) and override the validation error using the
If the recipient started systemic therapy for minimal residual disease, persistent disease, or relapse during the reporting period, report “Known” for question 86 and indicate the date started in question 87. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If the recipient started therapy for minimal residual disease, persistent disease, or relapse in a prior reporting period and continued the therapy into the current reporting period, report “Previously reported” and go to question 88.

For recipients who start and stop therapy multiple times post-infusion, first determine whether the recipient stopped therapy for at least 30 days. If not, consider the therapy continuous. Only report a new therapy start date if all three of the below conditions are met

1. The recipient stopped all therapy given for minimal residual disease, persistent disease, or relapse during a prior reporting period; and
2. The recipient restarted therapy for minimal residual disease, persistent disease, or relapse during the current reporting period; and
3. Therapy was restarted at least 30 days after the therapy stop date.

**Question 88-89: Specify systemic therapy given**

Select all systemic therapy (see question 40 for definition) given for minimal residual disease, persistent disease, or relapse during the reporting period. If a therapy is given, but not listed as an option in question 88, select “Other systemic therapy” and specify the drug in question 89.

**Question 90: Cellular therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “Yes” if the recipient received cellular therapy as treatment for minimal residual disease, persistent disease, or relapse during the reporting period. If not, report “No.”

**Question 91: Subsequent HCT**

Indicate whether the recipient received a HCT since the date of the last report (or since infusion if
completing this is the 100 day follow-up form). Hematopoietic stem cells (HSC) are defined as mobilized peripheral blood stem cells, bone marrow, or cord blood. The source of HSC may be allogeneic unrelated, allogeneic related, or autologous. For more information on how to distinguish infusion types (example: HCT versus DCI), see Appendix D.

Question 92: Accelerated withdrawal of immunosuppression

Immunosuppressive medications may be tapered or entirely withdrawn in order to promote a graft vs leukemia effect in the setting of relapsed, progressive, or persistent disease. For reporting purposes, accelerated withdrawal is defined as any decrease in immunosuppression to promote graft versus leukemia effect.

If the recipient undergoes an accelerated withdrawal immunosuppression during the reporting period in order to treat disease, report “yes.” If not, report “no.”

Question 93-94: Other therapy

Indicate if the recipient received any other treatment for minimal residual disease, persistent disease, or relapse during the reporting period. If “Yes,” specify the type of treatment administered in question 94. If “No,” go to question 95.
Q95-130: Disease Status at the Time of Evaluation for This Reporting Period

Question 95: Does the current disease status reflect the disease detected in this reporting period section (as captured in questions 51-89), without subsequent therapy?

This section of the form is intended to capture the most recent disease assessment. The most recent disease assessments may have already been reported in questions 48-80 and, if that is the case, it is not necessary to report those same disease assessments in questions 95-128. Refer to the instructions below to determine how to complete this section of the form. Reporting scenarios have also been provided below.

Report “Yes” for question 95 and go to question 129 if the most recent disease assessments have already been reported in questions 48-80. Also, report “Yes” for question 95 and go to question 129 if assessments were reported in questions 48-80 and no therapy was given to treat disease between the date(s) of the reported assessments and the date of contact for this reporting period.

Report “No” for question 95 and go to question 96 in any of the following scenarios:

- disease was not detected by any method of assessment during the reporting period; or
- disease was detected by at least one method of assessment during the reporting period (reported in questions 48-80), but the most recent assessments have not yet been reported on the form.

Report “Not applicable” for question 95 and submit the form if the disease was not assessed during the reporting period. Only report this option if the recipient did not have any disease evaluations, including a physical exam by their primary care provider, performed during the reporting period. Obtain clarification from your center’s liaison if there are questions regarding whether a visit or test should be reported as a disease assessment.

Disease Status Evaluation Reporting Scenarios:

A. A recipient has a bone marrow assessment on D+30 (1/15/2016) including morphology review, flow cytometry, and PCR testing for FLT3-ITD (FLT3-ITD was detected at diagnosis). Disease was not detected by any of these three assessments. Subsequently, on D+95 (3/20/2016), a repeat bone marrow assessment is performed including morphology and flow cytometry. Testing for molecular markers is not done. Both assessments (morphology and flow) are negative. The date of contact for the 100 Day Follow-Up Form is 3/20/2016.
100 Day Follow-Up Form:

Questions 48-80: No assessments will be reported here since the recipient’s disease did not relapse, did not persist or have evidence of minimal residual disease. In this scenario, questions 51, 63, 70, 80, and 87 must be answered “No”.

Question 95: Report “No” for question 95. Disease was not detected by any method of assessment during the reporting period.

Questions 96-128: Report the results of the most recent assessment by each method including:

- PCR testing for FLT3-ITD performed on 1/15/2016.
- Flow cytometry testing performed on the bone marrow on 3/20/2016.
- Morphology review performed on the bone marrow on 3/20/2016.

B. A recipient has a bone marrow assessment on D+30 (1/15/2016) including morphology review, flow cytometry, and PCR testing for FLT3-ITD (FLT3-ITD was detected at diagnosis). Disease was not detected by any of these three assessments. Subsequently, on D+95 (3/20/2016), all three tests are repeated and are positive indicating disease relapse. The date of contact for the 100 Day Follow-Up Form is 3/20/2016.

100 Day Follow-Up Form:

Questions 48-80: All three disease assessments performed on 3/20/2016 (PCR test for FLT3-ITD as well as morphology and flow cytometry on the bone marrow) will be reported because they were the earliest positive assessments of disease during the reporting period.

Question 95: Report “Yes” for question 95. The most recent assessments have already been reported in questions 48-80.

Questions 96-128: These questions will be left blank.

C. A recipient has a bone marrow assessment on D+30 (1/15/2016) including morphology review, flow cytometry, and PCR testing for FLT3-ITD (FLT3-ITD was detected at diagnosis). Disease was not detected by any of these three assessments. Subsequently, on D+95 (3/20/2016), a repeat bone marrow assessment is performed including morphology and flow cytometry. Testing for molecular markers is not done. Both assessments (morphology and flow) are positive indicating disease relapse. The date of contact for the 100 Day Follow-Up Form is 3/20/2016.

100 Day Follow-Up Form:

Questions 48-80: Morphology and flow cytometry assessments of the bone marrow on 3/20/2016 will be reported because they were the earliest positive assessments of disease during the reporting period. Testing for molecular markers was not done at the time of relapse and should not be reported here.

Question 95: Report “Yes” for question 95 since the most recent test results were reported in Q48-80.

Questions 96-128: These questions will be left blank.
D. A recipient has a bone marrow assessment on D+30 (1/15/2016) including morphology review, flow cytometry, and PCR testing for FLT3-ITD. All three assessments detect disease. Subsequently, on D+95 (3/20/2016), a repeat bone marrow assessment is performed including morphology and flow cytometry. Testing for molecular markers is not done. Both assessments (morphology and flow) are again positive for disease. The date of contact for the 100 Day Follow-Up Form is 3/20/2016.

100 Day Follow-Up Form:

Questions 48-80: All three disease assessments performed on 1/15/2016 (PCR test for FLT3-ITD as well as morphology and flow cytometry on the bone marrow) will be reported because they were the earliest positive assessments of disease during the reporting period.

Question 95-128: Report “Yes” for question 95 and leave questions 96-128 blank if no therapy was given to treat the disease between 1/15/2016 and 3/20/2016. If therapy was used to treat the disease during this time frame, “No” and report the most recent test results in questions 96-128.

Question 96: Were tests for molecular markers performed (e.g. PCR, NGS)?

Negative Disease Assessments
Prior versions of the ALL Post-Infusion Data Form have only permitted reporting of testing for molecular abnormalities known to be associated with the recipient’s ALL (i.e., only report testing that has been positive least once between diagnosis and the date of the assessment being reported). The wording of this question has been updated to include any testing for molecular markers of ALL regardless of previous or current test results. When completing questions 96-100, consider all testing for molecular markers performed during the reporting period. Testing may be reported in these fields even if it has never been positive.

Refer to question 4 for a description of testing for molecular markers. If molecular testing was performed during the reporting period, report “Yes” and go to question 97. If testing was not performed during the reporting period or it is not known whether testing was performed, report “No” or “Unknown” respectively and go to question 101.

Question 97-100: Specify results

For each molecular marker in questions 97-98, report whether testing was “Positive,” “Negative,” or “Not done” at the time of the most recent assessment during the reporting period. If the most recent testing performed during the reporting period identified a molecular marker other than those listed in questions 97-98, report the result in question 99 and specify the marker in question 100.

If multiple “Other molecular marker[s]” were tested at the time of best response, report one instance (i.e., copy) of question 99-100 for each “Other molecular marker” tested. If greater than 3 “Other molecular
marker[s]" were tested, do the following:

  - report one instance of question 99-100; and
  - report “Positive” if any of the “Other molecular marker[s]” were positive, otherwise, report “Negative;” and
  - report “see attachment” in question 100; and
  - attach any / all reports documenting the results of testing for “Other molecular marker[s].”

**Question 101: Was the disease status assessed via flow cytometry?**

Refer to [question 9](#) for a description of flow cytometry. Only testing performed on the blood or bone marrow may be reported in questions 101-109. If flow cytometry was performed on the blood and / or bone marrow during the reporting period, report “Yes” and go to question 101. If testing was not performed during the reporting period, report “No” and go to question 106.

**Question 102-105: Flow cytometry testing on blood**

If flow cytometry was performed on the blood during the reporting period, report “Yes” for question 102 and go to question 103. If testing was not performed during the reporting period, report “No” and go to question 106.

If “Yes” has been reported for question 102, report the date of collection and results for the most recent assessment performed during reporting period in questions 103 and 104 respectively. If disease was detected by the most recent assessment, report the percent disease detected (i.e., percent leukemic blasts) in question 105. Otherwise, go to question 106.

**Question 106-109: Flow cytometry testing on bone marrow**

If flow cytometry was performed on the bone marrow during the reporting period, report “Yes” for question 106 and go to question 107. If testing was not performed during the reporting period, report “No” and go to question 110.

If “Yes” has been reported for question 106, report the date of collection and results for the most recent assessment performed during reporting period in questions 107 and 108 respectively. If disease was detected by the most recent assessment, report the percent disease detected (i.e., percent leukemic blasts) in question 109. Otherwise, go to question 110.
Question 110: Were cytogenetics tested (karyotyping or FISH)?

Negative Disease Assessments
Prior versions of the ALL Post-Infusion Data Form have only permitted reporting of cytogenetic testing if it has been positive least once between diagnosis and the date of the assessment being reported. The wording of this question has been updated to include any cytogenetic testing regardless of previous or current test results. When completing questions 110-120, consider all cytogenetic testing performed during the reporting period. Testing may be reported in these fields even if it has never been positive.

Refer to question 18 for a description of cytogenetic testing. If cytogenetic testing was performed during the reporting period, report “Yes” and go to question 111. If testing was not performed during the reporting period or it is not known whether testing was performed, report “No” or “Unknown” respectively and go to question 122.

If cytogenetic studies were attempted during the reporting period, but there were not adequate cells (metaphases) for any cytogenetic assessments, report “No,” and go to question 122.

Question 111-112: Were cytogenetics tested via FISH?

If FISH studies were performed during the reporting period, report “Yes” and indicate whether clonal abnormalities were detected on the most recent assessment in the reporting period in question 112. If FISH studies were not performed, report “No” for question 111 and go to question 116. Examples of this include: no FISH study performed or FISH sample was inadequate.

Question 113-115: Specify cytogenetic abnormalities (FISH)

Report the number of clonal abnormalities detected by the most recent FISH assessment in the reporting period in question 113. After indicating the number of abnormalities in question 113, select all clonal abnormalities detected in questions 114-115.

If a clonal abnormality is detected on the most recent FISH assessment in the reporting period, but not listed as an option in question 114, select “Other abnormality” and specify the abnormality in question 115. If multiple “Other abnormalities” were detected, report “see attachment” in question 115 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 116-117: Were cytogenetics tested via karyotyping?

If karyotyping was performed during the reporting period, report “Yes” for question 116 and indicate whether
clonal abnormalities were detected in question 117. If karyotyping was not performed, indicate “No” for question 116 and go to question 121. Examples of this include: karyotyping was not performed or karyotyping sample was inadequate.

**Question 118-120: Specify cytogenetic abnormalities (karyotyping)**

Report the number of clonal abnormalities detected by the most recent karyotype in the reporting period in question 118. After indicating the number of clonal abnormalities in question 118, select all abnormalities detected in questions 119-120.

If a clonal abnormality is detected on the most recent karyotype during the reporting period, but not listed as an option in question 119, select “Other abnormality” and specify the abnormality in question 120. If multiple “Other abnormalities” were detected, report “see attachment” in question 120 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 121: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping or FISH testing report is attached to support the cytogenetic findings reported in questions 110-120. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 122-124: Was disease detected by clinical / hematologic assessment?**

Clinical / hematologic assessments include, but are not limited to, biopsies, imaging assessments, complete blood counts, radiographic studies and physical exams. If clinical / hematologic testing was performed during the reporting period, report “Yes” for question 122 and report the date and result in questions 123 and 124 respectively. The date and results reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). Indicate the date the sample was collected for examination for pathological and laboratory evaluations; enter the date of physical examination. If no disease assessments were performed within approximately 30 days prior to the date of contact, report the results and date of the most recent assessment performed during the reporting period. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If no clinical / hematologic assessments (including a physical exam by the recipient’s primary care provider) were performed during the reporting period, report “No” for question 122 and go to question 125.

**Question 125-128: Was the disease status assessed by other assessment?**

Indicate in question 125 whether ALL was assessed by any method other than those included in questions
96-124 during the reporting period. If “Yes,” report the date of assessment and specify the type of assessment in questions 126 and 127 respectively. Also report the results of the assessment in question 128. If the exact date of assessment is not known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms. If ALL was not assessed by any methods other than those included in questions 96-124, report “No” for question 125 and go to question 129.

**Question 129: What is the current disease status?**

Indicate the hematologic disease status of ALL as of the last evaluation during the reporting period. Determine the current disease status using the international working group criteria provided in the ALL Response Criteria of the Forms Instructions Manual. Report “Complete Remission” for recipients who meet the criteria for complete remission (CR). Do not consider testing for molecular markers, testing for cytogenetic abnormalities, or testing by flow cytometry when reporting the hematologic disease status in question 129.

Some clinical judgment is required for evaluating whether a recipient meets the CR criteria, specifically neutrophil, platelet, and transfusion parameters. If a recipient does not meet these specifications, the underlying cause should be assessed; if the cause for not meeting one of these parameters is felt to be due to a reason other than underlying leukemia, such as renal insufficiency, hemolysis, or drug-related causes, the disease status may be reported as “complete remission.” If the cause for not meeting the parameters is judged to be leukemia-related, the disease status should be reported as “not in complete remission.”

If the recipient did not meet the criteria for CR report “Not in complete remission.”

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

**Question 130: Date assessed**

Enter the date of the most recent assessment establishing disease status within the reporting period. The date reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). In addition to clinician evaluation and physical examination, clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory analysis (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluation; the date the imaging took place for radiographic assessments, or the date of physical examination.
2012/2112: Chronic Myeloid Leukemia (CML)

Chronic myelogenous leukemia (CML) is a slow-progressing cancer of the myeloid white blood cells. It is characterized by the increased proliferation of immature white blood cells (granulocytes) with damaged DNA, or blasts, which accumulate in the blood and bone marrow. Normal blasts develop into white blood cells which function to fight infection. The symptoms of CML are caused by the replacement of normal bone marrow with leukemic cells, resulting in a drop in red blood cells, platelets, and normal white blood cells.

The Chronic Myelogenous Leukemia Pre-infusion Data Form is one of the Comprehensive Report Forms. This form captures CML-specific pre-infusion data such as: the recipient's hematologic and cytogenetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-infusion treatments administered, and disease status prior to the preparative regimen.

The Chronic Myelogenous Leukemia Post-Infusion Data Form (Form 2112) is one of the Comprehensive Report Forms. This form captures CML-specific post-infusion data such as: the recipient's best response to HCT or cellular therapy; planned treatments post-infusion; disease relapse data including treatment administered for relapse or persistent disease; and disease status for the reporting period.

CML Response Criteria
2012: CML Pre-Infusion
2112: CML Post-Infusion
CML Response Criteria

Complete Hematologic Remission (CR)

A treatment response where all of the following criteria are met:

- White blood count is $< 10 \times 10^9/L$, without immature granulocytes and with $< 5\%$ basophils
- Platelet count $< 450 \times 10^9/L$
- Non-palpable spleen

Chronic Phase

Characterized by relatively few blasts ($<10\%$) present in the blood and bone marrow. Symptoms are often not present. The chronic phase may last several months to years, depending on the recipient and the treatment they receive.

Accelerated Phase

One or more of the following must be present:

- 10%-19% blasts in blood or marrow
- $\geq 20\%$ basophils in peripheral blood
- Clonal marrow cytogenetic abnormalities in addition to the single Philadelphia chromosome (clonal evolution)
- Increasing spleen size, unresponsive to therapy
- Increasing WBC, unresponsive to therapy
- Thrombocytopenia (platelets $< 100,000$), unrelated to therapy
- Thrombocytosis (platelets $> 1,000,000$), unresponsive to therapy

Blast Phase

Characterized by having $\geq 20\%$ blasts (formerly $\geq 30\%$) in the peripheral blood or bone marrow. Having extramedullary blastic infiltrates (i.e., myeloid sarcoma, granulocytic sarcoma, or chloroma) also qualifies as blast phase. The red cell, platelet, and neutrophil counts may decrease and episodes of infection and bleeding may result. Symptoms such as fatigue, shortness of breath, abdominal pain, bone pain, and spleen enlargement may occur.

When tiredness, fever, and an enlarged spleen occur during the blast phase, it is called blast crisis.¹ Blast crisis is similar to acute leukemia in its signs and its effects on the recipient, and can involve lymphoid or
myeloid lineages (so-called lymphoid blast crisis or myeloid blast crisis). For reporting purposes, blast crisis should be reported as blast phase on the CIBMTR data collection forms.

**Relapse**

For reporting purposes, relapse is defined as recurrence of disease after complete hematologic remission. In general, relapse should be confirmed by a clinical / hematologic assessment (e.g., pathology, CBC, or clinical exam).

Do not report recurrence of disease by molecular, cytogenetic (karyotype / FISH), or flow cytometry assessment as relapse unless the findings are documented as such by the primary care provider. If the findings are not addressed in the available notes, request documentation from the primary care provider.

**Progression**

For reporting purposes, progression is defined as any of the following changes in disease status:

- Advancement from **chronic phase** to **accelerated phase**.
- Advancement from **chronic phase** to **blast phase**.
- Advancement from **accelerated phase** to **blast phase**.

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**2012: CML Pre-Infusion Data**

Chronic myelogenous leukemia (CML) is a slow-progressing cancer of the myeloid white blood cells. It is characterized by the increased proliferation of immature white blood cells (granulocytes) with damaged DNA, or blasts, which accumulate in the blood and bone marrow. Normal blasts develop into white blood cells which function to fight infection. The symptoms of CML are caused by the replacement of normal bone marrow with leukemic cells, resulting in a drop in red blood cells, platelets, and normal white blood cells.

The Chronic Myelogenous Leukemia Pre-infusion Data Form is one of the Comprehensive Report Forms. This form captures CML-specific pre-infusion data such as: the recipient's hematologic and cytogenetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-infusion treatments administered, and disease status prior to the preparative regimen.

This form must be completed for all recipients whose primary disease, reported on Pre-TED Disease Classification Form (Form 2402), is CML. This includes CML with the following chromosomal abnormalities: Philadelphia chromosome, complex variation and/or variant form, or BCRABL gene rearrangement.

This form must be completed for all recipients whose primary disease, reported on Pre-TED Disease Classification Form (Form 2402), is CML. This includes CML with the following chromosomal abnormalities: Philadelphia chromosome, complex variation and/or variant form, or BCR/ABL gene rearrangement. The CML Post-Infusion Data Form must be completed in conjunction with each Post-Infusion Data Form (Form 2100) completed. The post-infusion forms are designed to capture specific data occurring within the timeframe of each reporting period (i.e. between day 0 and day 100 date of contact for the 100 day follow-up, between day 100 date of contact and the six-month date of contact for the six-month follow-up, etc.).

**Is this the report of a second or subsequent transplant or cellular therapy for the same disease?**

Report “no” and go to question 1 in any of the following cases:

- This is the first infusion reported to the CIBMTR;
- This is a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than Chronic Myelogenous Leukemia);
- This is a second or subsequent infusion for the same disease subtype and if this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior infusion, prior infusion was autologous with no consent, etc.).

If this is a report of a second or subsequent infusion for the same disease and this baseline CML disease insert was completed previously, report “yes” and go to question 186.
Links to Sections of Form:

Q1-17: Disease Assessment at Diagnosis  
Q18-83: Laboratory Studies at Diagnosis  
Q84-185: Pre-HCT or Pre-Infusion Therapy  
Q186-191: Disease Assessment at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion  
Q192-252: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion  
Q253-256: Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

Manual Updates:

Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text. If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/24/17</td>
<td>2012: CML Pre-Infusion Data Form</td>
<td>Modify</td>
<td>Corrected an error in Table 3 by adding the text in red below to the definition of complex variation. Translocation of three or more chromosomes, one of which must be chromosome 22 [e.g., t(3; 9; 22)]</td>
</tr>
</tbody>
</table>
**Q1-17: Disease Assessment at Diagnosis**

**Question 1: What was the date of diagnosis?**

Report the date of the first pathological diagnosis (e.g., bone marrow) of CML. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathologic or laboratory assessment is available, the dictated date of diagnosis within a physician’s note may be reported. The date of diagnosis is important because the interval between diagnosis and HCT or cellular therapy is often a significant indicator for the recipient’s prognosis post-infusion.

If the exact pathologic diagnosis date is unknown, use the process described for reporting partial or unknown dates in General Instructions, *General Guidelines for Completing Forms*.

**Question 2: What was the disease status? (at diagnosis)**

The pre-infusion disease status/phase is determined by a disease assessment, such as hematologic testing, pathology study, and/or physician assessment.

**WHO definition of CML phases:**

- **Chronic phase:** Peripheral blood blasts less than 10% in the blood and bone marrow

- **Accelerated phase:** Blasts 10-19% of WBCs in peripheral and/or nucleated bone marrow cells; persistent thrombocytopenia (<100 x 10^9>1000 x 10^9/L) unresponsive to therapy; increasing WBCs and spleen size unresponsive to therapy; cytogenetic evidence of clonal evolution

- **Blast phase:** Peripheral blood blasts >20% of peripheral blood white blood cells or nucleated bone marrow cells; extramedullary blast proliferation; and large foci or clusters of blasts on bone marrow biopsy.

If the recipient’s disease status at diagnosis is **chronic phase**, go to question 3.

If the recipient’s disease status at diagnosis is **accelerated phase**, go to question 10.

If the recipient’s disease status at diagnosis is **blast phase**, go to question 9.

**Question 3-8: Specify the chronic phase risk score? (at diagnosis)**

The risk score for recipients in chronic phase at the time of diagnosis may be determined using different
formulas. Report the formula and score as documented in the provider notes. If a score is not provided in the available documentation, have the primary care provider at your facility determine whether a score can be determined. The criteria for three common scales are provided below for reference.

Table 1. CML Prognostic Score

<table>
<thead>
<tr>
<th>Formula</th>
<th>Score Calculation</th>
<th>Risk Assignment</th>
</tr>
</thead>
</table>
| EUTOS¹  | 4 x spleen size (cm below costal margin) +7 x basophils (% in peripheral blood) | ≤ 87 low
|         |                   | > 87 high       |
| Hasford²| 0.6666 x age (0 when < 50 years, 1 otherwise) + 0.042 x spleen size (cm below costal margin) + 0.0584 x percent blasts + 0.0413 x percent eosinophils + 0.2039 x basophils (0 when < 3%, 1 otherwise) + 1.0956 x platelet count (0 when <1500, 1 otherwise) x 100 | ≤ 780 low
|         |                   | > 780 and ≤ 1480 intermediate
|         |                   | >1480 high      |
| Sokal²  | 0.0116 x (age in years – 4.34) + 0.0345 (spleen – 7.51) + 0.188 ((platelets / 700)^2 – 0.563) + 0.0887 (percentage of blasts – 2.1) | < 0.8 good prognosis
|         |                   | 0.8-1.2 moderate prognosis
|         |                   | >1.2 poor prognosis |

¹ EUTOS: http://www.eutos.org/content/home/eutos_score/index_eng.html
² Hasford and Sokal: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1731441/pdf/v054p00491.pdf

Once a scale has been reported in question 3, report the documented risk score in the corresponding field (questions 4-7). If “other” was reported for the scale (question 3), the center must specify the scale used in question 8.

**Question 9: Specify the blast phenotype?**

Question 9 should only be answered if “blast phase” has been reported in question 3. Assessments performed on the bone marrow or peripheral blood may be used to determine the blast phenotype at the time of best response. Indicate which phenotype was detected. If phenotype cannot be determined from the assessments performed, report “unknown.”

**Question 10-11: Specify the criteria used to establish accelerated phase or blast phase**

Multiple accelerated and blast phase criteria are currently available. Report the criteria used to confirm the recipient was in accelerated / blast phase at the time of diagnosis. If the criteria used to confirm the recipient’s disease status are not specified in the available documentation, ask the primary care provider to
confirm the disease status and document the criteria used. Below is a summary of accelerated phase as defined by four separate institutions: World Health Organization (WHO), International Bone Marrow Transplant Registry (IBMTR), MD Anderson Cancer Center (MDACC), and The European LeukemiaNet (ELN).

Table 2. Accelerated Phase Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>WHO</th>
<th>IBMTR</th>
<th>MDACC</th>
<th>ELN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blasts</td>
<td>PB or BM 10-19%</td>
<td>PB or BM ≥ 10%</td>
<td>PB or BM 10-19%</td>
<td>PB or BM 15-29%</td>
</tr>
<tr>
<td>Blasts and Promyelocytes</td>
<td>NA</td>
<td>PB or BM ≥ 20%</td>
<td>≥ 30%</td>
<td>≥ 30% with blasts &lt; 30%</td>
</tr>
<tr>
<td>Basophils</td>
<td>PB ≥ 20%</td>
<td>PB ≥ 20%</td>
<td>PB or BM ≥ 20%</td>
<td>PB ≥ 20%</td>
</tr>
<tr>
<td>Platelets</td>
<td>&gt; 1000 × 10^9 / L or &lt; 100 × 10^9 / L, unresponsive to therapy</td>
<td>Persistent thrombocytosis</td>
<td>&gt; 1000 × 10^9 / L or &lt; 100 × 10^9 / L, unresponsive to therapy</td>
<td>Persistent thrombocytopenia (&lt; 100 × 10^9 / L) unrelated to therapy</td>
</tr>
<tr>
<td>WBC</td>
<td>Increasing WBC count unresponsive to therapy</td>
<td>Difficult to control</td>
<td>&gt; 10 × 10^9</td>
<td>NA</td>
</tr>
<tr>
<td>Anemia</td>
<td>NA</td>
<td>Unresponsive to therapy</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Splenomegally</td>
<td>Increasing spleen size</td>
<td>Increasing spleen size</td>
<td>Persistent splenomegaly unresponsive to sustained therapy</td>
<td>NA</td>
</tr>
<tr>
<td>Cytogenetic</td>
<td>CE no present at time of diagnosis</td>
<td>CE</td>
<td>NA</td>
<td>Clonal chromosome abnormalities in Ph+ cells (CCA / Ph1), major route, on treatment</td>
</tr>
<tr>
<td>Others</td>
<td>Large foci or clusters of blasts in bone marrow biopsy</td>
<td>Myelofibrosis, chloromas</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

Blast Phase

**WHO Criteria**

One or more of the following must be present:

- Blasts in blood or marrow ≥ 20%
- Extramedullary blast proliferation, apart from spleen
- Large foci or clusters of blasts in the bone marrow biopsy

**European Leukemia Net Criteria**

One or more of the following must be present:

- Blasts in blood or marrow ≥ 30%
- Extramedullary blast proliferation, apart from spleen

If the criteria used to confirm the recipient’s disease status at diagnosis are not included in the option choices for question 10, report “other” and indicate the criteria used in question 11. Otherwise, go to question 12.

If the recipient’s disease status at diagnosis is documented as accelerated phase or blast phase, but the criteria used were not documented, ask the primary care provider to confirm whether the criteria can be determined. If not, report “unknown” and go to question 12.

**Question 12: Specify the spleen size**

Report the recipient’s spleen size below the left costal margin, in centimeters, at the time of diagnosis. If the physical exam at diagnosis does not find any evidence of splenomegaly, report “0.” If the physical exam findings at diagnosis are not documented, leave question 12 blank and override the validation error using the code “unknown.” If the recipient had a splenectomy prior to their CML diagnosis, leave question 12 blank and override the validation error using the code “not applicable.”

**Question 13-17: Did the recipient have extramedullary leukemia at diagnosis?**

Extramedullary refers to disease found in organs or tissue outside the bone marrow or blood stream (e.g. central nervous system, skin, soft tissue, etc.). Examples of extramedullary disease in CML patients include granulocytic sarcoma, subcutaneous nodules, leukemia cutis, and meningeal leukemia. If there is evidence of extramedullary disease at the time of diagnosis, indicate “yes” and go to question 14. If there is no
evidence of extramedullary disease at the time of diagnosis, indicate “no”, or if “unknown”, go to question 18.

Note, if granulocytic sarcoma (question 15) is reported “yes,” the disease status at diagnosis (question 2) must be “blast phase.”

Q18-83: Laboratory Studies at Diagnosis

All values reported in questions 18-83 must reflect testing performed prior to any treatment of CML. If testing was not performed near the time of diagnosis and prior to the initiation of treatment, report unknown for that value.

If the exact date of sample collection is unknown, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

Questions 18-20: WBC

Indicate whether the white blood count (WBC) is “known” or “unknown” at diagnosis. If “known,” report the laboratory value, unit of measure, and date of sample collection.

If “unknown,” go to question 21.

Questions 21-24: Hemoglobin

Indicate whether the hemoglobin is “known” or “unknown” at diagnosis. If “known,” report the laboratory value, unit of measure, and date of sample collection. Also, report whether a RBC transfusion was given within 30 days prior to the date of sample collection (question 23).

If the hemoglobin level at diagnosis is “unknown,” go to question 25.

Questions 25-28: Platelets

Indicate whether the platelet count is “known” or “unknown” at diagnosis. If “known,” report the laboratory value, unit of measure, and date of sample collection. Also, report whether a platelet transfusion was given within 7 days prior to the date of sample collection (question 27).

If the platelet level at diagnosis is “unknown,” go to question 29.

Questions 29-31: Eosinophils

Indicate whether the percentage of eosinophils is “known” or “unknown” at diagnosis. If “known,” report the percentage and the date of sample collection.

If “unknown,” go to question 32.
Questions 32-34: Basophils

Indicate whether the percentage of basophils is “known” or “unknown” at diagnosis. If “known,” report the percentage and the date of sample collection.

If “unknown,” go to question 35.

Questions 35-37: Blasts in blood

The percentage of blasts in the peripheral blood may be evaluated by a manual or automated differential as well as a flow cytometry assessment. Any of these methods may be used to complete questions 35-37. If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form (question 36).

Indicate whether the percentage of blasts in the peripheral blood is “known” or “unknown” at diagnosis. If “known,” report the percentage and the date of sample collection.

If “unknown,” go to question 38.

Questions 38-40: Blasts in bone marrow

The percentage of blasts in the bone marrow may be evaluated by a differential or by flow cytometry. Report the percentage of blasts as identified by a differential performed on the bone marrow aspirate when available. If a differential on a bone marrow aspirate sample was not performed at diagnosis, the center should report questions 38-40 using either a differential performed on an alternative bone marrow sample or a flow cytometry assessment.

Indicate whether the percentage of blasts in the bone marrow is “known” or “unknown” at diagnosis. If “known,” report the percentage and the date of sample collection.

If the percentage of blasts is reported as a range, enter the average of the range rounded to the nearest whole number (e.g., if 0%-5%, enter 3%). If the pathology report states >90% blasts, packed marrow, or sheets of blasts, enter 91% on the form. If the report states <5% blasts, enter 4% on the form.

If blasts in the bone marrow is “unknown,” skip questions 39-40 and continue with question 41.

Question 41: Were cytogenetics tested (karyotyping or FISH)?

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing
methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

FISH is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in CML. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells. FISH may be used as surveillance for changes associated with post-therapy malignancy.

If cytogenetic studies were obtained at diagnosis, report “yes” and go to question 42.

If cytogenetic studies were not obtained at time of diagnosis, report “no” and go to question 56.

If it is unknown whether cytogenetic studies were performed, report “unknown” and go to question 56.

**Questions 42-43: Were cytogenetics tested via karyotyping?**

Report whether karyotyping was performed at diagnosis. A description of karyotyping can be found in the instructions for question 41. If karyotyping was performed, report “yes” and indicate the date the sample was collected in question 43.

If karyotyping was not performed or it is unknown, report “no” or “unknown” respectively and go to question 49.

**Question 44: Results of test**

Indicate if cytogenetic studies identified any clonal abnormalities (any karyotype other than 46XX or 46XY) at the time of diagnosis. For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If chromosomal abnormalities were detected, indicate “abnormalities identified,” go to question 45.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified, go to question 49.
**Question 45: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)**

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 3. Often, karyotype reports will specify the number of cells demonstrating a specific abnormality, but will not document the percent. In this case, divide the number of Ph+ cells by the total number of metaphases examined (20 is very common). Multiply this value by 100 to determine the percent Ph+ cells present.

**Table 3. CML Chromosomal Abnormalities Classification.**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philadelphia chromosome t(9;22)(q34;q11)</td>
<td>An exchange of genetic material between region q34 of chromosome 9 and region q11 of chromosome 22.</td>
</tr>
<tr>
<td>Complex variation</td>
<td>Translocation of three or more chromosomes, one of which must be chromosome 22 [e.g., t(3; 9; 22)]</td>
</tr>
<tr>
<td>Variant form</td>
<td>Any translocation involving 22(q11), or 22(q11.2) in which CML is the suspected diagnosis [e.g., t(13; 22)(p3;q11)].</td>
</tr>
</tbody>
</table>

**Question 46-47: Other abnormality**

Indicate whether karyotyping at the time of diagnosis demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 47. For complex karyotypes revealing many other abnormalities, centers should report “see report” in question 47 and attach a copy of the karyotype report to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

If no other abnormalities were detected, report “no” for question 46 and go to question 48.

**Question 48: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the karyotype report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 49-50: Were cytogenetics tested via FISH?**

Report whether FISH studies were performed at diagnosis. A description of FISH testing can be found in the
instructions for question 41. If FISH studies for cytogenetic abnormalities were performed, report “yes” and indicate the date the sample was collected in question 50.

If FISH studies were not performed or it is unknown, report “no” or “unknown” respectively and go to question 56.

**Question 51: Results of test**

Indicate if FISH studies identified any clonal abnormalities at diagnosis. For FISH studies, a clonal abnormality is defined as an abnormality occurring at a frequency (percentage of cells) above the upper limit of normal. The upper limit of normal will vary according the specific test being performed. If the upper limit of normal is not included on the FISH report and it is unclear whether an abnormality was detected, contact your center’s laboratory to obtain documentation of the upper limit of normal for the assay(s) performed.

If cytogenetic abnormalities were detected, indicate “abnormalities identified,” go to question 52.

If the sample collected was not sufficient to perform the ordered FISH studies, report “no evaluable metaphases.” If FISH studies were successfully performed and all tests were negative, report “no abnormalities” identified. In either case, go to question 56.

**Question 52: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)**

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 3. Results of FISH studies are often reported in percentages; however, if this is not the case, divide the number of Ph+ cells by the total number of cells examined (200 is very common). Multiply this value by 100 to determine the percent Ph+ cells present.

**Question 53-54: Other abnormality**

Indicate whether FISH studies at diagnosis demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For FISH studies, a clonal abnormality is defined as an abnormality occurring at a frequency (percentage of cells) above the upper limit of normal. See question 51 for further instructions on reporting clonal abnormalities as detected by FISH methods.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 54. In cases where FISH studies reveal many other abnormalities, centers should report “see report” in question 54 and attach a copy of the FISH report(s) to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

If no other abnormalities were detected, report “no” for question 53 and go to question 55.
Question 55: Was documentation submitted to the CIBMTR?

Indicate whether a copy of the FISH report was attached to the form in FormsNet3<sup>SM</sup>. For further instructions on how to attach documents in FormsNet3<sup>SM</sup>, refer to the Training Guide.

Question 56-57: Were tests for molecular markers performed (e.g., PCR)?

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient’s primary disease. Testing for these sequences is often performed using PCR based methods; however, lower sensitivity testing, including FISH, may also be used to detect molecular markers (e.g., BCR / ABL). Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue.

If testing for molecular markers was performed at diagnosis, report “yes” and indicate the sample collection date in question 57.

If no molecular marker testing was performed or it is unknown if testing was done, report “no” or “unknown” respectively and go to question 84.

Question 58-60: Was BCR / ABL detected?

Report whether testing for BCR / ABL was positive at diagnosis. Typically, testing will be performed by PCR to establish a baseline from which a response to treatment can be measured. Multiple tests for BCR / ABL may be performed to identify the specific location at which the mutation occurred. The final report for the tests performed should specify which breakpoint(s) were tested. If the specific breakpoints are not specified, contact your center’s laboratory to obtain documentation of the breakpoints which were tested.

If any test for BCR / ABL was positive at diagnosis, report “yes” and specify the breakpoint in question 59. If the breakpoint identified does not match the options provided, report “other breakpoint” for question 59 and specify the breakpoint identified in question 60. If the breakpoint cannot be determined from the testing performed, report “unknown” for question 59.

If all testing for BCR / ABL performed at diagnosis was negative, report “no” for question 58 and go to question 84.

Question 61-82: Was BCR / ABL kinase domain mutation analysis performed?

Identification of kinase domain (KD) mutations can inform treatment decisions regarding use of tyrosine kinase inhibitors (TKIs). Mutations may be identified at diagnosis or later on as a recipient’s disease develops resistance to TKI therapy.
If testing for KD mutations was performed at diagnosis, report “yes” for question 61 and complete questions 62-81. If a KD mutation was tested at diagnosis, but is not included in questions 62-80, report the test result in question 81 and specify the mutation tested in question 82.

**Question 83: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the molecular testing report was attached to the form in FormsNet3SM For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.
Q84-185: Pre-HCT or Pre-Infusion Therapy

The FormsNetSM application allows questions 85-185 to be reported multiple times. Complete these questions for each line of therapy administered prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given). When submitting the paper version of the form for more than two lines of therapy, copy the “Pre-infusion or Pre-Infusion Therapy” section and complete questions 85-185 for each line of therapy administered.

A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.). If a recipient’s disease status changes resulting in a change to treatment, a new line of therapy should be reported. Additionally, if therapy is changed because a favorable disease response was not achieved, a new line of therapy should be reported.

**Question 84: Was therapy given?**

Indicate if the recipient received treatment for their primary disease between diagnosis and the start of the preparative regimen (or prior to infusion if no preparative regimen was given). If “yes,” continue with question 85. If “no” or “unknown,” go to question 186.

**Question 85: Systemic therapy**

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally. Common systemic therapies used to treat CML include tyrosine kinase inhibitors and chemotherapy.

If systemic therapy was administered, report “yes” and continue with question 86. If not, report “no” and go to question 112.

**Questions 86-87: Date therapy started**

Indicate whether the therapy start date is “known” or “unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 87. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

**Questions 88: Was therapy stopped?**

Indicate whether therapy was stopped prior to the start of the preparative regimen (or prior to infusion if not preparative regimen was administered). Only report “no” for therapies continued after the date the
preparative regimen was started (or after the date of infusion if no preparative regimen was given).

If the line of therapy being reported was stopped, continue with question 89. Otherwise, go to question 93.

**Questions 89-90: Date therapy stopped**

Indicate if therapy stop date is “known” or “unknown.” If the therapy is being given in cycles, report the date the recipient started the last cycle for this line of therapy in question 90. Otherwise, report the final administration date for the therapy being reported. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](https://CIBMTR.org).

If the date therapy stopped is “unknown,” go to question 91.

**Questions 91-92: Specify reason therapy stopped**

Treatment for CML may be stopped for different reasons including side effects of treatment or poor disease response. Report the reason treatment was stopped as documented in the provider’s notes. If it is not clear why therapy was stopped, ask the provider to provide documentation indicating the most appropriate reason. If the documented reason does not match any of the options provided in question 91, report “other” and specify the reason in question 92.

**Questions 93-111: Specify therapy given**

Treatments vary based on protocol and in most cases are administered in the outpatient setting. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. For the line of therapy being reported, report “yes” for any drug administered. Report “no” for any drug(s) not given. Do not leave any responses blank. If the recipient received a systemic therapy which is not listed, report “yes” for question 110 and specify the treatment in question 111. Report the generic name of the agent, not the name brand.

Do not report supportive therapies (e.g., transfusions, growth factors) as systemic therapy.

**Question 112: Radiation therapy**

Radiation therapy utilizes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. For CML, radiation therapy may be used to shrink the spleen in cases of severe / painful splenomegaly. Radiation therapy may be given in conjunction with systemic chemotherapy or as a separate line of therapy.

If radiation therapy was given during or adjacent to administration of systemic therapy, report them together
as single line of therapy on the form (i.e., one copy of questions 85-185). Otherwise, capture the radiation treatment as a separate line of therapy.

If the recipient received radiation therapy between the time of diagnosis and the start of the preparative regimen, report “yes” and continue with question 113. If not, report “no” and go to question 120.

**Questions 113-114: Date therapy started**

Indicate whether the start date for radiation therapy is “known” or “unknown.” If known, enter the date radiation therapy began in question 114. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](https://CIBMTR.org).

**Questions 115-116: Date therapy stopped**

Indicate if the stop date for radiation therapy is “known” or “unknown.” If known, enter the final date radiation was administered in question 116. If the stop date is partially known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](https://CIBMTR.org).

**Questions 117-119: Specify site(s) of radiation therapy**

Report all sites of radiation therapy administered between the start and stop dates reported in questions 113-116. If “yes” is reported for “Other site,” specify all other sites in question 119.

**Question 120: Splenectomy**

If a splenectomy was performed during or adjacent to administration of systemic therapy or a period of radiation therapy report them together as single line of therapy on the form (i.e., one copy of questions 85-185). Otherwise, capture the surgery as a separate line of therapy.

If the recipient underwent a splenectomy for their primary disease, report “yes.” Otherwise, report “no.”

Do not report a history of a splenectomy performed prior to the diagnosis of CML.

**Question 121-122: Other therapy**

If therapy was given to treat the recipient’s primary disease, but cannot be reported as systemic therapy, radiation therapy, or splenectomy, report yes for question 121 and specify the treatment in question 122.

Do not report supportive therapies (e.g., transfusions, growth factors), cellular therapy, HCT, or any agents given as part of the preparative regimen in questions 121-122.
**Best Response to Therapy**

Questions 123-183 refer to testing performed at the time of the recipient’s best response to therapy (Q183) and prior to the initiation of any new therapy (including preparative regimen or infusion). Disease assessments may be performed multiple times during this time frame. When deciding which assessments to report, choose testing performed closest to the date reported in question 183. If testing was not performed during this time frame, report “unknown.”

**Question 123-125: WBC**

Indicate whether the white blood count (WBC) is “known” or “unknown” at the time of best response. If “known,” report the laboratory value, unit of measure, and date of sample collection. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If “unknown,” go to question 127.

**Question 126: Were immature cells (i.e., myelocytes, promyelocytes or myoblasts) noted on the WBC differential performed on the peripheral blood?**

Automated or manual differentials performed on the recipient’s peripheral blood will identify whether immature cells are present. Depending on the format of the results / report, immature cells may not be listed if none were detected. If a differential was performed, but no immature cells are noted, assume none were detected.

If immature cells were noted on the WBC differential performed on the peripheral blood, report “yes.” If a differential was performed, but no immature cells were noted, report “no.” If a differential was not performed at the time of best response, report “unknown.”

**Question 127-128: Basophils**

Indicate whether the basophil percentage is “known” or “unknown” at the time of best response. If “known,” report the percentage in question 128. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If “unknown,” go to question 129.

**Questions 129-132: Platelets**

Indicate whether the platelet count is “known” or “unknown” at the time of best response. If “known,” report the laboratory value, unit of measure, and date of sample collection. If the exact date is not known, use the
process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

Also, report whether a platelet transfusion was given within 7 days prior to the date of sample collection (question 131).

If the platelet level at the time of best response is “unknown,” go to question 133.

Question 133: Were cytogenetics tested (karyotyping or FISH)?

Indicate whether karyotyping or FISH assessments were performed at the time the best response. If karyotyping or FISH assessments were done during this time period, report “yes” and continue with question 134. If not, report “no” and go to question 148.

Refer to question 41 for further instructions on reporting karyotyping and FISH studies.

Questions 134-135: Were cytogenetics tested via karyotyping?

Report whether karyotyping was performed at the time of best response. If karyotyping was performed, report “yes” and indicate the date the sample was collected in question 135. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If karyotyping was not performed or it is unknown, report “no” or “unknown” respectively and go to question 141.

Question 136: Results of test

Indicate if cytogenetic studies identified any clonal abnormalities (any karyotype other than 46XX or 46XY) at the time of best response. For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If chromosomal abnormalities were detected, report “abnormalities identified,” continue with question 137.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified, go to question 141.

Question 137: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 3. Refer to
question 45 for further instructions on reporting Ph+ testing by karyotype.

**Question 138-139: Other abnormality**

Indicate whether karyotyping at the time of best response demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 139. For complex karyotypes revealing many other abnormalities, centers should report “see report” in question 139 and attach a copy of the karyotype report to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

If no other abnormalities were detected, report “no” for question 138 and got to question 140.

**Question 140: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the karyotype report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 141-142: Were cytogenetics tested via FISH?**

Report whether FISH studies were performed at the time of best response. A description of FISH testing can be found in the instructions for question 41. If FISH studies for cytogenetic abnormalities were performed, report “yes” and indicate the date the sample was collected in question 50. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If FISH studies were not performed or it is unknown, report “no” or “unknown” respectively and go to question 148.

**Question 143: Results of test**

If cytogenetic abnormalities were detected, report “abnormalities identified," continue with question 144. Refer to question 51 for further instructions on reporting FISH results.

If the sample was not sufficient to perform the ordered FISH studies, report “no evaluable metaphases." If FISH studies were successfully performed and all tests were negative, report “no abnormalities” identified. In either case, go to question 148.
**Question 144: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)**

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 3. Refer to [question 52](#) for further instructions on reporting Ph+ testing by FISH.

**Question 145-146: Other abnormality**

Indicate whether FISH studies at the time of best response demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For FISH studies, a clonal abnormality is defined as an abnormality occurring at a frequency (percentage of cells) above the upper limit of normal. See [question 51](#) for further instructions on reporting clonal abnormalities as detected by FISH methods.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 146. In cases where FISH studies reveal many other abnormalities, centers should report “see report” in question 146 and attach a copy of the FISH report(s) to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the [Training Guide](#).

If no other abnormalities were detected, report “no” for question 145 and go to question 147.

**Question 147: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the FISH report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the [Training Guide](#).

**Question 148-149: Were tests for molecular markers performed (e.g., PCR)?**

If testing for molecular markers was performed at diagnosis, report “yes” and indicate the sample collection date in question 149. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](#).

If no molecular marker testing was performed or it is unknown if testing was done, report “no” or “unknown” respectively and go to question 179.

Refer to [questions 56-57](#) for further instructions on reporting testing for molecular markers.

**Question 150: Was BCR / ABL detected?**

If any test for BCR / ABL was positive at the time of best response, report “yes” and continue with question 151. If all testing for BCR / ABL was negative, report “no” for question 150 and go to question 153.
**Question 151: Specify level of detection**

The results of quantitative PCR tests for BCR / ABL mutations are typically reported as a percentage. This value corresponds to the ratio of total number of BCR / ABL copies divided by the total number of control copies. Report the result of testing performed closest to the date of best response (question 183).

If it is not clear how to report the level of detection documented in the lab report, contact your center’s liaison for assistance.

**Question 152: Was BCR / ABL level of detection reported on the Standardized International Scale (IS)?**

Methods of quantifying BCR / ABL transcripts vary between laboratories making it difficult to compare documented responses to therapy across centers. An international scale (IS) was established in 2005 to standardize BCR / ABL testing and to allow different laboratories convert their findings so centers could accurately measure disease response. The laboratory report must either report test results converted to IS or report the conversion factor specific to the test method used to be able to determine the IS level of detection.

If the result reported in question 151 is adjusted to IS, report “yes.” If not, report “no.”

**Question 153: Were two consecutive tests performed? (quantitative and / or nested; of adequate quality [sensitivity > 104])**

Indicate whether two consecutive quantitative tests for BCR / ABL were obtained at the time of best response (question 183). Both tests should be performed prior to the initiation of any new treatment for the recipient’s primary disease. Ensure the sensitivity of both tests is greater than 1:10,000. If consecutive tests were obtained and the sensitivity of both tests > 1: 10,000, report “yes,” otherwise, report “no.”

If question 150 was answered “yes,” go to question 154. If not, go to question 178.

**Question 154-155: Specify BCR / ABL breakpoint**

Indicate the breakpoint identified on the BCR / ABL testing reported in questions 150-151. If the breakpoint identified does not match the options provided, report “other breakpoint” for question 154 and specify the breakpoint identified in question 155. If the breakpoint cannot be determined from the testing performed, report “unknown” for question 154.

**Question 156-177: Was BCR / ABL kinase domain mutation analysis performed?**

If testing for kinase domain (KD) mutations was performed at the time of best response, report “yes” for question 156 and complete questions 157-176. If a KD mutation was tested at the time of best response, but is not included in questions 157-175, report the test result in question 176 and specify the mutation tested in
question 177.

**Question 178: Was documentation submitted to the CIBMTR?**

*Indicate whether a copy of the molecular testing report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the “Guide.”*

**Question 179: Specify the spleen size**

Report the spleen size in centimeters below the left costal margin as assessed by physical exam at the time of best response. If the physical exam does not find any evidence of splenomegaly, report “0.” If the physical exam findings are not documented, leave question 179 blank and override the validation error using the code “unknown.”

*Note, question 179 will be skipped if the center has reported a prior splenectomy (question 120).*

**Question 180: Best response to line of therapy**

Indicate the best response to the line of therapy using the international working group criteria provided in CML Response Criteria section of the Forms Instructions Manual. The best response is determined by a disease assessment, such as hematologic testing, pathology study, and/or physician assessment.

If the best response to the line of therapy is “complete hematologic response” or “chronic phase,” go to question 181.

If the best response to the line of therapy is “accelerated phase,” go to question 183.

If the best response to the line of therapy is “blast phase,” go to question 182.

**Question 181: Specify level of best response**

If the recipient’s best response to therapy (question 180) is “complete hematologic remission” or “chronic phase,” specify the cytogenetic / molecular response. Refer to Table 4 for definitions of cytogenetic and molecular responses.

### Table 4. Definitions of Cytogenetic and Molecular Responses to Therapy

<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete molecular remission * (most favorable)*</td>
<td>0% BCR / ABL transcripts detected in peripheral blood or bone marrow</td>
</tr>
</tbody>
</table>
Major molecular remission | > 0 – 0.1% BCR / ABL transcripts detected in peripheral blood or bone marrow
Complete cytogenetic response | 0% Ph+ cells detected in bone marrow
Partial cytogenetic response | > 0 – 35% Ph+ cells in bone marrow
Minor cytogenetic response | > 35 – 65% Ph+ cells in bone marrow
Minimal cytogenetic response | > 65 – 95% Ph+ cells in bone marrow
No cytogenetic response (least favorable) | > 95% Ph+ cells in bone marrow.


The responses in Table 4 are listed from most favorable (complete molecular remission) to least favorable (no cytogenetic response). Centers should report the most favorable response achieved. For example, if a recipient has achieved a major molecular remission by PCR testing as well as a complete cytogenetic response by karyotyping / FISH, the center should report “major molecular remission” for question 181. Answer question 181 based on the molecular and cytogenetic tests performed closest to the date of best hematologic response (question 183). Do not consider any tests performed after the initiation of a subsequent line of therapy.

**Question 182: Specify blast phase phenotype**

Assessments performed on the bone marrow or peripheral blood may be used to determine the blast phenotype at the time of best response. Indicate which phenotype was detected. If phenotype cannot be determined from the assessments performed, report “unknown.”

**Question 183: Date assessed**

Report the date the best response to the line therapy was established. This should be the earliest date all international working group criteria (see CML Response Criteria) were met for the response reported in question 180. Enter the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically evaluated the recipient’s response.

If the best response was achieved prior to starting the line of therapy being reported, indicate the date of the first assessment which was performed after initiating the current line of therapy and confirms the sustained response.
If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

**Question 184: Did disease relapse/progress following this line of therapy?**

Refer to the guidelines in the CML Response Criteria section of the Forms Instructions Manual for more information on how to determine recurrence or progression of disease. Report “yes” if the recipient had documented relapse or progression after starting this line of therapy and prior to starting a subsequent line of therapy.

Report “no” if the recipient never relapsed or progressed following this line of therapy. Also, report “no” if the recipient relapsed or progressed after beginning a subsequent line of therapy. This episode of relapse/progression will be captured in the instance (i.e., copy) of questions 85-185 completed for the subsequent line of therapy.

If this is the last line of therapy administered prior to HCT, only report “yes” if relapse or progression occurred prior to infusion. Relapse or progression occurring after the infusion date will be reported on the CML Post-Infusion Data Form (Form 2112).

**Question 185: Date of relapse/progression**

Enter the assessment date that relapse or progression was established following initiation of this line of therapy. Report the date of the pathologic evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathologic and laboratory evaluations. If extranodal disease is detected upon radiographic examination (e.g., X-rays, CT scans, MRI scans, PET scans), enter the date the imaging took place. If the physician determines evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.
Q186-191: Disease Assessment at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

Questions 186-191 refer to the most recent assessments performed prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given).

Question 186: Specify the spleen size

Report the spleen size in centimeters below the left costal margin as assessed by physical exam. If the physical exam does not find any evidence of splenomegaly, report “0.” If the physical exam findings are not documented, leave question 186 blank and override the validation error using the code “unknown.”

Note, question 186 will be skipped if the center has reported a prior splenectomy (question 120).

Questions 187-191: Was extramedullary disease present?

Extramedullary refers to disease found in organs or tissue outside the bone marrow or blood stream (e.g., central nervous system, testes, skin, soft tissue, etc.). Examples of extramedullary disease in CML patients include CNS involvement and granulocytic sarcoma. If there is evidence of extramedullary disease on the most recent assessment(s), report “yes” and indicate any sites of disease in questions 188-191. If extramedullary disease is present, but does not fit in the options provided, report “yes” for question 191 and specify any other sites of disease in question 191.

If there is no evidence of extramedullary disease on the most recent assessment(s), indicate “no” and go to question 192.

Note, if granulocytic sarcoma (question 189) is reported “yes,” the disease status prior to the start of the preparative regimen (question 253) must be “blast phase.”

Splenomegaly

Do not report splenomegaly in questions 187-191 (extramedullary disease). Splenomegaly will be captured in question 186 and should not be reported again in questions 188-191.
Questions 192-252 refer to the most recent laboratory studies performed prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given). “Unknown” should only be reported if there isn’t any documentation or it’s unclear from the documentation to be able to answer the question.

**Question 192: Were immature cells (i.e., myelocytes, promyelocytes or myoblasts) noted on the WBC differential performed on the peripheral blood?**

Automated or manual differentials performed on the recipient’s peripheral blood will identify whether immature cells are present. Depending on the format of the results / report, immature cells may not be listed if none were detected. If a differential was performed, but no immature cells are noted, assume none were detected.

If immature cells were noted on the WBC differential performed on the peripheral blood, report “yes.” If a differential was performed, but no immature cells were noted, report “no.”

**Question 193-195: Eosinophils**

Indicate whether the percentage of eosinophils is “known” or “unknown.” If “known,” report the percentage and date the sample was collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If “unknown,” go to question 129.

**Questions 196-198: Basophils**

Indicate whether the percentage of basophils is “known” or “unknown.” If “known,” report the percentage and the date the sample was collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If “unknown,” go to question 199.

**Questions 199-201: Blasts in blood**

The percentage of blasts in the peripheral blood may be evaluated by a manual or automated differential as
well as a flow cytometry assessment. Any of these methods may be used to complete questions 199-201. If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form (question 200).

Indicate whether the percentage of blasts in the peripheral blood is “known” or “unknown” at the time of diagnosis. If “known,” report the percentage and the date of sample collection. If the exact date is not known, use the process described for reporting partial or unknown dates in General Guidelines for Completing Forms.

If “unknown,” go to question 202.

**Questions 202-204: Blasts in bone marrow**

The percentage of blasts in the bone marrow in the bone marrow may be evaluated by a differential or by flow cytometry. Report the percentage of blasts as identified by a differential performed on the bone marrow aspirate when available. If a differential on a bone marrow aspirate sample is not available, the center should report questions 202-204 using either a differential performed on an alternative bone marrow sample or a flow cytometry assessment.

Indicate whether the percentage of blasts in the bone marrow is “known” or “unknown.” If “known,” report the percentage and the date the sample was collected. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If the percentage of blasts is reported as a range, enter the average of the range rounded to the nearest whole number (e.g., if 0%-5%, enter 3%). If the pathology report states >90% blasts, packed marrow, or sheets of blasts, enter 91% on the form. If the report states <5% blasts, enter 4% on the form.

If blasts in bone marrow is “unknown,” go to question 205.

**Questions 205-206: What was the status of bone marrow fibrosis prior to the preparative regimen / infusion?**

Fibrosis describes the replacement of bone marrow by fibrous (scar) tissue. This distinction is made on the pathology report of a bone marrow examination.

Indicate the degree of bone marrow fibrosis documented on the most recent pathology report. If the degree of fibrosis is not addressed in the report, select “unknown.” Report the date of the most recent bone marrow biopsy in question 206. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.
Questions 207: Were cytogenetics tested (karyotyping or FISH)?

Indicate whether karyotyping or FISH assessments were performed prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given). If karyotyping or FISH assessments were done during this time period, report “yes” and go to question 208. If not, report “no” and go to question 222.

Refer to question 41 for further instructions on reporting karyotyping and FISH studies.

Questions 208-209: Were cytogenetics tested via karyotyping?

Report whether karyotyping was performed. If karyotyping was performed, report “yes” and indicate the date the sample was collected in question 209. If karyotyping was not performed or it is unknown, report “no” or “unknown” respectively and go to question 215.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

Question 210: Results of test

Indicate if cytogenetic studies identified any clonal abnormalities (any karyotype other than 46XX or 46XY). For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If chromosomal abnormalities were detected, indicate “abnormalities identified,” go to question 211.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified, go to question 215.

Question 211: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 3. Refer to question 45 for further instructions on reporting Ph+ testing by karyotype.

Question 212-213: Other abnormality

Indicate whether karyotyping at the time of last evaluation prior to the start of the preparative regimen demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 139. For complex karyotypes revealing many other abnormalities, centers should report “see report” in question...
213 and attach a copy of the karyotype report to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

If no other abnormalities were detected, report “no” for question 212 and go to question 214.

**Question 214: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the karyotype report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 215-216: Were cytogenetics tested via FISH?**

Report whether FISH studies were performed. A description of FISH testing can be found in the instructions for question 41. If FISH studies for cytogenic abnormalities were performed, report “yes” and indicate the date the sample was collected in question 216. If FISH studies were not performed or it is unknown, report “no” or “unknown” respectively and go to question 222.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

**Question 217: Results of test**

If cytogenetic abnormalities were detected by FISH, report “abnormalities identified,” go to question 218.

If the sample collected was not sufficient to perform the ordered FISH studies, report “no evaluable metaphases.” If FISH studies were successfully performed and all tests were negative, report “no abnormalities” identified. In either case, go to question 222.

Refer to question 51 for further instructions on reporting FISH results.

**Question 218: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)**

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 3. Refer to question 52 for further instructions on reporting Ph+ testing by FISH.

**Question 219-220: Other abnormality**

Indicate whether FISH studies at the time of last evaluation prior to the start of the preparative regimen demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For FISH studies, a clonal abnormality is defined as an abnormality occurring at a frequency
(percentage of cells) above the upper limit of normal. See question 51 for further instructions on reporting clonal abnormalities as detected by FISH methods.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 220. In cases where FISH studies reveal many other abnormalities, centers should report “see report” in question 220 and attach a copy of the FISH report(s) to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

If no other abnormalities were detected, report “no” for question 219 and go to question 221.

**Question 221: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the FISH report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 222-223: Were tests for molecular markers performed (e.g., PCR)?**

If testing for molecular markers was performed at last evaluation prior to the start of the preparative regimen, report “yes” and indicate the sample collection date in question 223. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If no molecular marker testing was performed or it is unknown if testing was done, report “no” or “unknown” respectively and go to question 253.

Refer to questions 56-57 for further instructions on reporting testing for molecular markers.

**Question 224: Was BCR / ABL detected?**

If any test for BCR / ABL was positive at the time of last evaluation prior to the start of the preparative regimen, report “yes” and continue with question 225. If all testing for BCR / ABL was negative or testing was not performed, report “no” for question 224 and go to question 227.

**Question 225: Specify level of detection**

Report the result of testing performed prior to the start of the preparative regimen (or infusion if no preparative regimen given). Refer to question 151 for further instructions on reporting BCR / ABL test results.
Question 226: Was BCR / ABL level of detection reported on the Standardized International Scale (IS)?

Indicate whether the result reported in question 225 is adjusted to International Scale (IS). Refer to question 152 for more information about standardized results.

Question 227: Were two consecutive tests performed? (quantitative and / or nested; of adequate quality [sensitivity > 104])

Indicate whether two consecutive quantitative tests for BCR / ABL were obtained prior to the start of the preparative regimen (or infusion if no preparative regimen given). Ensure the sensitivity of both tests is greater than 1:10,000. If consecutive tests were obtained and the sensitivity of both tests > 1:10,000, report “yes,” otherwise, report “no.”

Question 228-229: Specify BCR / ABL breakpoint

Indicate the breakpoint identified on the BCR / ABL testing reported in questions 224-225. If the breakpoint identified does not match the options provided, report “other breakpoint” for question 228 and specify the breakpoint identified in question 229. If the breakpoint cannot be determined from the testing performed, report “unknown” for question 228.

Question 230-251: Was BCR / ABL kinase domain mutation analysis performed?

If testing for kinase domain (KD) mutations was performed, report “yes” for question 230 and go to question 231. If a KD mutation was tested at the time of best response, but is not included in questions 231-249, report the test result in question 250 and specify the mutation tested in question 251.

Question 252: Was documentation submitted to the CIBMTR?

Indicate whether a copy of the molecular testing report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.
Q253-256: Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

Questions 253-256 refer to the most recent assessments performed prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given).

**Question 253: What was the disease status?**

Indicate the disease status using the international working group criteria provided in CML Response Criteria section of the Forms Instructions Manual. The disease status is determined by a disease assessment, such as hematologic testing, pathology study, and/or physician assessment.

If the disease status is “complete hematologic response” or “chronic phase,” go to question 254.

If the disease status is “accelerated phase,” go to question 256.

If the disease status is “blast phase,” go to question 255.

**Question 254: Specify level of response**

If the recipient’s disease status (question 253) is “complete hematologic remission” or “chronic phase,” specify the cytogenetic / molecular response. Refer to Table 4 for definitions of cytogenetic and molecular responses. Centers should report the most favorable response achieved prior to the start of the preparative regimen.

**Question 255: Specify blast phase phenotype**

Assessments performed on the bone marrow or peripheral blood may be used to determine the blast phenotype at the time of best response. Indicate which phenotype was detected. If phenotype cannot be determined from the assessments performed, report “unknown.”

**Question 256: Date assessed**

Enter the date of the most recent assessment. Report the date of the pathologic evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-rays, CT scans, MRI scans, PET scans), or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathologic and laboratory evaluations; enter the date the imaging took place for radiographic assessments. If no pathologic,
radiographic, or laboratory assessment was performed within the pre-transplant work-up time period, report the most recent office visit in which the physician assessed the recipient's disease status.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.
Chronic myelogenous leukemia (CML) is a slow-progressing cancer of the myeloid white blood cells. It is characterized by the increased proliferation of immature white blood cells (granulocytes) with damaged DNA, or blasts, which accumulate in the blood and bone marrow. Normal blasts develop into white blood cells which function to fight infection. The symptoms of CML are caused by the replacement of normal bone marrow with leukemic cells, resulting in a drop in red blood cells, platelets, and normal white blood cells.

The Chronic Myelogenous Leukemia Post-Infusion Data Form (Form 2112) is one of the Comprehensive Report Forms. This form captures CML-specific post-infusion data such as: the recipient's best response to HCT or cellular therapy; planned treatments post-infusion; disease relapse data including treatment administered for relapse or persistent disease; and disease status for the reporting period.

This form must be completed for all recipients whose primary disease, reported on Pre-TED Disease Classification Form (Form 2402), is CML. This includes CML with the following chromosomal abnormalities: Philadelphia chromosome, complex variation and/or variant form, or BCR/ABL gene rearrangement. The CML Post-Infusion Data Form must be completed in conjunction with each Post-Infusion Data Form (Form 2100) completed. The post-infusion forms are designed to capture specific data occurring within the timeframe of each reporting period (i.e. between day 0 and day 100 date of contact for the 100 day follow-up, between day 100 date of contact and the six-month date of contact for the six-month follow-up, etc.).

Links to Sections of Form:

- Q1-63: Disease Assessment at the Time of Best Response
- Q64-99: Post-HCT / Post-Infusion Planned Therapy
- Q100-109: Disease Relapse or Progression Post-HCT / Post-Infusion
- Q110-194: Post-HCT / Post-Infusion Therapy
- Q195-198: Disease Status at Time of Evaluation for this Reporting Period

Manual Updates:

Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text. If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.
<table>
<thead>
<tr>
<th>Date</th>
<th>Title</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
</table>
| 3/19/18    | Comprehensive Disease Specific Manuals     | Add    | Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119).
|            |                                            |        | *The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.* |
| 1/31/17    | 2112: CML Post-Infusion Data Form          | Add    | Version 1 of the 2012: CML Post-Infusion Data Form section of the Forms Instructions Manual released. Version 1 corresponds to revision 2 of the Form 2112. |
Q1-63: Disease Assessment at the Time of Best Response

**Question 1:** What was the best response to HCT or cellular therapy since the date of the last report? (include response to any therapy given for post-HCT maintenance or consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease)

The intent of this question is to determine the best overall response to HCT / cellular therapy. This is assessed in each reporting period. When evaluating the best response, determine the disease status within the reporting period using the international working group criteria provided in the in CML Response Criteria section of the Forms Instructions Manual. Compare this response to all previous post-infusion reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status. See question 4 to indicate that this disease status was previously reported.

Include response to any post-infusion treatment planned as of Day 0. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR or as preemptive therapy for recipients with minimal residual disease, consider this “planned therapy,” even if this was not documented prior to the transplant. **Do not include response to any treatment administered as a result of relapse, progression, or persistent disease.** If a recipient has started treatment for relapse, progression, or persistent disease, report the best response confirmed prior to the initiation of treatment (even if this was confirmed in a prior reporting period).

If the best response to the line of therapy is **complete hematologic response** or **chronic phase**, go to question 2.

If the best response to the line of therapy is **accelerated phase**, go to question 4.

If the best response to the line of therapy is **blast phase**, go to question 3.

**Question 2: Specify level of best response**

If the recipient’s best response to therapy (question 1) is “complete hematologic remission” or “chronic phase,” specify the cytogenetic / molecular response. Refer to Table 1 for definitions of cytogenetic and molecular responses.

**Table 1. Definitions of Cytogenetic and Molecular Responses to Therapy**
<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete molecular remission <em>(most favorable)</em></td>
<td>0% BCR / ABL transcripts detected in peripheral blood or bone marrow</td>
</tr>
<tr>
<td>Major molecular remission</td>
<td>&gt; 0 – 0.1% BCR / ABL transcripts detected in peripheral blood or bone marrow</td>
</tr>
<tr>
<td>Complete cytogenetic response</td>
<td>0% Ph+ cells detected in bone marrow</td>
</tr>
<tr>
<td>Partial cytogenetic response</td>
<td>&gt; 0 – 35% Ph+ cells in bone marrow</td>
</tr>
<tr>
<td>Minor cytogenetic response</td>
<td>&gt; 35 – 65% Ph+ cells in bone marrow</td>
</tr>
<tr>
<td>Minimal cytogenetic response</td>
<td>&gt; 65 – 95% Ph+ cells in bone marrow</td>
</tr>
<tr>
<td>No cytogenetic response <em>(least favorable)</em></td>
<td>&gt; 95% Ph+ cells in bone marrow.</td>
</tr>
</tbody>
</table>


The responses in Table 1 are listed from most favorable (complete molecular remission) to least favorable (no cytogenetic response). Centers should report the most favorable response achieved. For example, if a recipient has achieved a major molecular remission by PCR testing as well as a complete cytogenetic response by karyotyping / FISH, the center should report “major molecular remission” for question 2. Answer question 2 based on the molecular and cytogenetic tests performed closest to the date of best hematologic response (question 1).

**Question 3: Specify blast phase phenotype**

Assessments performed on the bone marrow or peripheral blood may be used to determine the blast phenotype at the time of best response. Indicate which phenotype was detected. If phenotype cannot be determined from the assessments performed, report “unknown.”

**Question 4: Was the date of best response previously reported?**

If the best response to HCT or cellular therapy (question 1) was first documented during the current reporting period, report “no” and go to question 5. If the best response was already documented during a prior reporting period, report “yes” and skip questions 6-63. It is not necessary re-report questions 6-63 for improvements in cytogenetic / molecular response to HCT or cellular therapy (question 2).

Do not report “yes” if completing this form for the 100 Day reporting period.
**Question 5: Date assessed**

Report the date the best response to the line therapy was established. This should be the earliest date all international working group criteria (see CML Response Criteria) were met for the response reported in question 1. Enter the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically evaluated the recipient’s response.

If the best response was achieved prior to starting the line of therapy being reported, indicate the date of the first assessment which was performed after initiating the current line of therapy and confirms the sustained response.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

**Questions 6-8: WBC**

Indicate whether the white blood count (WBC) is “known” or “unknown” at the time of best response. If “known,” report the laboratory value, unit of measure, and date of sample collection. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If “unknown,” go to question 10.

**Question 9: Were immature cells (i.e., myelocytes, promyelocytes or myoblasts) noted on the WBC differential performed on the peripheral blood?**

Automated or manual differentials performed on the recipient’s peripheral blood will identify whether immature cells are present. Depending on the format of the results / report, immature cells may not be listed if none were detected. If a differential was performed, but no immature cells are noted, assume none were detected.

If immature cells were noted on the WBC differential performed on the peripheral blood, report “yes.” If a differential was performed, but no immature cells were noted, report “no.” If a differential was not performed at the time of best response, report “unknown.”

**Questions 10-11: Basophils**

Indicate whether the percentage of basophils is “known” or “unknown” at the time of best response. If “known,” report the percentage.
If “unknown,” go to question 12.

**Questions 12-15: Platelets**

Indicate whether the platelet count is “known” or “unknown” at the time of best response. If “known,” report the laboratory value, unit of measure, and date of sample collection. Also, report whether a platelet transfusion was given within 7 days prior to the date of sample collection (question 14).

If the platelet level at diagnosis is “unknown,” go to question 16.

**Question 16: Were cytogenetics tested (karyotyping or FISH)?**

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

FISH is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in CML. These probes are mixed with cells from the recipient's blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells. FISH may be used as surveillance for changes associated with post-therapy malignancy.

If cytogenetic studies were obtained at time of best response report “yes” and go to question 17.

If cytogenetic studies were not obtained at time of best response report “no” and go to question 31.

If it is unknown whether chromosome studies were performed, report “unknown” and go to question 31.

**Questions 17-18: Were cytogenetics tested via karyotyping?**

Report whether karyotyping was performed at time of best response. If karyotyping was performed, report “yes” and indicate the date the sample was collected in question 18.

If karyotyping was not performed or it is unknown, report “no” or “unknown” respectively and go to question 24.
**Question 19: Results of test**

Indicate if cytogenetic studies identified any clonal abnormalities (any karyotype other than 46XX or 46XY) at the time of best response. For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If chromosomal abnormalities were detected, indicate “abnormalities identified,” go to question 20.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified, go to question 24.

**Question 20: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)**

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 2. Often, karyotype reports will specify the number of cells demonstrating a specific abnormality, but will not document the percent. In this case, divide the number of Ph+ cells by the total number of metaphases examined (20 is very common). Multiply this value by 100 to determine the percent Ph+ cells present.

**Table 2. CML Chromosomal Abnormalities Classification**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philadelphia chromosome t(9;22)(q34;q11)</td>
<td>An exchange of genetic material between region q34 of chromosome 9 and region q11 of chromosome 22.</td>
</tr>
<tr>
<td>Complex variation</td>
<td>Translocation of three or more chromosomes, one of which must be chromosome 22 [e.g., t(9; 22)]</td>
</tr>
<tr>
<td>Variant form</td>
<td>Any translocation involving 22(q11), or 22(q11.2) in which CML is the suspected diagnosis [e.g., t(13; 22)(p3;q11)].</td>
</tr>
</tbody>
</table>

**Questions 21-22: Other abnormality**

Indicate whether karyotyping at the time of best response demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 22. For complex karyotypes revealing many other abnormalities, centers should report “see report” in question 22 and attach a copy of the karyotype report to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.
If no other abnormalities were detected, report “no” for question 21 and go to question 23.

**Question 23: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the karyotype report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Questions 24-25: Were cytogenetics tested via FISH?**

Report whether FISH studies were performed at the time of best response. A description of FISH testing can be found in the instructions for question 16. If FISH studies for cytogenetic abnormalities were performed, report “yes” and indicate the date the sample was collected in question 25.

If FISH studies were not performed or it is unknown, report “no” or “unknown” respectively and go to question 31.

**Question 26: Results of test**

Indicate if FISH studies identified any clonal abnormalities at the time of best response. For FISH studies, a clonal abnormality is defined as an abnormality occurring at a frequency (percentage of cells) above the upper limit of normal. The upper limit of normal will vary according the specific test being performed. If the upper limit of normal is not included on the FISH report and it is unclear whether an abnormality was detected, contact your center’s laboratory to obtain documentation of the upper limit of normal for the assay(s) performed.

If cytogenetic abnormalities were detected, indicate “abnormalities identified,” go to question 27.

If the sample collected was not sufficient to perform the ordered FISH studies, report “no evaluable metaphases.” If FISH studies were successfully performed and all tests were negative, report “no abnormalities” identified. In either case, go to question 31.

**Question 27: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)**

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 2. Results of FISH studies are often reported in percentages; however, if this is not the case, divide the number of Ph+ cells by the total number of cells examined (200 is very common). Multiply this value by 100 to determine the percent Ph+ cells present.
Questions 28-29: Other abnormality

Indicate whether FISH studies performed at the time of best response demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For FISH studies, a clonal abnormality is defined as an abnormality occurring at a frequency (percentage of cells) above the upper limit of normal. See question 26 for further instructions on reporting clonal abnormalities as detected by FISH methods.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 29. In cases where FISH studies reveal many other abnormalities, centers should report “see report” in question 29 and attach a copy of the FISH report(s) to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

If no other abnormalities were detected, report “no” for question 28 and go to question 30.

Question 30: Was documentation submitted to the CIBMTR?

Indicate whether a copy of the FISH report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 31-32: Were tests for molecular markers performed (e.g., PCR)?

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient’s primary disease. Testing for these sequences is often performed using PCR based methods; however, lower sensitivity testing, including FISH, may also be used to detect molecular markers (e.g., BCR / ABL). Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue.

If testing for molecular markers was performed at the time of best response, report “yes” and indicate the sample collection date in question 32.

If no molecular marker testing was performed or it is unknown if testing was done, report “no” or “unknown” respectively and go to question 62.

Question 33: Was BCR / ABL detected?

If any test for BCR / ABL was positive at the time of best response, report “yes” and continue with question 34. If all testing for BCR / ABL was negative, report “no” for question 33 and go to question 36.
Question 34: Specify level of detection

The results of quantitative PCR tests for BCR / ABL mutations are typically reported as a percentage. This value corresponds to the ratio of total number of BCR / ABL copies divided by the total number of control copies. Report the result of testing performed closest to the date of best response (question 5).

If it is not clear how to report the level of detection documented in the lab report, contact your center’s liaison for assistance.

Question 35: Was BCR / ABL level of detection reported on the Standardized International Scale (IS)?

Methods of quantifying BCR / ABL transcripts vary between laboratories making it difficult to compare documented responses to therapy across centers. An international scale (IS) was established in 2005 to standardize BCR / ABL testing and to allow different laboratories convert their findings so centers could accurately measure disease response. The laboratory report must either report test results converted to IS or report the conversion factor specific to the test method used to be able to determine the IS level of detection.

If the result reported in question 34 is adjusted to IS, report “yes.” If not, report “no.”

Question 36: Were two consecutive tests performed? (quantitative and / or nested; of adequate quality [sensitivity > 104])

Indicate whether two consecutive quantitative tests for BCR / ABL were obtained at the time of best response (question 5). Both tests should be performed prior to the initiation of any new treatment for the recipient’s primary disease. Ensure the sensitivity of both tests is greater than 1:10,000. If consecutive tests were obtained and the sensitivity of both tests > 1: 10,000, report “yes,” otherwise, report “no.”

If question 33 was answered “yes,” go to question 37. If not, go to question 61.

Questions 37-38: Specify BCR / ABL breakpoint

Indicate the breakpoint identified on the BCR / ABL testing reported in questions 33-34. If the breakpoint identified does not match the options provided, report “other breakpoint” for question 37 and specify the breakpoint identified in question 38. If the breakpoint cannot be determined from the testing performed, report “unknown” for question 37.

Questions 39-60: Was BCR / ABL kinase domain mutation analysis performed?

If testing for kinase domain (KD) mutations was performed at the time of best response, report “yes” for question 39 and complete questions 40-60. If a KD mutation was tested at the time of best response, but is not included in questions 40-59, report the test result in question 49 and specify the mutation tested in
question 60.

**Question 61: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the molecular testing report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Questions 62-63: Spleen size**

Report the spleen size in centimeters below the left costal margin as assessed by physical exam at the time of best response. If the physical exam does not find any evidence of splenomegaly, report “0.” If the physical exam findings are not documented, report “unknown.”
Q64-99: Post-HCT / Post-Infusion Planned Therapy

**Question 64:** Was therapy given since the date of last report for reasons other than relapse or progressive disease? (Include any maintenance and consolidation therapy.)

Indicate if the recipient received treatment post-Infusion for reasons other than relapse, progressive, or persistent disease (excluding minimal residual disease (MRD)) during the current reporting period. Recipients are generally transplanted under a specific protocol that defines radiation and/or systemic therapy the recipient is intended to receive as a preparative regimen prior to the HCT or cellular therapy; infection and GVHD prophylaxis to be administered pre- and/or post-HCT; as well as any systemic therapy, radiation, and/or other treatments to be administered post-HCT or cellular therapy as planned (or maintenance) therapy. Planned (maintenance or consolidation) therapy is given to assist in prolonging a remission. Planned therapy may be described in a research protocol or standard of care protocol and these should be referred to when completing this section. If post-transplant therapy is given as prophylaxis or maintenance for recipients in CR, or as preemptive therapy for recipients with minimal residual disease, consider this “planned therapy,” even if this was not documented prior to the transplant. For example, if a physician decides to put the recipient on imatinib maintenance therapy post-HCT or cellular therapy, even if it the intent wasn’t documented prior to transplant, report it in this section of the form. Do not include any treatment administered as a result of relapse, progression, or persistent disease (excluding MRD).

If planned therapy, including therapy given for maintenance or consolidation, was given during the reporting period, report “yes” and go to question 65. If “no,” go to question 100.

**Questions 65-96: Systemic Therapy**

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally. Common systemic therapies used to treat CML include chemotherapy and monoclonal antibodies.

Report “yes” if systemic therapy was given as planned treatment (including maintenance and consolidation treatments) during the reporting period and complete questions 66-96. Use the following guidelines when reporting start and stop dates:

**Date Therapy First Started:** For any systemic therapies first given during the reporting period, indicate “no” for Was the date therapy first started previously reported? and report the first date the therapy was actually given. Do not re-report the start date of any therapy continued from a prior reporting period.
**Date Therapy Stopped:** For any systemic therapies given and then stopped during the reporting period, indicate “no” for *Was this therapy still being given at the date of last contact?* and report the final date the therapy was actually given as the date therapy was stopped. If therapy was continued through the date of death, the center should report “yes” for *Was this therapy still being given at the date of last contact?* and the date stopped should be left blank.

If a systemic therapy was given, but is not one of the options provided in questions 66-86, report “yes” for other systemic therapy (question 91) and specify any other systemic therapies given in question 92. Do not report cellular therapies or subsequent transplants in questions 91-92 as these therapies are captured in other sections of the form.

If systemic therapy was not given as planned therapy during the reporting period, report “no” and go to question 97.

**Question 97: Cellular therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “yes” if the recipient received cellular therapy as planned therapy post-HCT (including maintenance and consolidation treatments) during the reporting period. If not, report “no.” Note, reporting “yes” for question 97 will prompt a Pre-Cellular Therapy Essential Data Form (Form 4000) to come due. This form will capture additional information about the cellular therapy administered.

**Question 98-99: Other therapy**

Indicate if the recipient received any other treatment as planned therapy post-HCT (including maintenance and consolidation treatments). If “yes,” specify the type of treatment administered using question 99. If “no,” and go to question 100.
Q100-109: Disease Relapse or Progression Post-HCT / Post-Infusion

Questions 100-109 are intended to capture the detection of relapse or progression of CML by molecular, cytogenetic, and clinical / hematologic assessments performed during the reporting period. Molecular and cytogenetic detection of relapse / progression should be confirmed by the recipient’s primary care provider. Refer to the CML Response Criteria for more information on how to determine recurrence or progression of the recipient’s primary disease.

Questions 100-101: Was a disease relapse or progression detected by molecular testing (e.g., PCR)?

Molecular testing involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection, and can indicate known genetic abnormalities. PCR is an example of a molecular test method. If molecular testing detected the recipient’s primary disease (e.g., BCR-ABL) during the reporting period, confirm with the recipient’s primary care provider whether this should be reported as evidence of relapse / progression of CML.

If relapse / progression was detected by molecular testing performed during the reporting period, report “yes” for question 100 and indicate the date the sample was collected in question 101.

If relapse / progression was not detected by molecular testing during the reporting period, report “no” for question 100 and go to question 102.

Question 102: Was a disease relapse or progression detected by cytogenetic testing (karyotyping or FISH)?

Refer to question 16 for descriptions of karyotyping and FISH testing. If cytogenetic testing detected the recipient’s primary disease during the reporting period, confirm with the recipient’s primary care provider whether this should be reported as evidence of relapse / progression of CML.

If relapse / progression was detected by cytogenetic testing performed during the reporting period, report “yes” for question 102 and go to question 103.

If relapse / progression was not detected by cytogenetic testing during the reporting period, report “no” for question 102 and go to question 107.

Questions 103-104: Was a disease relapse or progression detected via karyotyping?

If relapse / progression was detected by karyotyping performed during the reporting period, report “yes” for
question 103 and indicate the date the sample was collected in question 104.

If relapse / progression was not detected by karyotyping during the reporting period, report “no” for question 103 and go to question 105.

**Questions 105-106: Was a disease relapse or progression detected via FISH?**

If relapse / progression was detected by FISH testing performed during the reporting period, report “yes” for question 105 and indicate the date the sample was collected in question 106.

If relapse / progression was not detected by FISH testing during the reporting period, report “no” for question 105 and go to question 107.

**Questions 107-108: Was a disease relapse or progression detected by clinical / hematologic assessment?**

Clinical and hematologic assessments are the least sensitive methods of establishing a patient’s disease status. Examples of those include: pathologic evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination.

If clinical and/or hematologic assessments identified disease relapse or progression, report “yes” and indicate the date of assessment in question 108. Report the date disease was detected by radiographic examination (e.g., CT, MRI, PET, or PET/CT scans), bone marrow examination, peripheral blood assessment, or clinical assessment. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If clinical and/or hematologic assessments did not identify disease relapse or progression, report “no” for question 107 and go to question 109. This option should rarely be used as this question will only be completed if the criteria for hematologic relapse / progression were met during the reporting period.

**Question 109: Specify CML phase**

If relapse or progression was detected by clinical / hematologic assessments during the reporting period, indicate the CML phase on the date of relapse or progression (question 108). Refer to the CML Response Criteria section of the Forms Instructions Manual for definitions of each phase.

If relapse was not detected by clinical / hematologic methods during the reporting period (question 107) go to question 110.
Q110-194: Post-HCT / Post-Infusion Therapy

Therapy for Persistent Disease
Report treatment for persistent disease (excluding MRD) in questions 110-132. Do not include therapy which has already been reported in questions 64-99 (planned therapy including maintenance and consolidation) unless the treatment is continued after the recipient’s disease has relapsed or progressed.

Question 110: Was any therapy given for relapse or progressive disease since the date of last report?

Systemic therapy, radiation, and/or other treatments may be administered for relapse, progressive or persistent disease. Indicate if the recipient received treatment post-infusion for relapse or progressive disease since the date of last report.

Questions 111-127: Systemic Therapy
Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally. Common systemic therapies used to treat CML include chemotherapy and monoclonal antibodies.

Report “yes” if systemic therapy was given during the reporting period to treat relapse, progressive, or persistent disease during the reporting period and complete questions 112-127. If known, report the date systemic therapy was first administered during the reporting period to treat relapse, progressive, or persistent disease in question 113. If therapy was continued from a prior reporting period, report “yes” for question 112 and go to question 114.

If a systemic therapy was given, but is not one of the options provided in questions 114-125, report “yes” for other systemic therapy (question 126) and specify any other systemic therapies given in question 127. Do not report cellular therapies or subsequent transplants in questions 126-127 as these therapies are captured in other sections of the form.

If systemic therapy was not given as planned therapy during the reporting period, report “no” and go to question 128.

Question 128: Withdrawal of immunosuppression
Immunosuppressive medications may be tapered or entirely withdrawn in order to promote a graft vs leukemia effect in the setting of relapsed, progressive, or persistent (excluding MRD) disease post-HCT.
If immunosuppression is reduced or stopped during the reporting period in order to treat disease, report “yes.” If not, report “no.”

**Question 129: Cellular therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “yes” if the recipient received cellular therapy during the reporting period to treat relapsed, progressive, or persistent disease. If not, report “no.” Note, reporting “yes” for question 129 will prompt a Pre-Cellular Therapy Essential Data Form (Form 4000) to come due. This form will capture additional information about the cellular therapy administered.

**Question 130: Subsequent HCT**

If the recipient received a subsequent HCT to treat relapse, progression, or persistence of the recipient's primary disease, report “yes.” If not, report “no.”

If a subsequent HCT was performed during the reporting period, ensure this was reported on the Post-Infusion Data Form (Form 2100) as well. Reporting a subsequent HCT given to treat the recipient’s primary disease will prompt a new Pre-TED Form (Form 2400) to come due in FormsNet3SM.

**Questions 131-132: Other therapy**

Indicate if the recipient received any other treatment for relapsed, progressive, or persistent (excluding MRD) disease during the reporting period. If “yes,” specify the type of treatment administered using question 132. If “no,” go to question 133.

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**Best Response to Therapy**

Questions 133-194 refer to testing performed at the time of the recipient’s best response to therapy (Q194) during the reporting period. Disease assessments may be performed multiple times during this time frame. When deciding which assessments to report, choose testing performed closest to the date reported in question 194. If testing was not performed during this time frame, report “unknown.”

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**Response to Therapy**

*Questions 133-194 are intended to capture the best response to any therapy given during the reporting period for relapsed, progressive, or persistent disease (therapy reported in questions 110-132). Report*
assessments performed at the time of the best response was achieved / confirmed. If the recipient’s best response was achieved in a prior reporting period, report the first assessments performed during the current reporting period which confirm a continued response.

**Example 1.** Continued treatment, sustained response
A recipient receives therapy for progression shortly after HCT and their best response during the 100 day reporting period is a return to chronic phase. Treatment continues into the 6 month reporting period, during which chronic phase is maintained, but a complete hematologic response (CHR) is never achieved.

- **On the 100 day CML Post-Infusion Data Form:**
  Report testing performed during the reporting period and closest to the time point at which chronic phase was achieved / detected.

- **On the six month CML Post-Infusion Data Form:**
  Report the earliest testing performed during the reporting period which confirms the recipient continues to be in chronic phase.

**Example 2.** Continued treatment, improved response
A recipient receives therapy for progression shortly after HCT and their best response during the 100 day reporting period is a return to chronic phase. Treatment continues into the 6 month reporting period, during which a CHR is achieved.

- **On the 100 day CML Post-Infusion Data Form:**
  Report testing performed during the reporting period and closest to the time point at which chronic phase was achieved / detected.

- **On the six month CML Post-Infusion Data Form:**
  Report testing performed during the reporting period and closest to the time point at which CHR was achieved / detected.

**Questions 133-135: WBC**
Indicate whether the white blood count (WBC) is “known” or “unknown” at the time of best response (question 194). If “known,” report the laboratory value, unit of measure, and date of sample collection. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If “unknown,” skip questions 134-135 and go to question 136.

**Question 136: Were immature cells (i.e., myelocytes, promyelocytes or myoblasts) noted on the WBC**
**differential performed on the peripheral blood?**

Automated or manual differentials performed on the recipient's peripheral blood will identify whether immature cells are present. Depending on the format of the results/report, immature cells may not be listed if none were detected. If a differential was performed, but no immature cells are noted, assume none were detected.

If immature cells were noted on the WBC differential performed on the peripheral blood, report “yes.” If a differential was performed, but no immature cells were noted, report “no.” If a differential was not performed at the time of best response, report “unknown.”

**Questions 137-138: Basophils**

Indicate whether the percentage of basophils is “known” or “unknown” at the time of best response (question 194). If “known,” report the percentage.

If “unknown,” skip question 138 and go to question 139.

**Questions 139-142: Platelets**

Indicate whether the platelet count is “known” or “unknown” at the time of best response (question 194). If “known,” report the laboratory value, unit of measure, and date of sample collection. Also, report whether a platelet transfusion was given within 7 days prior to the date of sample collection (question 141).

If the platelet count is “unknown,” go to question 143.

**Question 143: Were cytogenetics tested (karyotyping or FISH)?**

Refer to question 16 for a description of cytogenetic testing. Only report testing performed during the reporting period.

If cytogenetic studies were obtained at the time of best response (question 194), report “yes” and go to question 144.

If cytogenetic studies were not obtained at the time of best response (question 194), report “no” and go to question 158.

If it is unknown whether chromosome studies were performed, report “unknown” and go to question 158.

**Questions 144-145: Were cytogenetics tested via karyotyping?**

Report whether karyotyping was performed at the time of best response (question 194). Only report testing
performed during the reporting period. If karyotyping was performed, report “yes” and indicate the date the sample was collected in question 145.

If karyotyping was not performed or it is unknown, report “no” or “unknown” respectively and go to question 151.

**Question 146: Results of test**

Indicate if cytogenetic studies identified any clonal abnormalities (any karyotype other than 46XX or 46XY). For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If chromosomal abnormalities were detected, indicate “abnormalities identified,” go to question 147.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified, go to question 151.

**Question 147: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)**

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 2. Often, karyotype reports will specify the number of cells demonstrating a specific abnormality, but will not document the percent. In this case, divide the number of Ph+ cells by the total number of metaphases examined (20 is very common). Multiply this value by 100 to determine the percent Ph+ cells present.

**Questions 148-149: Other abnormality**

Indicate whether karyotyping demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 149. For complex karyotypes revealing many other abnormalities, centers should report “see report” in question 149 and attach a copy of the karyotype report to the form in FormsNet3\textsuperscript{SM}. For further instructions on how to attach documents in FormsNet3\textsuperscript{SM}, refer to the Training Guide.

If no other abnormalities were detected, report “no” for question 148 and go to question 150.

**Question 150: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the karyotype report was attached to the form in FormsNet3\textsuperscript{SM}. For further
instructions on how to attach documents in FormsNet3\textsuperscript{SM}, refer to the Training Guide.

**Questions 151-152: Were cytogenetics tested via FISH?**

Report whether FISH studies were performed at the time of best response (question 194). Only report testing performed during the reporting period. A description of FISH testing can be found in the instructions for question 16. If FISH studies for cytogenetic abnormalities were performed, report “yes” and indicate the date the sample was collected in question 152.

If FISH studies were not performed or it is unknown, report “no” or “unknown” respectively and go to question 158.

**Question 153: Results of test**

Refer to question 26 for assistance interpreting FISH reports.

If cytogenetic abnormalities were detected, indicate “abnormalities identified,” go to question 154.

If the sample collected was not sufficient to perform the ordered FISH studies, report “no evaluable metaphases.” If FISH studies were successfully performed and all tests were negative, report “no abnormalities” identified. In either case, go to question 158.

**Question 154: Percent Ph+ metaphases (t(9;22)(q34;q11) and variants)**

Report the percent of cells demonstrating a Philadelphia chromosome. Typically, this is observed as t(9;22)(q34;q11), but sites should include any cells matching the descriptions provided in Table 2. Results of FISH studies are often reported in percentages; however, if this is not the case, divide the number of Ph+ cells by the total number of cells examined (200 is very common). Multiply this value by 100 to determine the percent Ph+ cells present.

**Questions 155-156: Other abnormality**

Indicate whether FISH studies performed at the time of best response (question 194) demonstrated any clonal abnormalities other than the Philadelphia chromosome (t(9;22)(q34;q11) and variants). For FISH studies, a clonal abnormality is defined as an abnormality occurring at a frequency (percentage of cells) above the upper limit of normal. See question 26 for further instructions on reporting clonal abnormalities as detected by FISH methods.

If other abnormalities were detected, report “yes” and indicate all other clonal abnormalities in question 156. In cases where FISH studies reveal many other abnormalities, centers should report “see report” in question 156 and attach a copy of the FISH report(s) to the form in FormsNet3\textsuperscript{SM}. For further instructions on how to
attach documents in FormsNet3SM, refer to the Training Guide.

If no other abnormalities were detected, report “no” for question 155 and go to question 157.

**Question 157: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the FISH report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Questions 158-159: Were tests for molecular markers performed (e.g., PCR)?**

Refer to questions 31-32 for a description testing for molecular markers. If testing for molecular markers was performed at the time of best response (question 194), report “yes” and indicate the sample collection date in question 159. Only report testing performed during the reporting period.

If no molecular marker testing was performed or it is unknown if testing was done, report “no” or “unknown” respectively and go to question 189.

**Question 160: Was BCR / ABL detected?**

If any test for BCR / ABL was positive at the time of best response (question 194), report “yes” and continue with question 161. If all testing for BCR / ABL was negative, report “no” for question 160 and go to question 163.

**Question 161: Specify level of detection**

The results of quantitative PCR tests for BCR / ABL mutations are typically reported as a percentage. This value corresponds to the ratio of total number of BCR / ABL copies divided by the total number of control copies. Report the result of testing performed closest to the date response to therapy was assessed.

If it is not clear how to report the level of detection documented in the lab report, contact your center’s liaison for assistance.

**Question 162: Was BCR / ABL level of detection reported on the Standardized International Scale (IS)?**

Refer to question 35 for a description of the Standardized International Scale (IS). If the result reported in question 161 is adjusted to IS, report “yes.” If not, report “no.”

**Question 163: Were two consecutive tests performed? (quantitative and / or nested; of adequate quality [sensitivity > 104])**

Indicate whether two consecutive quantitative tests for BCR / ABL were obtained at the time of best
response (question 194). Ensure the sensitivity of both tests is greater than 1:10,000. If consecutive tests were obtained and the sensitivity of both tests > 1: 10,000, report “yes,” otherwise, report “no.”

If question 160 is answered “yes,” go to question 164. Otherwise, go to question 188.

**Questions 164-165: Specify BCR / ABL breakpoint**

Indicate the breakpoint identified on the BCR / ABL testing reported in questions 160-161. If the breakpoint identified does not match the options provided, report “other breakpoint” for question 164 and specify the breakpoint identified in question 165. If the breakpoint cannot be determined from the testing performed, report “unknown” for question 164.

**Questions 166-187: Was BCR / ABL kinase domain mutation analysis performed?**

If testing for kinase domain (KD) mutations was performed at the time of best response (question 194), report “yes” for question 166 and complete questions 167-187. Only report testing performed during the reporting period. If a KD mutation was tested, but is not included in questions 167-186, report the test result in question 186 and specify the mutation tested in question 187.

**Question 188: Was documentation submitted to the CIBMTR?**

Indicate whether a copy of the molecular testing report was attached to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Questions 189-190: Spleen size**

Report the spleen size in centimeters below the left costal margin as assessed by physical exam at the time of best response. If the physical exam does not find any evidence of splenomegaly, report “0.” If the physical exam findings are not documented, report “unknown.”

**Question 191: What was the best response to therapy?**

Indicate the best response to therapy using the international working group criteria provided in CML Response Criteria section of the Forms Instructions Manual. The best response is determined by a disease assessment, such as hematologic testing, pathology study, and/or physician assessment.

If the best response to the line of therapy is complete hematologic response or chronic phase, go to question 192.

If the best response to the line of therapy is accelerated phase, go to question 194.
If the best response to the line of therapy is blast phase, go to question 193.

**Question 192: Specify level of best response**

If the recipient's best response to therapy (question 191) is “complete hematologic remission” or “chronic phase,” specify the cytogenetic / molecular response. Refer to Table 1 for definitions of cytogenetic and molecular responses.

**Question 193: Specify blast phase phenotype**

Assessments performed on the bone marrow or peripheral blood may be used to determine the blast phenotype at the time of best response. Indicate which phenotype was detected. If phenotype cannot be determined from the assessments performed, report “unknown.”

**Question 194: Date assessed**

Report the date the best response to the line therapy was established. This should be the earliest date all international working group criteria (see CML Response Criteria) were met for the response reported in question 191. Enter the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically evaluated the recipient’s response.

If the best response was achieved prior to starting the line of therapy being reported, indicate the date of the first assessment which was performed after initiating the current line of therapy and confirms the sustained response.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.
Q195-198: Disease Status at Time of Evaluation for this Reporting Period

Question 195: What was the disease status?

Report the recipient’s disease status at the time of evaluation for this reporting period. Ensure the disease status is consistent with the international working group criteria provided in the CML Response Criteria section of the Forms Instructions Manual.

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

Question 196: Specify level of response:

If the recipient's current disease status (question 195) is “complete hematologic remission” or “chronic phase,” specify the cytogenetic / molecular response. Refer to Table 1 for definitions of cytogenetic and molecular responses.

Question 197: Specify blast phase phenotype

Assessments performed on the bone marrow or peripheral blood may be used to determine the blast phenotype at the time of best response. Indicate which phenotype was detected. If phenotype cannot be determined from the assessments performed, report “unknown.”

Question 198: Date assessed

Report the date the current disease status was established. Report the date of the most recent disease-specific assessment performed within approximately 30 days of the date of contact. Enter the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessment was performed within approximately 30 days of the date of contact, report the office visit in which the physician clinically evaluated the recipient's response.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.
**2013/2113: Chronic Lymphocytic Leukemia (CLL)**

Chronic lymphocytic leukemia (CLL) is a cancer of the B lymphocytes. B lymphocytes are white blood cells that develop in the bone marrow and circulate throughout the blood to fight infection. In CLL, lymphocytes with damaged DNA proliferate within the blood, accumulating in the bone marrow, lymph nodes, and organs. The damaged lymphocytes do not fight infections as well as healthy lymphocytes. Symptoms of CLL are generally caused by the replacement of healthy blood cells (including red blood cells and white blood cells) with leukemic cells in the bone marrow and lymph nodes. Symptoms include frequent infections, fever, fatigue, splenomegaly, night sweats, etc.

Small lymphocytic lymphoma (SLL) describes the condition in which abnormal lymphocytes with the same morphology and immunophenotype as CLL present primarily in the lymph nodes.

Hairy cell leukemia is similar to CLL, but the lymphocytes have a distinct “hairy” appearance under the microscope.

Prolymphocytic leukemias are identified by the presence of abnormal prolymphocytes, the precursor to lymphocytes. These leukemias are more aggressive and are split into two subtypes: B-cell prolymphocytic leukemia and T-cell prolymphocytic leukemia.

**CLL Response Criteria**

2013: CLL Pre-Infusion

2113: CLL Post-Infusion
**CLL Response Criteria**

**Complete Response (CR)**¹

All of the following:

- No evidence of lymphadenopathy
- No organomegaly
- Neutrophils $\geq 1.5 \times 10^9/L$
- Platelets $> 100 \times 10^9/L$
- Hemoglobin $> 11$ g/dL
- Lymphocytes $< 4 \times 10^9/L$
- Bone marrow $< 30\%$ lymphocytes
- Absence of constitutional symptoms (including weight loss, fever, and night sweats)


² Absence of significant lymphadenopathy (e.g., lymph nodes $> 1.5$ cm in diameter) by physical examination. In clinical trials, a CT scan of the abdomen, pelvis, and thorax is desirable if previously abnormal. Lymph nodes should not be larger than 1.5 cm in diameter.

**Partial Response (PR)**

All of the following, if applicable:

- $\geq 50\%$ decrease in peripheral blood lymphocyte count from pretreatment value
- $\geq 50\%$ reduction in lymphadenopathy if present pretreatment
- $\geq 50\%$ reduction in liver and/or spleen size if enlarged pretreatment

In addition, one or more of the following:

- Neutrophils $\geq 1.5 \times 10^9/L$ or $50\%$ improvement over baseline
- Platelets $> 100 \times 10^9/L$ or $50\%$ improvement over baseline
• Hemoglobin > 11 g/dL or 50% improvement over baseline

**Stable Disease (SD)**

No change (not complete response, partial response, or progressive disease)

**Progressive Disease (Prog)**

One or more of the following:

- ≥ 50% increase in the sum of the products of ≥ 2 lymph nodes (≥ 1 lymph node must be ≥ 2 cm) or new nodes
- ≥ 50% increase in liver or spleen size, or new hepatomegaly or splenomegaly
- ≥ 50% increase in absolute lymphocyte count to ≥ 5 ×10⁹/L
- Transformation to a more aggressive histology

*Report relapse from CR using this response indicator.*

**Untreated**

No chemotherapy given in the six months prior to the HCT

**Not Assessed**

No evaluation performed


**Manual Updates:**

Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.
<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/23/17</td>
<td>Remove</td>
<td>Removed criteria for <strong>Nodular Partial Remission</strong> as this disease status is no longer captured on the forms.</td>
</tr>
<tr>
<td>3/5/15</td>
<td>Add</td>
<td>The disease status criteria for CLL, formerly available in the Pre-TED section of the Forms Instruction Manual, has been moved to a new section of the manual titled <strong>CLL Response Criteria</strong>.</td>
</tr>
</tbody>
</table>
The Chronic Lymphocytic Leukemia Pre-Infusion Data Form is one of the Comprehensive Report Forms. This form captures CLL-specific pre-infusion data such as: disease assessment at diagnosis, laboratory studies at diagnosis, pre-infusion treatment for CLL, most recent disease assessment prior to the start of the preparative regimen, laboratory studies prior to the preparative regimen or cellular therapy, and disease status at the last assessment prior to the preparative regimen or cellular therapy.

This form must be completed for all recipients assigned to the CRF track whose disease, reported on Pre-TED Disease Classification Form (Form 2402), is chronic lymphocytic leukemia (CLL), B-cell/small lymphocytic leukemia (SLL), or prolymphocytic leukemia (PLL). Both Form 2013 (Chronic Lymphocytic Leukemia Pre-Infusion Data) and Form 2018 (Hodgkin and Non-Hodgkin Lymphoma Pre-Infusion Data), must be completed if the recipient had a Richter’s transformation from CLL to diffuse large B-cell lymphoma prior to transplant or cellular therapy.

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1.

If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than CLL), begin the form at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, check the indicator box and continue with question 149.

Q1-21: Disease Assessment at Diagnosis
Q22-73: Laboratory Studies at Diagnosis
Q74-148: Pre-HCT or Pre-Infusion Therapy
Q149-191: Disease Assessment at Last Evaluation Prior to the Start of the Preparative Regimen
Q192-193: Disease Status at the Last Assessment Prior to the Preparative Regimen

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference
the retired manual section on the [Retired Forms Manuals](#) webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
<tr>
<td>12/12/2016</td>
<td>2013: CLL Pre-Infusion</td>
<td>Modify</td>
<td>Instructions for Revision 2 of the CLL Pre- and Post-HCT Forms were retired and instructions for Revision 3 of the CLL Pre- and Post-Infusion Forms were released.</td>
</tr>
</tbody>
</table>
**Q1-21: Disease Assessment at Diagnosis**

*Subsequent Infusion*

If this is a report of a second or subsequent transplant or cellular therapy, check “yes” under the Subsequent Transplant or Cellular Therapy section of the form and continue with question 149.

**Questions 1-2: What was the date of diagnosis of Chronic Lymphocytic Leukemia?**

Report the date of the first pathologic diagnosis (e.g., bone marrow biopsy or flow cytometric analysis of the peripheral blood) of CLL, SLL, or PLL. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathologic or laboratory assessment is available, the dictated date of diagnosis within a physician’s note may be reported. Do not report the date symptoms first appeared. The date of diagnosis is important because the interval between diagnosis and HCT or cellular therapy is often a significant indicator for the recipient’s prognosis post-infusion.

If the exact pathologic diagnosis date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

Indicate if documentation (e.g., pathology report) was submitted to the CIBMTR in question 2. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 3: Did a histologic transformation occur at any time after CLL diagnosis?**

Histologic transformation may occur after CLL diagnosis. Indicate if CLL transformed into another disease, such as diffuse large B-cell lymphoma (known as Richter’s transformation or Richter’s syndrome). If CLL transformed, report “yes” and continue with question 4. If CLL did not transform, report “no” and continue with question 8.

**Question 4: Date of transformation:**

Report the date of assessment that determined the disease transformation. Use the date of the pathologic evaluation (e.g., lymph node biopsy) and enter the date the sample was collected.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.
Questions 5-7: Specify the disease classification after transformation:

Indicate if the new disease classification is diffuse large B-cell lymphoma (Richter syndrome) or other histology.

Richter’s Syndrome occurs when CLL transforms into diffuse large B-cell lymphoma. If the recipient transforms to diffuse large cell lymphoma, report Non-Hodgkin Lymphoma (NHL) on question 357 of Form 2400 (Revision 4) as the primary disease for HCT. In addition to this form, Form 2018 (Hodgkin and Non-Hodgkin Lymphoma Pre-HCT Data) must be completed.

In rare cases, CLL may transform into another disease such as Hodgkin Lymphoma or a T-cell lymphoma. Evolution to a component of B-cell prolymphocytic leukemia (B-PLL) during the natural history of relapsed CLL/SLL is also common. If CLL transforms into another histology, specify using question 6.

Indicate whether documentation (pathology report) was submitted to the CIBMTR in question 7. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 8-11: Autoimmune disorder(s) at diagnosis:

Autoimmune cytopenias appear in 5-10% of patients with CLL. Treatment for these disorders may include corticosteroids or even splenectomy if unresponsive. Indicate whether any of the following autoimmune disorders were present at diagnosis:

- Immune Hemolytic Anemia: the destruction of red blood cells by the immune system. This disorder is typically diagnosed using a Direct Antiglobulin Test (DAT) also known as the Coombs Test. This assay will determine whether the body is producing antibodies which will target red blood cells.

- Immune Thrombocytopenia: the destruction of platelets by the immune system. This is typically a clinical diagnosis and platelet specific antibodies are not routinely ordered due to their low sensitivity and specificity. However, if platelet specific antibodies were tested for and found to be present this would support a diagnosis of immune thrombocytopenia. A clinical diagnosis should be confirmed if the provider notes are unclear.

If the recipient had an autoimmune disorder at diagnosis which is not listed above (e.g., pure red cell aplasia), report “other” and specify the other autoimmune disorder in question 11.

Questions 12-13: Rai stage (at diagnosis):

Using the criteria in Table 1 below, indicate the Rai stage at diagnosis. If the Rai stage at diagnosis is not clear from the available documentation, consult with a physician and have them document the stage. If the
Rai stage at diagnosis is unknown, select “unknown” for question 12 and skip question 13.

Table 1. Rai Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Risk</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Low Risk</td>
<td>Lymphocytosis (&gt; 15,000 × 10^9/L) in blood or bone marrow only without adenopathy, hepatosplenomegaly, anemia or thrombocytopenia</td>
</tr>
<tr>
<td>Stage I</td>
<td>Intermediate Risk</td>
<td>Lymphocytosis plus enlarged lymph nodes (lymphadenopathy) without hepatosplenomegaly, anemia, or thrombocytopenia</td>
</tr>
<tr>
<td>Stage II</td>
<td>Intermediate Risk</td>
<td>Lymphocytosis plus enlarged liver or spleen with or without lymphadenopathy</td>
</tr>
<tr>
<td>Stage III</td>
<td>High Risk</td>
<td>Lymphocytosis plus anemia (hemoglobin &lt; 11 g/dL) with or without enlarged liver, spleen, or lymph nodes</td>
</tr>
<tr>
<td>Stage IV</td>
<td>High Risk</td>
<td>Lymphocytosis plus thrombocytopenia (platelet count &lt; 100 × 10^9/L) with or without anemia or enlarged liver, spleen, or lymph nodes</td>
</tr>
</tbody>
</table>

Question 14-15: What was the Binet stage at diagnosis?

Using the criteria in Table 2 below, indicate the Binet stage at diagnosis. If the Binet stage at diagnosis is not clear from the available documentation, consult with a physician and have them document the stage. If the Binet stage at diagnosis is unknown, report “unknown” and skip question 15.

The Binet staging focuses on lymphoid bearing areas: axillary, cervical, inguino-femoral, liver, and spleen.

Table 2. Binet Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage A</td>
<td>Two or fewer lymphoid bearing areas enlarged, without anemia or thrombocytopenia</td>
</tr>
<tr>
<td>Stage B</td>
<td>Three or more lymphoid bearing areas enlarged, without anemia or thrombocytopenia</td>
</tr>
<tr>
<td>Stage C</td>
<td>Presence of anemia (hemoglobin &lt; 10.0 g/dL) or thrombocytopenia (platelet count &lt; 100 × 10^9/L or 100,000/μL)</td>
</tr>
</tbody>
</table>

Question 16: Were systemic symptoms (B symptoms) present?

Using the criteria below, indicate if the recipient had “B symptoms” (also known as systemic or constitutional symptoms) at the time of diagnosis. If the symptoms at diagnosis are not clear from the available documentation, consult with a physician and have them document the presence or absence of “B"
symptoms. If the symptomology at diagnosis is unknown, select “unknown” for question 16 and continue with question 17.

Table 3. Systemic Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>None of the symptoms listed in B below</td>
</tr>
</tbody>
</table>
| B        | • Unexplained fever > 38° C (100.4° F);  
|          | • Night sweats; or, 
|          | • Unexplained weight loss of > 10% of body weight in six months before treatment |

Question 17: Was extranodal disease present at diagnosis?

Extranodal disease involves sites other than the lymph nodes, spleen and thymus. Common areas of extranodal involvement include the bone marrow, central nervous system, liver, and lungs. Extranodal involvement is most often detected utilizing imaging techniques or pathologic findings.

If there was extranodal involvement at diagnosis, indicate “yes” and complete questions 18-21.

If there was no evidence of extranodal involvement, select “no” and skip questions 18-21.

Questions 18-21: Specify site(s) of extranodal involvement

Specify the site(s) of extranodal involvement. If “other site” is reported, specify any other sites of involvement in question 21.

Q22-73: Laboratory Studies at Diagnosis

All values reported in questions 22-73 must reflect testing performed prior to any treatment of CLL/SLL/PLL. If testing was not performed near the time of diagnosis and prior to the initiation of treatment, the center should report unknown for that value. An exception is question 40, leukemia cell type, which may not be confirmed until after treatment is started. Centers should report the cell type if confirmed at any time prior to HCT or cellular therapy.

Question 22-23: WBC

Indicate whether the white blood count (WBC) in the peripheral blood is “known” or “unknown” at the time of diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “unknown,” skip question 23 and continue with question 24.

Question 24-25: Hemoglobin (untransfused):

Indicate whether the hemoglobin is “known” or “unknown” at the time of diagnosis. If the recipient is receiving red blood cell (RBC) transfusions, ensure no RBC transfusions have been given within 30 days of the value reported. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “unknown,” skip question 25 and continue with question 26.

Report “unknown” if no testing was performed at least 30 days after any RBC transfusions were being given at the time of diagnosis.

Question 26-27: Platelets (untransfused):

Indicate whether the platelet count is “known” or “unknown” at the time of diagnosis. If the recipient is receiving platelet transfusions, ensure no platelet transfusions have been given within 7 days of the value reported. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “unknown,” skip question 27 and continue with question 28.

Report “unknown” if no testing was performed at least 7 days after any platelet transfusions being given at the time of diagnosis.

Question 28-29: Lymphocytes:

Indicate whether the percentage of lymphocytes is “known” or “unknown” at the time of diagnosis. If “known,” report the laboratory value documented on the laboratory report. If “unknown,” skip question 29 and continue with question 30.
Question 30-31: Prolymphocytes

Indicate whether the percentage of prolymphocytes in the peripheral blood is “known” or “unknown” at the time of diagnosis. If “known,” report the laboratory value documented on the laboratory report. If “unknown,” skip question 31 and continue with question 32.

Question 32-34: LDH:

Indicate whether the lactate dehydrogenase (LDH) value is “known” or “unknown” at the time of diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “unknown,” skip question 33-34 and continue with question 35.

If known, indicate the upper limit of normal for LDH at the institution where testing was performed.

Question 35-37: Serum β2 microglobulin

Indicate whether the serum β2 microglobulin is “known” or “unknown” at the time of diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “unknown,” skip question 36-37 and continue with question 38.

If known, indicate the upper limit of normal for the serum β2 at the institution where testing was performed.

Question 38-39: Lymphocytes in bone marrow:

Indicate whether the percentage of lymphocytes in the bone marrow is “known” or “unknown” at the time of diagnosis. If “known,” report the laboratory value documented on the laboratory report. If “unknown,” skip question 39 and continue with question 40.

Question 40: Leukemia cell type (may be determined at any time after diagnosis)

Indicate the leukemic cell type: B-cell or T-cell. Cell type can be determined using immunophenotyping techniques such as flow cytometry. The cell type may be determined at any time after diagnosis and prior to HCT or cellular therapy. If the leukemic cell type is unknown, select “unknown” and continue with question 41.

Question 41-42: Were tests for molecular markers performed (e.g. PCR) at the time of diagnosis?

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient’s primary disease. Testing for these sequences is often performed using PCR based methods; however, lower sensitivity testing, including FISH, may also be used to detect molecular markers. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue.
If testing for molecular markers was performed at the time of CLL diagnosis, report “yes” and indicate the sample collection date in question 42. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If no molecular marker testing was performed or it is unknown if testing was done, report “no” or “unknown” respectively and skip questions 42-51.

**Question 43-51: Specify results**

For each molecular marker in questions 43-50, report whether testing was “positive,” “negative,” or “not done.” If tests identified a molecular marker other than those listed in questions 43-48, report the result in question 49 and specify the marker in question 50.

If multiple “other molecular markers” were tested at diagnosis, report “see attachment” in question 50 and attach the final reports for any other markers which were tested. In this scenario, report “positive” in question 49 if any of the “other molecular markers” were detected.

Indicate if documentation was submitted to the CIBMTR (e.g., pathology report) in question 51. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 52: Was flow cytometry (immunophenotyping) performed at the time of diagnosis?**

Flow cytometry (immunophenotyping) is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be detected on cellular material.

If flow cytometry (immunophenotyping) was performed at the time of diagnosis, report “yes” and continue with question 53. If not, report “no” and skip questions 53-60.

**Question 53-60: Specify flow cytometry results performed at the time of diagnosis**

For each cell surface marker in questions 53-60, report whether testing was “positive,” “negative,” or “not done.” If flow cytometry was not performed for a given marker, report “not done.”

**Question 61: Were cytogenetics tested (karyotyping or FISH) at the time of diagnosis?**

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the
dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

FISH is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in CLL. These probes are mixed with cells from the recipient's blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells. FISH may be used as surveillance for changes associated with post-therapy malignancy.

If cytogenetic studies were obtained at diagnosis, report “yes” and continue with question 62.

If cytogenetic studies were attempted, but there were not adequate cells (metaphases), report “yes,” and specify “no evaluable metaphases” in question 62; skip questions 63-73.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, report “no” or “unknown” respectively in question 63 and skip questions 63-73.

**Question 62: Results of test**

Indicate if cytogenetic studies identified any clonal abnormalities (any karyotype other than 46XX or 46XY) at the time of diagnosis. For karyotype studies, a clonal abnormality is defined as an abnormality detected in two or more cells. For FISH studies, the level of detection should be above the upper limit of normal as specified in the report. If an upper limit is not specified and the FISH result indicates an abnormality was present, consult a physician to determine whether the abnormality ought to be reported.

If chromosomal abnormalities were detected, indicate “abnormalities identified,” continue with question 63.

If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified, skip questions 63-73.

**Questions 63-73: Specify results**

For each cytogenetic abnormality, report whether testing was positive (yes) or negative (no). Refer to question 62 for further information on how to determine if a testing is positive or negative for a clonal abnormality. If an abnormality was detected, but cannot be reported in question 63-70, report “yes” for question 71 and specify any abnormalities detected and not already reported above in question 72.

For more information regarding cytogenetic terminology and nomenclature, see [Appendix C](#).

Indicate whether documentation (cytogenetic or FISH report) was submitted to the CIBMTR in question 73.
For further instructions on how to attach documents in FormsNet3\textsuperscript{SM}, refer to the \textit{Training Guide}.
Q74-148: Pre-HCT or Pre-Infusion Therapy

The FormsNet3 application allows questions 75-148 to be reported multiple times. Complete these questions for each line of therapy administered prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given). When submitting the paper version of the form for more than two lines of therapy, copy the “Pre-HCT or Pre-Infusion Therapy for Chronic Lymphocytic Leukemia” section and complete a “Line of Therapy” section for each line of therapy administered.

A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.). If a recipient’s disease status changes resulting in a change to treatment, a new line of therapy should be reported. Additionally, if therapy is changed because a favorable disease response was not achieved, a new line of therapy should be reported.

Question 74: Was therapy given between diagnosis and the start of the preparative regimen?

Indicate if the recipient received treatment for their primary disease between diagnosis and the start of the preparative regimen. If “yes,” continue with question 75. If “no” or “unknown,” skip questions 75-148.

Question 75: Systemic therapy

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally. Common systemic therapies used to treat CLL include chemotherapy and monoclonal antibodies.

If systemic therapy was administered, report “yes” and continue with question 76. If not, report “no” and skip questions 76-108.

Question 76-77: Date therapy started

Indicate whether the therapy start date is “known” or “unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 77. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in

Richter’s Transformation

If completing this form for a recipient whose disease has undergone Richter’s transformation prior to HCT, only report therapy administered prior to transformation on the CLL Pre-Infusion Data Form. Any therapy given post-transformation will be reported on the Lymphoma Pre-Infusion Data Form and should not be duplicated on this form.
the General Instructions, General Guidelines for Completing Forms.

**Question 78-79: Date therapy stopped**

Indicate if therapy stop date is “known” or “unknown.” If the therapy is being given in cycles, report the date the recipient started the last cycle for this line of therapy in question 79. Otherwise, report the final administration date for the therapy being reported. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy stopped is “unknown,” skip question 79.

**Question 80-81: Number of cycles**

Systemic therapy (e.g., chemotherapy, monoclonal Abs) is usually administered in cycles with rest periods in-between. This enables cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from the damage sustained during therapy. A cycle can last one or more days and can repeat weekly, bi-weekly, or monthly. A single systemic therapy course may consist of multiple cycles.

Indicate whether the number of cycles is “known” or “unknown.” If known, enter the number of cycles the recipient received in question 81. If “unknown,” continue with question 82.

If therapy is not being administered in cycles (e.g., daily chemotherapy), report “unknown” for question 80 and skip question 81.

**Questions 82-107: Specify therapy given**

Treatments vary based on protocol and in most cases are administered in the outpatient setting. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. For the line of therapy being reported, report “yes” for any drug administered. Report “no” for any drug(s) not given. Do not leave any responses blank. If the recipient received a systemic therapy which is not listed, report “yes” for “other treatment” and specify the treatment in question 107. Report the generic name of the agent, not the name brand.

**Question 108: Was this line of therapy given for stem cell mobilization (priming)?**

The release of stem cells from the bone marrow into the peripheral blood is called stem cell mobilization (priming). Chemotherapy agents (e.g., cyclophosphamide) may be used to stimulate the mobilization of these stem cells for future collections.

If this line of therapy was given for stem cell mobilization, report “yes.” If not, report “no.”
**Question 109: Radiation therapy**

Radiation therapy utilizes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. For CLL, radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes. Radiation therapy may be given in conjunction with systemic chemotherapy or as a separate line of therapy.

If radiation therapy was given during or adjacent to administration of systemic therapy, report them together as single line of therapy on the form (i.e., one copy of questions 75-148). Otherwise, capture the radiation treatment as a separate line of therapy.

If the recipient received radiation therapy between the time of diagnosis and the start of the preparative regimen, report “yes” and continue with question 110. If not, report “no” and skip questions 110-116.

**Question 110-111: Date therapy started**

Indicate whether the start date for radiation therapy is “known” or “unknown.” If known, enter the date radiation therapy began in question 111. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

**Questions 112-113: Date therapy stopped**

Indicate if the stop date for radiation therapy is “known” or “unknown.” If known, enter the final date radiation was administered in question 113. If the stop date is partially known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

**Question 114-116: Specify site(s) of radiation therapy**

Report all sites of radiation therapy administered between the start and stop dates reported in questions 110-113. If “yes” is reported for “Other site,” specify all other sites in question 116.

**Question 117: Surgery**

If surgery was performed during or adjacent to administration of systemic therapy or a period of radiation therapy report them together as single line of therapy on the form (i.e., one copy of questions 75-148). Otherwise, capture the surgery as a separate line of therapy.

If the recipient underwent surgical treatment for their primary disease, report “yes,” continue with question 118. If not, report “no” and skip questions 118-121.
Question 118: Date of surgery

Enter the date the surgery occurred. If the date of surgery is partially known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

Question 119-121: Specify surgery

Report all sites of surgery performed on the date reported in question 118. If “yes” is reported for “Other site,” specify all other sites in question 121.

Question 122: Best response to line of therapy

Indicate the best response to the line of therapy using the international working group criteria provided in CLL Response Criteria section of the Forms Instructions Manual. The best response is determined by a disease assessment, such as hematologic testing, pathology study, and/or physician assessment.

If the best response to the line of therapy was not evaluated, report “not assessed (NA)” and skip question 123-148.

If the best response to the line of therapy is unknown, report “unknown” and skip question 123-148.

Question 123: Date best response established

Report the date the best response to the line therapy was established. This should be the earliest date all international working group criteria were met for the response reported in question 122. Enter the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically evaluated the recipient’s response.

If the best response was achieved prior to starting the line of therapy being reported, indicate the date of the first assessment which was performed after initiating the current line of therapy and confirms the sustained response.
If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

**Question 124-125: Were tests for molecular markers performed (e.g. PCR)?**

Indicate whether testing for molecular markers was performed between the time the best response was achieved and starting a new line of therapy or the preparative regimen. If multiple tests were performed during this time period, report the testing performed closest to the date of best response (question 123). For further instructions on reporting testing for molecular markers, refer to questions 41-42.

If testing for molecular markers was done during this time period, report “yes” and indicate the sample collection date in question 125. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If testing for molecular markers was not during this time period, report “no” and skip questions 126-133.

**Question 126-133: Specify results**

For each molecular marker in questions 126-132, report whether testing was “positive,” “negative,” or “not done.” If tests identified a molecular marker other than those listed in questions 126-131, report the result in question 132 and specify the marker in question 133.

If multiple “other molecular markers” were tested at the time of best response, report “see attachment” in question 133 and attach the final reports for any other markers which were tested. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide. In this scenario, report “positive” in question 132 if any of the “other molecular markers” were detected.

**Question 134-135: Was the disease status assessed via flow cytometry (minimum 4-color flow) (immunophenotyping)?**

Indicate whether flow cytometry (immunophenotyping) was performed between the time the best response was achieved and starting a new line of therapy or the preparative regimen. If multiple tests were performed during this time period, report the testing performed closest to the date of best response (question 123).

If flow cytometry was done during this time period, report “yes” and indicate the sample collection date in question 135. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If flow cytometry was not during this time period, report “no” and skip questions 135-136.
**Question 136: Was disease detected?**

Indicate whether disease was detected by flow cytometry. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 137: Was the disease status assessed via cytogenetic testing (karyotyping or FISH)?**

Indicate whether karyotyping or FISH assessments were performed between the time the best response was achieved and starting a new line of therapy or the preparative regimen. If multiple tests were performed during this time period, report the testing performed closest to the date of best response (question 123).

If karyotyping or FISH assessments were done during this time period, report “yes” and continue with question 138. If not, report “no” and skip questions 138-143.

**Question 138-139: Was the disease status assessed via FISH?**

Indicate whether FISH testing was performed between the time the best response was achieved and starting a new line of therapy or the preparative regimen. If multiple tests were performed during this time period, report the testing performed closest to the date of best response (question 123).

If FISH testing was done during this time period, report “yes” and indicate the sample collection date in question 139. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](#).

If FISH testing was not done during this time period, report “no” and skip questions 139-140. Examples of this include: no FISH study performed or FISH sample was inadequate.

**Question 140: Was disease detected?**

Indicate whether disease was detected by FISH. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 141-142: Was the disease status assessed via conventional cytogenetics (karyotyping)?**

Indicate whether karyotyping was performed between the time the best response was achieved and starting a new line of therapy or the preparative regimen. If multiple tests were performed during this time period, report the testing performed closest to the date of best response (question 123).

If karyotyping was done during this time period, report “yes” and indicate the sample collection date in question 142. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](#).
If karyotyping was not done during this time period, report “no” and skip questions 135-136. Examples of this include: no conventional cytogenetics performed or conventional cytogenetic culture failed.

**Question 143: Was disease detected?**

Indicate if disease was detected by karyotyping. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 144-145: Was the disease status assessed by clinical/hematologic assessment?**

Clinical and hematologic assessments are the least sensitive methods of establishing a patient’s disease status. Examples include: pathologic evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination.

Indicate whether clinical and/or hematologic assessments were performed between the time the best response was achieved and starting a new line of therapy or the preparative regimen. If “yes,” report the date of assessment in question 145. The date reported should be that of the most-disease specific assessment performed at the time of best response (question 123). When determining the most disease-specific assessment, only consider studies which have previously shown or currently show evidence of disease. If all assessments are negative, report the date of the most sensitive test performed (e.g., report a bone marrow biopsy rather than a CBC) within the appropriate time period. If assessments are positive for disease, report the first assessment confirming the best response (question 122). If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If no clinical and/or hematologic assessments were performed during this time period, report “no” and skip questions 145-146. This option should rarely be reported given the inclusion of physician assessments.

**Question 146: Was disease detected?**

Indicate if disease was detected by clinical/hematologic assessment. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 147: Did disease relapse/progress following this line of therapy?**

Refer to the international working group criteria provided in CLL Response Criteria section of the Forms Instructions Manual for more information on how to determine recurrence or progression of disease. Report “yes” if the recipient met the criteria for relapse or progression after starting this line of therapy and prior to starting a subsequent line of therapy.
Report “no” if the recipient never relapsed or progressed following this line of therapy. Also, report “no” if the recipient relapsed or progressed after beginning a subsequent line of therapy. This episode of relapse / progression will be captured in the instance (i.e., copy) of questions 75-148 completed for the subsequent line of therapy.

If this is the last line of therapy administered prior to HCT, only report “yes” if relapse or progression occurred prior to infusion. Relapse or progression occurring after the infusion date will be reported on the CLL Post-HCT Data Form (Form 2113).

**Question 148: Date of relapse/progression**

Enter the assessment date that relapse or progression was established following initiation of this line of therapy. Report the date of the pathologic evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathologic and laboratory evaluations. If extranodal disease is detected upon radiographic examination (e.g., X-rays, CT scans, MRI scans, PET scans), enter the date the imaging took place. If the physician determines evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](https://www.cibmtr.org/forms/instructionmanual).
Q149-191: Disease Assessment at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

**Question 149: Did the recipient have known nodal involvement?**

Refer to Graphic 1 for identification of nodal areas. Nodal involvement may be assessed by a physician palpating lymph nodes, pathology from a lymph node biopsy, or radiological assessment (e.g., PET or CT imaging). If evidence of nodal involvement is indicated prior to the start of the preparative regimen/infusion, report “yes,” and continue with Question 150. If not, report “no,” and skip question 150.

*Graphic 1. Nodal Regions*¹
Question 150: Specify the size of the largest nodal mass

Report the size (measured in centimeters) of the largest known nodal mass. If the size of the largest nodal mass cannot be determined, leave question 150 blank and override the validation error using the code “Unknown.”

Question 151: Was extranodal disease present?

If extranodal involvement was identified at the last evaluation prior to the start of the preparative regimen, indicate “yes” and continue with question 152. If not, report “no” and skip questions 152-155.
For further information on reporting extranodal disease, refer to question 17.

**Question 152-155: Specify the site(s) of extranodal involvement**

For questions 152-154, indicate whether extranodal involvement was identified for each site. Do not leave any question unanswered. If there was extranodal involvement at a site other than those listed in questions 152-153, report “yes” for question 154 and specify all other sites of involvement in question 155.

**Questions 156-157: Prolymphocytes**

Indicate whether the percentage of prolymphocytes in the peripheral blood is “known” or “unknown” prior to the start of the preparative regimen (or prior to infusion if no preparative regimen given). If “known,” report the laboratory value documented on the laboratory report. If “unknown,” skip question 157 and continue with question 158.

**Question 158-160 Serum β2 microglobulin?**

Indicate whether the β2 microglobulin is “known” or “not known” prior to the start of the preparative regimen (or prior to infusion if no preparative regimen given). If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “unknown,” skip questions 159-160.

If known, indicate the upper limit of normal for the serum β2 at the institution where testing was performed.

Indicate the upper limit of normal for β2 microglobulin at the institution where testing was performed.

**Questions 161-162: Lymphocytes in bone marrow**

Indicate whether the percentage of lymphocytes in the bone marrow is “known” or “not known” prior to the start of the preparative regimen (or prior to infusion if no preparative regimen given). If “known,” report the laboratory value documented on the laboratory report. If “unknown,” skip question 162 and continue with question 163.

**Question 163-164: Were tests for molecular markers performed (e.g. PCR)?**

Indicate whether molecular testing was done prior to the start of the preparative regimen (or prior to infusion if no preparative regimen given). For further instructions on reporting testing for molecular markers, refer to question 41-42.

If molecular testing was done, report “yes” and indicate the sample collection date in question 164. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](#).
If no molecular testing was performed or it is unknown if testing was done, report “no” or “unknown” respectively and skip questions 165-173.

**Questions 165-173: Specify results**

For each molecular marker in questions 165-172, report whether testing was “positive,” “negative,” or “not done.” If tests identified a molecular marker other than those listed in questions 165-170, report the result in question 171 and specify the marker in question 172.

If multiple “other molecular markers” were tested at the time of best response, report “see attachment” in question 172 and attach the final reports for any other markers which were tested. In this scenario, report “positive” in question 171 if any of the “other molecular markers” were detected.

Indicate if documentation was submitted to the CIBMTR (e.g., pathology report) in question 173. For further instructions on how to attach documents in FormsNet3SM, refer to the [Training Guide](#).

**Question 174-175: Was disease assessed via flow cytometry (4-minimum color) (immunophenotyping)?**

Indicate whether flow cytometry (immunophenotyping) was performed prior to the start of the preparative regimen (or prior to infusion if no preparative regimen given). If “yes,” report the sample collection date in question 175. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](#).

If flow cytometry was not performed during this time period, report “no” and skip question 176.

**Question 176: Was disease detected?**

Indicate if disease was detected by flow cytometry. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 177: Were cytogenetics tested (karyotyping of FISH)?**

Indicate if karyotyping or FISH studies were obtained prior to the start of the preparative regimen (or prior to infusion if no preparative regimen given). For further information on reporting karyotyping and FISH assessments, refer to [questions 61-62](#).

If “yes,” continue with question 178. If “no,” skip questions 178-188.

**Question 178: Results of tests**

If chromosomal abnormalities were detected, indicate “abnormalities identified,” and continue with question 179. If cytogenetic studies yielded “no evaluable metaphases” or there were “no abnormalities” identified,
Questions 179-188: Specify results

For each cytogenetic abnormality, report whether testing was positive (yes) or negative (no). Refer to question 62 for further information on how to determine if a testing is positive or negative for a clonal abnormality. If an abnormality was detected, but cannot be reported in question 179-186, report “yes” for question 187 and specify any abnormalities detected and not already reported above in question 188.

Question 189-190: Was the disease assessed by clinical/hematologic assessment?

Clinical and hematologic assessments are the least sensitive methods of establishing a patient's disease status. Examples of those include: pathologic evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination.

If clinical and/or hematologic assessment were performed at the time of disease assessment prior to the start of the preparative regimen (or prior to infusion if no preparative regimen given), report “yes” and report the date of assessment in question 90. For further information on reporting the date of clinical/hematologic assessment, refer to questions 144-145.

If no clinical and/or hematologic assessments were performed at the time of disease assessment prior to the start of the preparative regimen (or prior to infusion if no preparative regimen given), report “no” and skip question 191.

Question 191: Was disease detected?

Indicate if disease was detected by clinical/hematologic assessment. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.
Q192-193: Disease Status at the Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

Question 192: What was the disease status at the last evaluation prior to the start of the preparative regimen?

Nodular Partial Response
Nodular partial response (nPR) is a listed disease status option on the Pre-TED Form (Form 2400), but not on the CLL Pre- and Post-HCT Data Forms (Form 2013 and 2113). If the disease status meets the criteria for nPR, report the disease status as partial response (PR) on Forms 2013 and 2113.

Indicate the disease status using the international working group criteria provided in CLL Response Criteria section of the Forms Instructions Manual. The pre-HCT disease status is determined by a disease assessment, such as hematologic testing, pathology study, and/or physician assessment.

If no chemotherapy was given within 6 months of the start of the preparative regimen, report “Untreated.”

If the best response to the line of therapy was not evaluated, report “not assessed (NA)” and skip question 193.

If the best response to the line of therapy is unknown, report “unknown” and skip question 193.

Question 193: Date of the most recent assessment for disease status prior to the preparative regimen

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. Report the date of the pathologic evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-rays, CT scans, MRI scans, PET scans), or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathologic and laboratory evaluations; enter the date the imaging took place for radiographic assessments. If no pathologic, radiographic, or laboratory assessment was performed within the pre-transplant work-up time period, report the most recent office visit in which the physician assessed the recipient’s disease status.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.
The Chronic Lymphocytic Leukemia Post-Infusion Data Form is one of the Comprehensive Report Forms. This form captures CLL-specific post-infusion data such as: disease assessment at the time of best response to HCT or cellular therapy, laboratory studies at the time of best response to HCT or cellular therapy, post-infusion planned treatment for CLL, disease relapse or progression post-infusion, and disease status at the time of assessment for this reporting period. For an overview of CLL, refer to the instructions for the CLL Pre-Infusion Data Form.

This form must be completed for all recipients assigned to the CRF track whose disease, reported on Pre-TED Disease Classification Form (Form 2402), is chronic lymphocytic leukemia (CLL), B-cell/small lymphocytic leukemia (SLL), or prolymphocytic leukemia (PLL). If the recipient underwent a transformation to diffuse large B-cell lymphoma (Richter’s transformation), only the CLL Pre-Infusion Data Form (Form 2013) must be completed. Do not complete a CLL Post-Infusion Data Form (Form 2113).

The Chronic Lymphocytic Leukemia Post-Infusion Data (Form 2113) must be completed in conjunction with each Post-Infusion Data Follow-up Form. The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100, between day 100 and the six-month date of contact, between the date of contact for the six-month follow-up Form 2200 and one-year date of contact, etc.).

Q1-3: Disease Assessment at the Time of Best Response to HCT or Cellular Therapy
Q4-26: Disease Assessment at Time of Best Response
Q27-42: Post-HCT / Post-Infusion Planned Therapy
Q43-88: Disease Relapse or Progression Post-HCT / Post-Infusion
Q89-113: Disease Status at the Time of Evaluation for This Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

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<td>Comprehensive Disease-Specific Manuals</td>
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<td>2113: CLL Post-Infusion</td>
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Q1-3: Disease Assessment at the Time of Best Response to HCT or Cellular Therapy

Question 1: Compared to the disease status prior to the preparative regimen, what was the best response to HCT or cellular therapy since the date of the last report? (Include response to any therapy given for post-HCT maintenance or consolidation, but exclude any therapy given for relapsed, persistent or progressive disease.)

The intent of this question is to determine the best overall response to HCT / cellular therapy. This is assessed in each reporting period. When evaluating the best response, determine the disease status within the reporting period using the international working group criteria provided in the CLL Response Criteria of the Forms Instructions Manual. Compare this response to all previous post-infusion reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status. See question 2 to indicate that this disease status was previously reported.

Include response to any post-infusion treatment planned as of Day 0. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR or as preemptive therapy for recipients with minimal residual disease, consider this “planned therapy,” even if this was not documented prior to the transplant. Do not include response to any treatment administered as a result of relapse, progression, or persistent disease. If a recipient has started treatment for relapse, progression, or persistent disease, report the best response confirmed prior to the initiation of treatment (even if this was confirmed in a prior reporting period).

Question 2: Was the date of best response previously reported?

If the best response to HCT or cellular therapy was first documented during the current reporting period, report “no” and continue with question 3. If the best response was already documented during a prior reporting period, report “yes” and skip questions 3-26.

Nodular Partial Response
Nodular partial response (nPR) is a listed disease status option on the Pre-TED Form (Form 2400 Revision 4), but not on the CLL Pre- and Post-Infusion Data Forms (Form 2013 and 2113). If the disease status meets the criteria for nPR, report the disease status as partial response (PR) on Forms 2013 (Revision 3) and 2113.

* CIBMTR.org Forms Instruction Manual - 1
Do not report “yes” if completing this form for the 100 Day reporting period.

**Question 3: Date assessed**

Report the date the best response to HCT or cellular therapy was established. This should be the earliest date when all international working group criteria for the response being reported in question 1 were met. Report the date the sample was collected for pathologic evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). If no pathologic, radiographic, or laboratory assessments were performed to establish the best response, report the office visit in which the physician clinically evaluated the response to HCT or cellular therapy.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](https://cibmtr.org/forms-instruction-manual-1).
Q4-26: Disease Assessment at the Time of Best Response

Question 4-5: Were tests for molecular markers performed (e.g. PCR)?

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods; however, lower sensitivity testing, including FISH, may also be used to detect molecular markers. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue.

If testing for molecular markers was performed at the time of best response, report “yes” and indicate the sample collection date in question 5. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.

If no molecular marker testing was performed or it is unknown if testing was done, report “no” or “unknown” respectively and skip questions 5-13.

Question 6-13: Specify results

For each molecular marker in questions 6-12, report whether testing was “positive,” “negative,” or “not done.” If tests identified a molecular marker other than those listed in questions 6-11, report the result in question 12 and specify the marker in question 13.

If multiple "other molecular markers" were tested at the time of best response, report “see attachment” in question 13 and attach the final reports for any other markers which were tested. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide. In this scenario, report “positive” in question 12 if any of the "other molecular markers" were detected.

Question 14-15: Was the disease status assessed via flow cytometry (minimum 4 color flow) (immunophenotyping)?

Flow cytometry (immunophenotyping) is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be detected on cellular material.

If flow cytometry (immunophenotyping) was performed at the time of best response, report “yes” and indicate the sample collection date in question 15. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, General Guidelines for Completing Forms.
If flow cytometry (immunophenotyping) was not performed, report “no” and skip questions 15-16.

**Question 16: Was disease detected?**

Indicate whether disease was detected by flow cytometry. If this is not clear from the laboratory report, consult with a physician and have them document whether evidence of disease is present.

**Question 17: Was the disease status assessed via cytogenetic testing (karyotyping or FISH)?**

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality which reflects the recipient’s disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see [Appendix C](#).

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

FISH is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in CLL. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells. Additionally, the FISH probe panel should reflect the patient’s current disease; FISH may be used as surveillance for changes associated with post-therapy malignancy.

FISH testing for sex chromosomes after sex-mismatched allogeneic HCT should not be considered a disease assessment as the purpose is to determine donor chimerism.

If cytogenetic (karyotyping or FISH) studies were obtained at the time of best response, report “yes” and continue with question 18.

If cytogenetic studies were attempted at the time of best response, but there were not adequate cells (metaphases), report “no,” and skip questions 18-26.

If no cytogenetic studies were obtained at the time of best response, indicate “no” and skip questions 18-26.

**Question 18-19: Was the disease status assessed via FISH?**

If FISH studies were performed at the time of best response to HCT or cellular therapy, report “yes” and indicate the sample collection date in question 19. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).
If FISH studies were not performed, indicate “no” and skip questions 19-20. Examples of this include: no FISH study performed or FISH sample was inadequate.

**Question 20: Was disease detected?**

Indicate whether disease was detected by FISH. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 21-22: Was the disease status assessed via karyotyping?**

If karyotyping (conventional cytogenetic) studies were performed at time of best response to HCT or cellular therapy, report “yes” and indicate the date sample collection date in question 22. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If karyotyping was not performed, report “no” and skip questions 22-23. Examples of this include: no karyotyping was performed or karyotyping culture failed.

**Question 23: Was disease detected?**

Indicate whether disease was detected by conventional cytogenetics (karyotyping). If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 24-25: Was the disease status assessed by clinical/hematologic assessment?**

Clinical and hematologic assessments are the least sensitive methods of establish a patient’s disease status. Examples include: pathologic evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination.

Indicate whether clinical and/or hematologic assessments were performed at the time the best response. If “yes,” report the date of assessment in question 25. The date reported should be that of the most-disease specific assessment performed at the time of best response (question 3). When determining the most disease-specific assessment, only consider studies which have previously or currently show evidence of disease. If all assessments are negative, report the date of the most sensitive test performed (e.g., report a bone marrow biopsy rather than a CBC) within the appropriate time period. If assessments are positive for disease, report the first assessment confirming the best response (question 1). If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If no clinical and/or hematologic assessments were performed during this time period, report “no” and skip
questions 25-26. This option should rarely be reported given the inclusion of physician assessments.

**Question 26: Was disease detected?**

Indicate whether disease was detected by clinical/hematologic assessment. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.
Q27-42: Post-HCT / Post-Infusion Planned Therapy

Question 27: Was therapy given since the date of last report for reasons other than relapse or progressive disease? (Include any maintenance and consolidation therapy.)

Indicate if the recipient received treatment post-Infusion for reasons other than relapse, progressive, or persistent disease (excluding minimal residual disease (MRD)) during the current reporting period. Recipients are generally transplanted under a specific protocol that defines radiation and/or systemic therapy the recipient is intended to receive as a preparative regimen prior to the HCT or cellular therapy; infection and GVHD prophylaxis to be administered pre- and/or post-HCT; as well as any systemic therapy, radiation, and/or other treatments to be administered post-HCT or cellular therapy as planned (or maintenance) therapy. Planned (maintenance or consolidation) therapy is given to assist in prolonging a remission. Planned therapy may be described in a research protocol or standard of care protocol and these should be referred to when completing this section. If post-transplant therapy is given as prophylaxis or maintenance for recipients in CR, or as preemptive therapy for recipients with minimal residual disease, consider this “planned therapy,” even if this was not documented prior to the transplant. For example, if a physician decides to put the recipient on rituximab maintenance therapy post-HCT or cellular therapy, even if the intent wasn’t documented prior to transplant, report it in this section of the form. Do not include any treatment administered as a result of relapse, progression, or persistent disease (excluding MRD).

If planned therapy, including therapy given for maintenance or consolidation, was given during the reporting period, report “yes” continue with question 28. If “no” or “unknown,” continue skip questions 28-42.

Question 28: Systemic therapy

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally. Common systemic therapies used to treat CLL include chemotherapy and monoclonal antibodies.

Report “yes” if systemic therapy was given as planned treatment post-HCT or cellular therapy (including maintenance and consolidation treatments) during the reporting period and continue with question 29.

If systemic therapy was not given as planned therapy during the reporting period, report “no and skip questions 29-38.
Question 29: Chemotherapy

Indicate whether chemotherapy was given as planned treatment post-HCT or cellular therapy (including maintenance and consolidation treatments) during the reporting period. Do not report immune therapy / monoclonal antibodies (e.g., rituximab) as these treatments will be captured in questions 30-38.

Questions 30-38: Immune therapy/monoclonal antibody (mAb)

Indicate whether immune therapy/monoclonal antibody (mAb) was given as planned treatment post-HCT or cellular therapy (including maintenance and consolidation treatments) during the reporting period.

If “yes,” report the treatment(s) given using questions 31-38. If the recipient received a monoclonal antibody which is not listed, report “Other mAb” for question 35 and specify any other monoclonal antibodies given in question 36. If the recipient received an immune therapy which is not listed, report “yes” in question 37 and specify the other immune therapy in question 38.

If “no,” skip questions 31-38.

Question 39: Radiation

Radiation therapy utilizes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. For CLL, radiation therapy may be used to kill cells which have invaded other tissues and lymph nodes. Radiation therapy may be given in conjunction with systemic chemotherapy or as a separate line of therapy.

Report “yes” if the recipient received radiation as planned therapy post-HCT or cellular therapy (including maintenance and consolidation treatments) during the reporting period. If not, report “no.”

Question 40: Cellular therapy

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “yes” if the recipient received cellular therapy as planned therapy post-HCT (including maintenance and consolidation treatments) during the reporting period. If not, report “no.”

Question 41-42: Other therapy

Indicate if the recipient received any other treatment as planned therapy post-HCT (including maintenance and consolidation treatments). If “yes,” specify the type of treatment administered using question 42. If “no,” skip question 42.
Q43-88: Disease Relapse or Progression Post-HCT / Post-Infusion

Question 43: Was a disease relapse or progression detected since the date of last report?

Refer to the international working group criteria provided in CLL Response Criteria section of the Forms Instructions Manual for more information on how to determine recurrence or progression of disease. If the recipient met the criteria for relapse or progression during the reporting period, report “yes” and continue with question 44. Do not report persistent disease in this section of the form.

If the recipient’s disease did not relapse or progress during the reporting period, report “no” and skip questions 44-54. Questions 44-52 are meant to capture the recipient’s molecular, immunophenotypic, and cytogenetic status at the time of hematologic relapse / progression. Therefore, these questions will only be completed if the recipient has met the criteria for clinical/hematologic relapse or progression during the reporting period.

Question 44-45: Was a disease relapse or progression detected by molecular testing (e.g. PCR)?

If relapse or progression was identified by molecular testing, report “yes” and indicate the sample collection date in question 45. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

Only consider testing performed via molecular methods (e.g., PCR or other methods of equal or greater sensitivity) when completing question 44. Do not consider lower sensitivity testing such as FISH, flow cytometry, karyotyping, or clinical/hematologic methods.

If relapse or progression was not identified by molecular testing, report “no” and skip question 45.

Question 46-47: Was a disease relapse or progression detected via flow cytometry?

If relapse or progression was identified by flow cytometry (immunophenotyping), report “yes” and indicate the sample collection date in question 47. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If relapse or progression was not detected by flow cytometry, report “no” and skip question 47.
**Question 48: Was a disease relapse or progression detected by cytogenetic testing (karyotyping or FISH)?**

Indicate if cytogenetic studies (karyotyping or FISH) were obtained at the time of hematologic relapse / progression. If either of these methods detected relapse / progression, report “yes” and continue with question 49. If “no,” skip questions 49-52.

**Question 49-50: Was a disease relapse or progression detected via FISH?**

If FISH studies identified disease relapse or progression, report “yes” and indicate the date of sample collection in question 50. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If FISH studies did not identify disease relapse or progression, report “no” and skip question 50. Examples of this include: no FISH studies performed or FISH sample was inadequate.

**Question 51-52: Was a disease relapse or progression detected via karyotyping?**

If conventional cytogenetics identified disease relapse or progression, indicate “yes” and report the date of sample collection in question 52. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If conventional cytogenetics did not identify disease relapse or progression, report “no” and skip question 52. Examples of this include: no conventional cytogenetics performed or conventional cytogenetic culture failed.

**Question 53-54: Was a disease relapse or progression detected by clinical/hematologic assessment?**

Clinical and hematologic assessments are the least sensitive methods of establishing a patient's disease status. Examples of those include: pathologic evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination.

If clinical and/or hematologic assessments identified disease relapse or progression, report “yes” and indicate the date of assessment in question 54. Enter the date of the clinical/hematologic disease assessment that documented disease relapse or progression. Report the date disease was detected by radiographic examination (e.g., CT, MRI, PET, or PET/CT scans), bone marrow examination, peripheral blood assessment, or clinical assessment. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.
If clinical and/or hematologic assessments did not identify disease relapse or progression, report “no” and skip question 54.

**Question 55: Was any therapy given for relapse or progressive disease since the date of last report?**

*Therapy for Persistent Disease*

Report treatment for persistent disease (excluding MRD) in questions 55-88. Do not include therapy which has already been reported in questions 27-42 (planned therapy including maintenance and consolidation) unless the treatment is continued after the recipient’s disease has relapsed or progressed.

Systemic therapy, radiation, and/or other treatments may be administered for relapse or progressive disease. Indicate if the recipient received treatment post-infusion for relapse or progressive disease since the date of last report.

**Question 56: Date started**

Enter the date the recipient first received treatment for relapse, progressive, or persistent (excluding MRD) disease during the current reporting period. If the therapy reported in this section is continued from a prior reporting period, leave question 56 blank and override the validation error using the code “Unable to Answer.” If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

**Question 57: Systemic therapy**

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein or given orally. Common systemic therapies used to treat CLL include chemotherapy and monoclonal antibodies.

Report “yes” if systemic therapy was given for relapsed, progressive, or persistent (excluding MRD) disease during the reporting period and continue with question 58.

If systemic therapy was not given for relapsed, progressive, or persistent (excluding MRD) disease during the reporting period, report “no and skip questions 58-83.

**Questions 58-83: Specify systemic therapy**

Report “yes” or “no” for each chemotherapy and immunotherapy drug listed on the form. If the recipient received a chemotherapy treatment that is not listed, report “yes” for “other treatment” and specify the treatment in question 83. Report the generic name of the agent, not the name brand.
Question 84: Radiation therapy

Radiation therapy utilizes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. For CLL, radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes. Radiation therapy may be given in conjunction with systemic chemotherapy or as a separate line of therapy.

Report “yes” if the recipient was given treatment for relapsed, progressive, or persistent (excluding MRD) disease during the reporting period. If not, report “no.”

Question 85: Cellular therapy

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “yes” if the recipient received cellular therapy as treatment for relapsed, progressive, or persistent (excluding MRD) disease during the reporting period. If not, report “no.”

Question 86: Withdrawal of immunosuppression

Immunosuppressive medications may be tapered or entirely withdrawn in order to promote a graft vs leukemia effect in the setting of relapsed, progressive, or persistent (excluding MRD) disease post-HCT.

If immunosuppression is reduced or stopped during the reporting period in order to treat disease, report “yes.” If not, report “no.”

Questions 87-88: Other therapy

Indicate if the recipient received any other treatment for relapsed, progressive, or persistent (excluding MRD) disease during the reporting period. If “yes,” specify the type of treatment administered using question 88. If “no,” skip question 88.
Q89-113: Disease Status at the Time of Evaluation for This Reporting Period

Question 89-90: Were tests for molecular markers performed (e.g. PCR)?

If testing for molecular markers was performed during the reporting period, report “yes” and report the sample collection date of the most recent testing performed during the reporting period in question 90. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If testing for molecular markers was not performed during the reporting period, report “no” or “unknown” and continue with question 99.

For more information on testing for molecular markers, refer to the instructions for questions 4-5.

Questions 91-98: Specify results

For each molecular marker in questions 91-97, report whether the most recent testing performed during the reporting period was “positive,” “negative,” or “not done.” If tests identified a molecular marker other than those listed in questions 91-96, report the result in question 97 and specify the marker in question 98.

If multiple “other molecular markers” were tested at the time of evaluation for this reporting period, report “see attachment” in question 98 and attach the final reports for any other markers which were tested. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 99-100: Was the disease status assessed via flow cytometry (minimum 4-color flow) (immunophenotyping)?

If flow cytometry (immunophenotyping) was performed during the reporting period, report “yes” and indicate the sample collection date of the most recent testing performed during the reporting period in question 100. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If flow cytometry (immunophenotyping) was not performed during the reporting period, report “no” and skip questions 100-101.

For more information on reporting flow cytometry, refer to the instructions for questions 14-15.
Question 101: Was disease detected?
Indicate whether disease was detected by the most recent flow cytometry assessment performed during the reporting period. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

Question 102: Was the disease status assessed by cytogenetic (karyotyping or FISH)?
Indicate whether cytogenetic studies (karyotyping or FISH) were obtained during the reporting period. If cytogenetic studies were obtained, report “yes” and continue with question 103. If not, report “no” and skip questions 103-108.

For more information on reporting karyotyping and FISH studies, refer to the instructions for question 17.

Question 103-104: Was the disease status assessed via FISH?
If FISH studies were performed during the reporting period, report “yes” and indicate the sample collection date of the most recent testing performed during the reporting period in question 104. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If FISH studies were not performed, report “no” and skip questions 104-105. Examples of this include: no FISH study performed or FISH sample was inadequate.

Question 105: Was disease detected?
Indicate whether disease was detected by the most recent FISH study performed during the reporting period. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

Question 106-107: Was the disease status assessed via karyotyping?
If conventional cytogenetic studies were obtained during the reporting period, report “yes” and report the sample collection date of the most recent testing performed during the reporting period in question 107. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If conventional cytogenetic studies were not performed, report “no” and continue with question 109. Examples of this include: no conventional cytogenetics performed or conventional cytogenetic culture failed.
**Question 108: Was disease detected?**

Indicate whether disease was detected by the most recent karyotyping study performed during the reporting period. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 109-110: Was the disease status assessed by clinical/hematologic assessment?**

Indicate whether any clinical and/or hematologic assessments were performed during the reporting period. If “yes,” report the date of assessment in question 110. The date reported should be that of the most-disease specific assessment performed within approximately 30 days of the date of contact (reported on the Post-Infusion Data Form). When determining the most disease-specific assessment, only consider studies which have previously or currently show evidence of disease. If all assessments are negative, report the date of the most sensitive test performed (e.g., report a bone marrow biopsy rather than a CBC) within the appropriate time period. If assessments are positive for disease, report the most recent positive assessment. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).

If no clinical and/or hematologic assessments were performed during this time period, report “no” and skip questions 110-111. This option should rarely be reported given the inclusion of physician assessments.

For more information on reporting clinical/hematologic assessments, refer to the instructions for questions 24-25.

**Question 111: Was disease detected?**

Indicate whether disease was detected by clinical/hematologic assessment on the date reported in question 110. If the findings are unclear, consult with a physician and have them document whether evidence of disease is present.

**Question 112: What is the current disease status?**

- **Nodular Partial Response**
  
  Nodular partial response (nPR) is a listed disease status option on the Pre-TED Form (Form 2400 Revision 4), but not on the CLL Pre- and Post-Infusion Data Forms (Form 2013 and 2113). If the disease status meets the criteria for nPR, report the disease status as partial response (PR) on Forms 2013 (Revision 3) and 2113 (Revision 3).

Report the recipient’s disease status at the time of evaluation for this reporting period. Ensure the disease status is consistent with the international working group criteria provided in the [CLL Response Criteria](#).
section of the Forms Instructions Manual. If the disease was not assessed, report “not assessed” and go to “First Name.” This option should rarely be used given the inclusion of physician assessments as disease evaluations.

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

**Question 113: Date assessed**

The date reported should be that of the most-disease specific clinical / hematologic assessment performed within approximately 30 days of the date of contact (reported on the Post-Infusion Data Form). When determining the most disease-specific assessment, only consider studies which have previously or currently show evidence of disease. If all assessments are negative, report the date of the most sensitive test performed (e.g., report a bone marrow biopsy rather than a CBC) within the appropriate time period. If assessments are positive for disease, report the most recent positive assessment. If the exact date is not known, use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms.](#)
The myelodysplastic syndromes (MDS) are a diverse group of clonal hematopoietic stem cell diseases characterized by cytopenia(s), dysplasia (abnormal growth or development leading to an alteration in size, shape, and organization of the cell) in one or more of the major cell lines (WBC, RBC, and/or platelets), ineffective hematopoiesis, and an increased risk of development of Acute Myelogenous Leukemia (AML). MDS occurs primarily in older adults with a median age of 70 years. The majority of patients present with symptoms related to cytopenias; most patients present with anemia requiring RBC transfusions.

Primary or de novo MDS occurs without a known history of chemotherapy or radiation exposure. Some inherited hematologic disorders, such as Fanconi anemia, dyskeratosis congenita, Shwachmann-Diamond syndrome, and Diamond-Blackfan syndrome are associated with an increased risk of MDS.

Myeloproliferative neoplasms (MPN) are characterized by the overproduction of blood cells (red blood cells, white blood cells, and/or platelets) or collagen in the bone marrow. Often the MPN will be identified due to a blood test for another condition, as some patients are asymptomatic. Common symptoms found in the array of myeloproliferative disorders include fatigue and the enlargement of the spleen (splenomegaly).

MDS/MPN Response Criteria
2014: MDS/MPN Pre-HCT
2114: MDS/MPN Post-HCT
MDS/MPN Response Criteria

MDS Response Criteria

Complete Remission (CR)

Requires all of the following maintained for a minimum of four weeks:

Bone marrow evaluation:

• < 5% myeloblasts with normal maturation of all cell lines

Peripheral blood evaluation:

• Hemoglobin ≥ 11 g/dL untransfused without erythropoietic support
• ANC ≥ 1000/mm$^3$ without myeloid growth factor support
• Platelets ≥ 100,000/mm$^3$ without thrombopoietic support
• 0% blasts in blood

Alternative CR criteria are accepted in the setting of pediatric MDS and are as follows:

• Complete donor chimerism (≥ 95% donor chimerism without recipient cells detected)
• Hemoglobin ≥ 11 g/dL untransfused without erythropoietic support
• ANC ≥ 1000/mm$^3$ without myeloid growth factor support
• Platelets ≥ 100,000/mm$^3$ without thrombopoietic support

In some cases, there may not be a four-week interval between completion of therapy and the pre-transplant disease assessment. In this case, CR should still be reported as the status at transplant since it represents the “best assessment” prior to HCT. This is an exception to the criteria that CR be durable beyond four weeks; the pre-transplant disease status should not be changed based on early relapse or disease assessment post-transplant.
Hematologic Improvement (HI)

Requires one measurement of the following maintained for at least eight weeks without ongoing cytotoxic therapy:

Hematologic improvement – erythropoietic (HI-E):

- Hemoglobin increase of $\geq 1.5$ g/dL untransfused
  or
- For RBC transfusions performed for hemoglobin $\leq 9.0$: reduction in RBC units transfused in 8 weeks by $\geq 4$ units compared to the number of units transfused in the 8 weeks prior to treatment

Hematologic improvement – platelets (HI-P):

- For pre-treatment platelet count of $\geq 20 \times 10^9$, platelet absolute increase of $\geq 30 \times 10^9$
- For pre-treatment platelet count of $< 20 \times 10^9$, platelet absolute increase of $\geq 20 \times 10^9$ and $\geq 100\%$ increase from pre-treatment level

Hematologic improvement – neutrophils (HI-N):

- Neutrophil count increase of $\geq 100\%$ from pre-treatment level and an absolute increase of $\geq 500$/mm$^3$

No Response (NR)/Stable Disease (SD)

Does not meet the criteria for at least HI, but no evidence of disease progression to AML

Progression from Hematologic Improvement (Prog from HI)

Requires at least one of the following in the absence of another explanation (e.g., infection, bleeding, ongoing chemotherapy, etc.):

- $\geq 50\%$ reduction from maximum response levels in granulocytes or platelets
- Reduction in hemoglobin by $\geq 1.5$ g/dL

Hypomethylating agents (e.g. Vidaza) should not be considered cytotoxic therapy; therefore, Hematologic Improvement may still be reported if the recipient meets the criteria below while continuing to receive hypomethylating agents.
• Transfusion dependence

Note: declining donor chimerism does not meet the criteria for progression. If the above criteria for progression have been met, but a hematologic improvement was not previously achieved, report “No Response (NR) / Stable Disease (SD)”.

Relapse from Complete Remission (Rel from CR)

Requires at least one of the following:

• Return to pre-treatment bone marrow blast percentage
• Decrease of ≥ 50% from maximum response levels in granulocytes or platelets
• Transfusion dependence or hemoglobin level ≥ 1.5 g/dL lower than prior to therapy

Note: declining donor chimerism does not meet the criteria for relapse.

Progression to AML

≥ 20% blasts in the blood or bone marrow

MPN Response Criteria

CR (requires each of the following)

• Bone marrow with ≤ 5% myeloblasts (including monocytic blast equivalents in CMML) with normal maturation of all cell lines and return to normal cellularity
• Myelofibrosis absent or ≤ grade 1 fibrosis (mild reticulin fibrosis)
• Peripheral blood counts showing:
  ◦ WBC ≤ 10 × 10^9/L
  ◦ Hgb ≥ 11 g/dL
  ◦ PLT ≥ 100 × 10^9/L; ≤ 450 × 10^9/L
  ◦ Blasts 0%
  ◦ Neutrophilic precursors reduced to ≤ 2%
  ◦ Monocytes ≤ 1 × 10^9/L
• Resolution of any extramedullary disease present prior to therapy; this includes cutaneous disease, disease-related serous effusions, and palpable hepatosplenomegaly

Myelofibrosis CR
• Bone marrow with ≤ 5% myeloblasts with normal maturation of all cell lines
• Myelofibrosis absent or ≤ grade 1 fibrosis (mild reticulin fibrosis)
• Peripheral blood counts showing:
  ◦ ANC ≥ 1.0 × 10^9/L and < upper limit of normal
  ◦ Hgb ≥ 11 g/dL and < upper limit of normal
  ◦ PLT ≥ 100 × 10^9/L and < upper limit of normal
  ◦ Neutrophilic precursors reduced to ≤ 2%
• Resolution of disease symptoms and no palpable hepatosplenomegaly; no evidence of extramedullary hematopoiesis

**Hematologic Improvement**

*Requires one measurement of the following maintained for at least eight weeks without ongoing cytotoxic therapy:*

• Response of erythroid line requires:
  ◦ Hgb increase ≥ 2.0 g/dL from baseline
  ◦ Transfusion independence for patients requiring at least 4 packed RBC transfusions in the previous 8 weeks
• Response of platelets requires:
  ◦ For pre-treatment platelet count of > 20 × 10^9/L, platelet absolute increase of ≥ 30 × 10^9/L
  ◦ For pre-treatment platelet count of ≤ 20 × 10^9/L, platelet absolute increase of ≥ 20 × 10^9/L and ≥ 100% increase from pre-treatment level
• Response of neutrophils requires:
  ◦ For pre-treatment ANC > 0.5 × 10^9/L and ≤ 1.0 × 10^9/L, neutrophils with ≥ 50% increase and an absolute increase of ≥ 0.5 × 10^9/L
  ◦ For pre-treatment ANC ≤ 0.5 × 10^9/L, neutrophils with ≥ 100% and an absolute increase of ≥ 0.5 × 10^9/L

**No response/stable disease**

• Does not meet the criteria for at least HI but no evidence of disease progression to AML

**Progression from Hematologic Improvement**

• Transfusion dependence defined by history of at least 2 units of red blood cell transfusions in the past month for a hemoglobin level < 8.5 g/dL without other explanation
• Reduction in hemoglobin by ≥ 1.5 g/dL
• ≥ 50% reduction from maximum response levels in granulocytes or platelets
Note: if the above criteria for progression have been met, but a hematologic improvement was not previously achieved, report “No Response (NR) / Stable Disease (SD)”.

Relapse from CR

• Reappearance of bone marrow disease, including blasts, monocytic blast equivalents, or fibrosis
• New extramedullary disease, including new or reappearance of splenomegaly, hepatomegaly, skin lesions, etc.


Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
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<tr>
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<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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<tbody>
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<td>6/7/17</td>
<td>MDS/MPN Response Criteria</td>
<td>Add</td>
<td>Added following bullet to CR criteria for Myelofibrosis: Myelofibrosis absent or ≤ grade 1 fibrosis (mild reticulin fibrosis)</td>
</tr>
<tr>
<td>9/27/15</td>
<td>MDS/MPN Response Criteria</td>
<td>Modify</td>
<td>Added language to NR/SD criteria: Does not meet the criteria for at least HI, but no evidence of disease progression to AML.</td>
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<tr>
<td>9/27/15</td>
<td>MDS/MPN Response Criteria</td>
<td>Add</td>
<td>Added MPN criteria</td>
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<td>Edited Progression to AML text to read: ≥ 20% blasts in the blood or bone marrow</td>
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<tr>
<td>6/5/15</td>
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<td>Modify</td>
<td>Changed the following text in HI-P:</td>
</tr>
<tr>
<td>Date</td>
<td>MDS/MPN Response Criteria</td>
<td>Action</td>
<td>Details</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>5/22/15</td>
<td>MDS/MPN Response Criteria</td>
<td>Add</td>
<td>Added the following text to CR: In some cases, there may not be a four-week interval between completion of therapy and the pre-transplant disease assessment. In this case, CR should still be reported as the status at transplant since it represents the “best assessment” prior to HCT. This is an exception to the criteria that CR be durable beyond four weeks; the pre-transplant disease status should not be changed based on early relapse or disease assessment post-transplant.</td>
</tr>
<tr>
<td>6/24/16</td>
<td>MDS/MPN Response Criteria</td>
<td>Add</td>
<td>Added information box to MDS Disease Status Criteria, Hematologic Improvement Section: Hypomethylating agents (e.g. Vidaza) should not be considered cytotoxic therapy; therefore, Hematologic Improvement may still be reported if the recipient meets the criteria below while continuing to receive hypomethylating agents.</td>
</tr>
<tr>
<td>6/24/16</td>
<td>MDS/MPN Response Criteria</td>
<td>Modify</td>
<td>Added language to note beneath Progression from Hematologic Improvement for MDS and MPN Response Criteria: If the above criteria for progression have been met, but a hematologic improvement was not previously achieved, report “No Response (NR) / Stable Disease (SD)”.</td>
</tr>
<tr>
<td>6/24/16</td>
<td>MDS/MPN Response Criteria</td>
<td>Add</td>
<td>Added language to MPN Disease Status Criteria, Hematologic Improvement: Requires one measurement of the following maintained for at least eight weeks without ongoing cytotoxic therapy:</td>
</tr>
</tbody>
</table>
2014: MDS/MPN Pre-HCT

The Myelodysplasia/Myeloproliferative Neoplasms Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures MDS/MPN-specific pre-HCT data such as: disease assessment at diagnosis, laboratory studies at diagnosis, pre-HCT therapy, disease transformation, most recent disease assessments, laboratory studies, and disease status prior to the preparative regimen.

This form must be completed for all recipients who are randomized to the Comprehensive Report Form (CRF) track and whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as “Myelodysplastic (MDS)/myeloproliferative (MPN) diseases (50) (Please classify all preleukemias)” and recipients with AML whose disease progressed from MDS/MPN.

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1.

If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than MDS/MPN), begin at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, select “yes” and continue with question 123.

Q1-18: Disease Assessment at Diagnosis
Q19-39: Laboratory Studies at Diagnosis
Q40-122: Pre-HCT Therapy
Q123-126: Transformation
Q127-153: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen
Q154-161: Disease Assessment at the Last Evaluation Prior to the Preparative Regimen

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.
<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/10/18</td>
<td>2014: MDS/MPN Pre-HCT</td>
<td>Added</td>
<td>Added an instructional blue box for question 123: <strong>Myelofibrosis that develops in patients with essential thrombocytemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. The CIBMTR forms capture disease subtype using the WHO classification of myeloid neoplasms and acute leukemia. Secondary myelofibrosis is not included as a separate category per the WHO classification. Therefore, when reporting the disease subtype <strong>at the time of transplant</strong> for recipients with secondary myelofibrosis, report “Primary Myelofibrosis (PMF)” to accurately capture these cases on the CIBMTR Forms.</strong></td>
</tr>
</tbody>
</table>
| 9/7/17     | 2014: MDS/MPN Pre-HCT | Modify         | Replaced note box regarding transformation of essential thrombocytopenia and polycythemia vera to myelofibrosis located below instructions for question 123 with Transformation to Myelofibrosis notebox. New text is highlighted red below while old text is struck out.  
**Recipients transplanted for post-essential thrombocytemia myelofibrosis (post-ET MF) or post-polycythemia vera myelofibrosis (post-PV MF) will be reported as ET or PV at diagnosis (Q2). Question 123: ‘Did the recipient progress or transform to a different MDS/MPN subtype between diagnosis and the start of the preparative regimen?’ must be answered “Yes”.”  
Myelofibrosis that develops in patients with essential thrombocytemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. Do not report this as a transformation; when a patient with ET or PV develops fibrosis, do not report primary myelofibrosis as the primary indication for transplant. |
| 8/1/17     | 2014: MDS/MPN Pre-HCT | Modify         | Added text (in red below) and removed text (struck out below) from instructions for question 121.  
**Refer to the MDS / MPN Response Criteria section when determining the recipient’s disease status. Indicate if the disease relapsed from CR or progressed from hematologic improvement. If the disease relapsed or progressed, answer “Yes” and go to question 122. If “No,” go to question 123.**  
Progression or relapse should be reported even if it was reported in the previous set of questions regarding response to therapy (questions 118-120).  
Relapse is the recurrence of disease after CR. MDS/MPN relapse requires one of the following:  
• Return to pre-treatment bone marrow blast percentage.  
• Decrease of ≥ 50% from maximum response levels in granulocytes or platelets  
• Transfusion dependence, or hemoglobin level ≥ 1.5 g/dL lower than prior to therapy.  
Progression is the worsening of the disease following hematologic improvement or stable disease. Progression requires at least one of the following in the absence of another explanation (e.g., |
- *infection, bleeding, ongoing chemotherapy, etc.)*:
  - ≥ 50% reduction from maximum response levels in granulocytes or platelets
  - Reduction in hemoglobin by ≥ 1.5 g/dL
  - Transfusion dependence
  - Progression to AML: ≥ 20% blasts in the blood or bone marrow

<table>
<thead>
<tr>
<th>Date</th>
<th>Activity</th>
<th>Description</th>
</tr>
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<tr>
<td>2/24/17</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
<tr>
<td>6/24/16</td>
<td>Add</td>
<td>Added information box to Question 157: “Never Treated” is not an option choice on revision three of the Myelodysplasia / Myeloproliferative Disorders Pre-HSCT Data (MDS) Form. When completing revision three of this form, centers should report “No Response (NR) / Stable Disease (SD)” for recipients who have only received supportive care prior to transplant.</td>
</tr>
<tr>
<td>3/31/16</td>
<td>Add</td>
<td>Added an information box about transformation of polycythemia vera and essential thrombocythemia to Question 123: Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. Do not report this as a transformation; when a patient with ET or PV develops fibrosis, do not report primary myelofibrosis as the primary indication for transplant.</td>
</tr>
<tr>
<td>9/27/15</td>
<td>Modify</td>
<td>Modified MDS transformation table to include RA, 5q- syndrome, MDS-U, and chronic eosinophilia transformations</td>
</tr>
<tr>
<td>6/26/15</td>
<td>Modify</td>
<td>Modified text of Questions 121 and 123 to include the following concept: Progression to AML: ≥ 20% blasts in the blood or bone marrow</td>
</tr>
</tbody>
</table>
Q1-18: Disease Assessment at Diagnosis

Question 1: What was the date of diagnosis?

Report the date of the first pathological diagnosis (i.e., bone marrow biopsy) of MDS/MPN. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared. The date of diagnosis is important because the interval between diagnosis and HCT is often a significant indicator for the recipient's prognosis post-HCT.

If the exact pathological diagnosis date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 2: What was the MDS/MPN subtype?

Please indicate the MDS/MPN subtype at diagnosis. For a list of MDS/MPN subtypes and their diagnostic criteria, see Appendix H.

Question 3: Was the disease (MDS/MPN) therapy related?

Agents such as the radiation or systemic chemotherapy used to treat other diseases (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, and breast cancer) can damage the marrow and lead to a secondary malignancy, such as MDS/MPN. If the diagnosis of MDS/MPN is therapy-related, select “yes” and continue with question 4. If the diagnosis of MDS/MPN is not therapy-related, select “no” and continue with question 12. If it is unknown if the MDS/MPN is therapy-related, select “unknown” and continue with question 12.

Do not answer this question “yes” if the recipient developed MDS/MPN after an environmental exposure (e.g., exposure to benzene).

Questions 4-5: Specify prior disease:

Indicate the recipient’s primary disease prior to the diagnosis of MDS/MPN.

If the recipient’s prior disease is not listed, select “other” and specify the disease using question 5.

Questions 6-7: Date of diagnosis of prior disease:

Specify if the date of diagnosis of the prior disease is “known” or “unknown.” If the date is “known,” continue with question 7 and report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of
the prior disease. Enter the date the sample was collected for examination. Do not report the date symptoms first appeared. This date must be prior to the MDS/MPN diagnosis date entered in question 1.

If the date is “unknown,” continue with question 8.

Questions 8-11: Specify therapy for prior disease:

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body. Systemic therapy in the setting of malignancy generally refers to chemotherapy or cytotoxic therapy.

Intrathecal therapy is administered via injection into the lumbar cerebral spinal fluid and acts on the central nervous system.

Radiation therapy uses high-energy, ionizing radiation to kill malignant cells. It is typically referred to as radiation therapy, x-ray therapy (XRT), or radiotherapy.

For each listed treatment, indicate “yes,” “no,” or “unknown.” If the treatment administered was “other treatment,” specify the type of treatment given using question 11. Select all that apply; do not leave any responses blank.

Question 12: Did the recipient have a predisposing condition prior to diagnosis of MDS/MPN?

A predisposing condition is a condition that contributes to the susceptibility of developing MDS/MPN. If the recipient has a documented history of a predisposing condition, select “yes” and continue with question 13. If there is no history of a predisposing condition or if predisposition is unknown, indicate “no” or “unknown” and continue with question 15.

Questions 13-14 Specify condition:

Aplastic anemia may progress to MDS and/or AML. Aplastic anemia is a broad classification referring to bone marrow failure characterized by pancytopenia and marrow hypoplasia. Also complete a CIBMTR Form 2028 – Aplastic Anemia Pre-HCT Data. If selected, continue with question 15.

Bloom syndrome is an autosomal recessive genetic disorder characterized by excessive chromosome breakage and corresponding rearrangements. It is characterized by proportional dwarfism and sun sensitivity. The chromosomal instability seen in Bloom syndrome is generally assumed to be responsible for these individuals' predisposition to malignancy. If selected, continue with question 15.

Down syndrome is also a chromosomal disorder (trisomy 21). It is characterized by an additional chromosome 21. Down syndrome patients exhibit a particular set of facial characteristics, growth deficiency,
and cognitive impairment. Although Down syndrome patients have a reduced risk of developing many common malignancies, they have an increased risk of developing leukemia. If selected, continue with question 15.

Fanconi anemia is a rare genetic blood disorder that prevents the body from producing a sufficient number of new blood cells to function properly. Abnormal blood cells may also be produced. These patients are short in stature, exhibit skeletal anomalies, and have an increased risk of developing solid tumors and leukemias. Also complete CIBMTR Form 2029 – Fanconi Anemia Pre-HCT Data. If selected, continue with question 15.

If the recipient had a predisposing condition not listed above, select “other condition” and specify the condition in question 14.

**Question 15: Did the recipient receive any RBC transfusions at the time of diagnosis and/or during the first year post diagnosis?**

Indicate if the recipient received any RBC transfusions in the first year after MDS/MPN was diagnosed. If the recipient required even one RBC transfusion as supportive care for the disease, select “yes.” Some discretion is required for this question; if the recipient required a RBC transfusion as part of a normal surgical procedure or for a reason other than their disease, indicate “no.” If it is unknown if the recipient received RBC transfusions during their first year after diagnosis, select “unknown.”

**Questions 16-18 refer to MPN subtypes only; if the diagnosis was other than MPN, continue with question 19.**

**Question 16: Were systemic symptoms (B symptoms) present (unexplained fever > 38°C; or night sweats; unexplained weight loss > 10% body weight in six months before diagnosis)?**

Indicate if systemic symptoms were present at the time of diagnosis. Systemic symptoms are often called “B” symptoms and include unexplained fever greater than 38°C (100.4°F), night sweats, or unexplained weight loss in the six months previous to diagnosis. Indicate “yes” if any systemic symptoms were present at diagnosis (or in the case of unexplained weight loss, within the six months previous to diagnosis). Indicate “no” if systemic symptoms were not present at diagnosis. Indicate “unknown” if it is not possible to determine the presence or absence of systemic symptoms at diagnosis.

**Question 17: Did the recipient have splenomegaly (spleen palpable > 3 cm below left costal margin)?**

Indicate if the spleen was palpable greater than 3 centimeters below the left costal margin at the time of diagnosis. Splenomegaly is often documented during the physician’s physical assessment of the patient and represents an abnormal finding. Indicate “yes” if splenomegaly was present at the time of diagnosis.
Indicate “no” if splenomegaly was not present at diagnosis. Indicate “unknown” if it is not possible to determine the presence or absence of splenomegaly at diagnosis.

**Question 18: Did the recipient have hepatomegaly (liver edge palpable > 3 cm below right costal margin)?**

Indicate if the edge of the liver was palpable greater than 3 centimeters below the right costal margin at the time of diagnosis. Hepatomegaly is often documented during the physician’s physical assessment of the patient and represents an abnormal finding. Indicate “yes” if hepatomegaly was present at the time of diagnosis. Indicate “no” if hepatomegaly was not present at diagnosis. Indicate “unknown” if it is not possible to determine the presence or absence of hepatomegaly at diagnosis.
Q19-39: Laboratory Studies at Diagnosis

Report findings laboratory results from prior to the start of first treatment of the primary disease for which the HCT is being performed. If the recipient’s MDS/MPS transformed, report the studies from the original diagnosis.

Questions 19-21: Monocytes:

Indicate whether the monocyte percentage in the blood was “known” or “unknown” at the time of MDS/MPN diagnosis. If “known,” report the percentage documented on the laboratory report in question 20 and the date of sample collection in question 21. If “unknown,” continue with question 22.

Questions 22-24: Blasts in blood:

Indicate whether the percentage of blasts in the blood was “known” or “unknown” at the time of MDS/MPN diagnosis. If “known,” report the percentage documented on the laboratory report in question 23 and the date of sample collection in question 24. If “unknown,” continue with question 25.

If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.

Questions 25-26: Was a bone marrow examination performed?

Indicate if a bone marrow examination was performed at the time of MDS/MPN diagnosis. If “yes,” indicate the date the sample was collected in question 26. If “no” or “unknown,” continue with question 29.

Question 27: Cellularity:

Cellularity describes the percentage of bone marrow occupied by hematopoietic cells compared to other tissues, such as adipose (fat) cells. In MDS/MPN, the percentage of hematopoietic cells is likely increased (hypercellular) due to proliferation of immature cells. In other cases, the cellularity may be normal (normocellular) or decreased (hypocellular). This distinction is made on the pathology report of a bone marrow examination.

Indicate whether the bone marrow examination revealed “decreased (hypocellular),” “normal (normocellular),” or “increased (hypercellular)” cellularity at diagnosis or prior to the first treatment. If a biopsy was not obtained or if the degree of cellularity is not addressed in the report, select “unknown.”
**Question 28: Fibrosis:**

Fibrosis describes the replacement of bone marrow by fibrous (scar) tissue. This is evident in MDS/MPN diseases such as chronic idiopathic myelofibrosis. This distinction is made on the pathology report of a bone marrow examination.

Indicate if fibrosis in the bone marrow was "present" or "absent." If the degree of fibrosis is not addressed in the report, select "unknown."

**Question 29: Were tests for molecular markers performed (e.g., PCR)?**

Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient’s disease. Molecular assessments are the most sensitive test for genetic abnormalities and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control.

Indicate if molecular studies were obtained at the time the recipient was diagnosed with MDS/MPN or prior to the start of treatment.

If molecular studies were obtained, select “yes” and continue with question 30.

If no molecular studies were obtained or it is unknown if molecular studies were performed, indicate “no” or “unknown” and continue with question 40.

**Question 30: Date sample collected:**

Report the date the sample was collected for molecular testing. If multiple studies were performed prior to the start of therapy, report the last assessment prior to the start of treatment.

**Questions 31-38: Specify abnormalities at diagnosis:**

If question 29 indicates that tests for molecular markers were performed, then each of questions 31-38 must be answered as “positive,” “negative,” or “not done.” Do not leave any response blank. If question 37 is answered “positive,” specify the identified molecular marker.

Note that the JAK2 mutation question only needs to be completed for recipients with MPN.

Questions 37-38 should be copied to report more than one other molecular marker.
Question 39: Was documentation submitted to the CIBMTR?

Indicate if a copy of the molecular report(s) is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the molecular report. Attaching a copy of the report may prevent additional queries.
**Q40-122: Pre-HCT Therapy**

Complete a “Pre-HCT Therapy” section for each line of therapy administered prior to the start of the preparative regimen. If multiple lines of therapy were administered, copy and complete questions 41-122 for each line of therapy.

**Question 40: Was therapy given?**

Indicate if the recipient received treatment for MDS/MPN after the time of diagnosis and before the start of the preparative regimen. If “yes,” continue with question 41. If “no,” continue with question 123.

**Questions 41-43: WBC**

Indicate whether the white blood cell (WBC) count was “known” or “unknown” prior to the start of this line of therapy. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 88 and the date of sample collection in question 89. If “unknown,” continue with question 90.

**Questions 44-46: Hemoglobin**

Indicate whether the hemoglobin was “known” or “unknown” prior to the start of this line of therapy. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 45 and the date of sample collection in question 46. If “unknown,” continue with question 48.

**Question 47: Were RBC transfused ≤ 30 days before the date of test?**

Currently there is an issue on the 2014 form regarding RBC transfusion dates. The question should read: “Were RBCs transfused ≤ 30 days before the date of test?”

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who received these cells from a transfusion.

Indicate if red blood cells were transfused less than or equal to 30 days prior to the testing.

**Questions 48-50: Platelets:**

Indicate whether the platelet count was “known” or “unknown” prior to the start of this line of therapy. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 49 and the date of sample collection in question 50. If “unknown,” continue with question 52.
**Question 51: Were platelets transfused \(\leq 7\) days before date of test?**

Currently there is an issue on the 2014 form regarding platelet transfusion dates. The question should read: “Were platelets transfused \(\leq 7\) days before the date of test?”

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who received these cells from a transfusion.

Indicate if platelets were transfused less than or equal to 7 days prior to the testing.

**Questions 52-54: Neutrophils:**

Indicate whether the neutrophil percentage in the blood was “known” or “unknown” prior to the start of this line of therapy. If “known,” report the value documented on the laboratory report in question 53 and the date of sample collection in question 54. If “unknown,” continue with question 55.

**Questions 55-57: Blasts in bone marrow:**

Indicate whether the percentage of blasts in the bone marrow was “known” or “unknown” prior to the start of this line of therapy. If “known,” report the percentage documented on the laboratory report in question 56 and the date of sample collection in question 57. If “unknown,” continue with question 58.

**Question 58: Were cytogenetics tested (conventional or FISH)?**

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient’s disease. Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained prior to the start of this line of therapy. If cytogenetic studies were obtained, select “yes” and continue with question 59.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select “no” or “unknown” and continue with question 87.

**Question 59: Date sample collected:**

Report the date the sample was collected for cytogenetic or FISH testing. If multiple studies were performed prior to the start of therapy, report the last assessment prior to the start of treatment.
Question 60: Results of test:

If cytogenetic studies identified abnormalities, indicate “abnormalities identified” and continue with question 61.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 87.

Question 61: Specify the number of distinct cytogenetic abnormalities:

Indicate the total number of abnormalities identified prior to this line of therapy.

Questions 62-86: Specify abnormalities identified prior to this line of therapy:

Report all abnormalities identified by all methods of cytogenetic assessment prior to the start of this line of therapy by selecting “yes” or “no” for each question. Do not leave any responses blank. If one or more abnormalities are best classified as “other abnormality” select “yes” for question 85 and specify the abnormality in question 86.

Question 87: Systemic Therapy:

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously to the whole body. These drugs enter the bloodstream and are distributed throughout the body.

Also report therapies for supportive care. These therapies include chelation therapy (for iron overload from chronic RBC transfusions) and treatment with growth factors (EPO, G-CSF, GM-CSF, etc.).

Indicate “yes” if the patient received systemic therapy and continue with question 88. If the patient did not receive systemic therapy, indicate “no” and continue with question 113.

Questions 88-89: Date therapy started:

Indicate “known” if the therapy start date is documented and use question 89 to specify the first date of systemic therapy administration. If the date is unknown, indicate “unknown” and continue with question 90.

Questions 90-91: Date therapy stopped:

Indicate “known” if the therapy completion date is documented and use question 91 to specify the date therapy stopped. If the patient is receiving systemic therapy in cycles, specify the first day of the last cycle of systemic therapy. If the patient is receiving a single line or single administration, indicate the last day systemic therapy was administered.
If the date is unknown, indicate “unknown” and continue with question 92.

**Questions 92-112: Specify systemic therapy:**

Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Drugs may be administered in an inpatient or outpatient setting, and treatment may consist of one drug or multiple drugs. Additionally, drugs may be administered on a single day, over consecutive days, or continuously.

Indicate “yes” or “no” for each therapy listed. Do not leave any responses blank. If the recipient received a chemotherapy agent that is not listed, select “yes” for “other systemic therapy” and specify the treatment.

**Question 113: Other therapy:**

Indicate if the recipient received therapy other than the systemic therapy listed above, including radiation and splenectomy. If the recipient received other therapy, select “yes” and continue with question 114. If the recipient did not receive other therapy, select “no” and continue with question 118.

**Questions 114-117: Specify other therapy:**

Indicate “yes” or “no” for each therapy listed. Do not leave any responses blank. If the recipient received therapy that is not listed, select “yes” for “other therapy” and specify the therapy in question 117.

**Question 118: Best response to line of therapy:**

Indicate the disease response of MDS/MPN to each line of therapy using the definitions found in the text on FormsNet. These definitions are also located in the MDS/MPN Response Criteria.

If the recipient’s disease status was “Complete remission (CR),” “No response (NR)/stable disease (SD),” “Progression from hematologic improvement (Prog from HI),” “Relapse from complete remission (Rel from CR),” or “Progression to AML (AML),” continue with question 120.

If the recipient’s disease status was “Hematologic improvement (HI),” continue with question 119.

If the disease status was “unknown” or “not assessed,” continue with question 123.

**Question 119: Specify the cell line examined to determine HI status:**

Indicate the cell line examined to determine hematologic improvement. Review the Hematologic Improvement criteria on the MDS/MPN Response Criteria section to determine the cell line.
Question 120: Date assessed:

Enter the date the best response to the line of therapy was established. Report the date of the pathological evaluation (e.g., bone marrow biopsy). If no pathologic evaluation was reported, report the date of blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and/or laboratory evaluations. If the recipient was treated for extramedullary disease and a radiological assessment (e.g., X-ray, CT scan, MRI scan, PET scan) was performed to assess disease response, enter the date the imaging took place for radiologic assessments. If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically assessed the recipient’s response.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 121: Did disease relapse/progress following this line of therapy?

Refer to the MDS/MPN Response Criteria section when determining the recipient's disease status. Indicate if the disease relapsed from CR or progressed from hematologic improvement. If the disease relapsed or progressed, answer “Yes” and go to question 122. If “No,” go to question 123.

Progression or relapse should be reported even if it was reported in the previous set of questions regarding response to therapy (questions 118-120).

Transformation to AML & Lines of Therapy

If the recipient’s disease transforms from MDS/MPN following this line of therapy, complete the form until question 126 and then skip to the signature lines. Any additional lines of therapy intended to treat the newly transformed AML should be reported on the Acute Myelogenous Leukemia (AML) Pre-HCT Form (F2010).

Indicate if the disease relapsed from CR or progressed from hematologic improvement or stable disease. If the disease relapsed or progressed, answer “yes” and continue with question 122. If “no,” continue with question 123.

Progression or relapse should be reported even if it was reported in the previous set of questions regarding response to transplant (questions 118-120).

Question 122: Date of relapse/progression:

Enter the date of the assessment that established relapse following the line of therapy. Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood
smear). Enter the date the sample was collected for pathological and laboratory evaluations. If extramedullary disease is detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place. If the physician determines cytogenetic or molecular relapse, enter the date of sample collection for cytogenetic or molecular evaluation. If the physician determines evidence of relapse following a clinical examination during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
**Q123-126: Transformation**

**Question 123:** Did the recipient progress or transform to a different MDS/MPN subtype between diagnosis and the start of the preparative regimen?

Indicate if the recipient’s disease progressed to AML or transformed into a different MDS/MPN subtype between initial diagnosis and the start of the preparative regimen. Approximately one-third of MDS cases transform into AML, which is usually associated with a poorer prognosis. Progression to AML is defined by an increase in blood or bone marrow blasts equal to or greater than 20%.

MDS/MPN subtypes may also transform from one into another. A progression from one subtype of MDS to another indicates that the number of cytopenias, number of blasts, and/or morphology of marrow sufficiently qualified them for a higher grade (i.e., more severe) MDS. For example, an MDS classified as RCUD at diagnosis whose blast count rises to 8% as documented on bone marrow aspirate would have progressed to RAEB-1.

Conversely, do not report a progression/transformation if the recipient’s assessments after diagnosis show that they qualify for a lower grade (i.e., less severe MDS). For example, a recipient who is diagnosed with RAEB-2, but whose assessments show that they meet the criteria for RAEB-1 as a response to treatment, would not qualify as a progression or transformation. In this example, the disease is lower grade (i.e., less severe), rather than a higher grade (i.e., more severe) so it should not be reported as a progression/transformation. See the table below for guidance in determining the severity of MDS/MPN progressions and transformations.

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**Transformation to Myelofibrosis**

Recipients transplanted for post-essential thrombocytemia myelofibrosis (post-ET MF) or post-polycythemia vera myelofibrosis (post-PV MF) will be reported as ET or PV at diagnosis (Q2). Question 123: ‘Did the recipient progress or transform to a different MDS/MPN subtype between diagnosis and the start of the preparative regimen?’ must be answered “Yes”.

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**Transformation to Myelofibrosis**

Myelofibrosis that develops in patients with essential thrombocytemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. The CIBMTR forms capture disease subtype using the WHO classification of myeloid neoplasms and acute leukemia. Secondary myelofibrosis is not included as a separate category per the WHO classification. Therefore, when reporting the disease subtype at the time of transplant for recipients with secondary...
Indicate if the recipient’s disease progressed to AML or transformed from one MDS/MPN subtype to another. If the recipient’s disease did transform or progress, select “yes” and continue with question 124. If there was no documented transformation or progression, select “no” and continue with question 127.

**Question 124: Was a subsequent complete remission achieved?**

Indicate if a subsequent complete remission was achieved. For recipients whose disease transformed from one MDS/MPN to another, complete remission is a treatment response that requires all of the following maintained for a minimum of four weeks:

**Bone marrow evaluation:**

- < 5% myeloblasts with normal maturation of all cell lines

**Peripheral blood evaluation:**

- Hemoglobin ≥ 11 g/dL untransfused without erythropoietic support
- ANC ≥ 1000/mm^3 without myeloid growth factor support
- Platelets ≥ 100,000/mm^3 without thrombopoietic support
- 0% blasts in blood

Alternative CR criteria are accepted in the setting of pediatric MDS and are as follows:
• Complete donor chimerism (≥ 95% donor chimerism without recipient cells detected)
• Hemoglobin ≥ 11 g/dL untransfused without erythropoietic support
• ANC ≥ 1000/mm³ without myeloid growth factor support
• Platelets ≥ 100,000/mm³ without thrombopoietic support

For recipients whose MDS/MPN transformed to AML, complete remission is a treatment response that requires all of the following maintained for a minimum of four weeks:

• < 5% blasts in the bone marrow
• Normal maturation of all cellular components in the bone marrow
• No blasts with Auer rods
• No extramedullary disease (e.g., central nervous system or soft tissue involvement)
• ANC of > 1,000/µL
• Platelets ≥ 100,000/µL
• Transfusion independence

**Question 125: Specify the date of the most recent transformation:**

Enter the date of the assessment that determined the most recent disease transformation (i.e., if there were multiple transformations, report the date of the most recent). Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 126: Specify the MDS/MPN subtype after transformation:**

Indicate the recipient’s current MDS/MPN subtype after transformation. If the recipient experiences more than one transformation after diagnosis, report the most recent subtype in this question. For MDS/MPN subtype characteristics, see Appendix H. Continue with question 127, unless the recipient transformed to AML.

If the disease transformed to AML, continue to the signature line. Also complete a CIBMTR Form 2010 – AML Pre-HCT Data.
Q127-153: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen

Questions 127-129: Monocytes:

Indicate whether the monocyte percentage in the blood was “known” or “unknown” prior to the start of the preparative regimen. If “known,” report the percentage documented on the laboratory report in question 128 and the date of sample collection in question 129. If “unknown,” continue with question 130.

Questions 130-132: Blasts in blood:

Indicate whether the percentage of blasts in the peripheral blood was “known” or “unknown” prior to the start of the preparative regimen. If “known,” report the percentage documented on the laboratory report in question 131 and the date of sample collection in question 132. If “unknown,” continue with question 133.

If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.

Questions 133-134: Was a bone marrow examination performed?

Indicate if a bone marrow examination was performed prior to the start of the preparative regimen. If “yes,” indicate the date sample was collected in question 134. If “no,” continue with question 137.

Question 135: Cellularity:

Cellularity describes the percentage of bone marrow occupied by hematopoietic cells compared to other tissues, such as adipose (fat) cells. In MDS/MPN, the percentage of hematopoietic cells is likely increased (hypercellular) due to proliferation of immature cells. In other cases, the cellularity may be normal (normocellular) or decreased (hypocellular). This distinction is made on the pathology report of a bone marrow examination.

Indicate whether the bone marrow examination revealed “decreased (hypocellular),” “normal (normocellular),” or “increased (hypercellular)” cellularity prior to the start of the preparative regimen. If a biopsy was not obtained or if the degree of cellularity is not addressed in the report, select “unknown.”
**Question 136: Fibrosis:**

Fibrosis describes the replacement of bone marrow by fibrous (scar) tissue. This is evident in MDS/MPN diseases such as chronic idiopathic myelofibrosis. This distinction is made on the pathology report of a bone marrow examination.

Indicate if fibrosis in the bone marrow was "present" or “absent” prior to the start of the preparative regimen. If the degree of fibrosis was not addressed in the report, select “unknown.”

**Question 137: Were tests for molecular markers performed (e.g., PCR)??**

Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient’s disease. Molecular assessments are the most sensitive test for genetic abnormalities and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control.

Indicate if molecular studies were obtained prior to the start of the preparative regimen.

If molecular studies were obtained, select “yes” and continue with question 138.

If no molecular studies were obtained or it is unknown if molecular studies were performed, indicate “no” or “unknown” and continue with question 147.

**Question 138: Date sample collected:**

Report the date the sample was collected for molecular testing. If multiple studies were performed prior to the start of the preparative regimen, report the last assessment prior to the start of treatment.

**Questions 139-146: Specify abnormalities at last evaluation prior to the start of the preparative regimen:**

If question 137 indicates that tests for molecular markers were performed, then each of the questions 139-145 must be answered as “positive,” “negative,” or “not done.” Do not leave any response blank. If question 145 is answered “positive,” specify the identified molecular marker in question 146.

Note that the JAK2 mutation question only needs to be completed for recipients with MPN.

Questions 145-146 should be copied to report more than one other molecular marker.
**Question 147: Was flow cytometry performed?**

Flow cytometry assessment is a method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics; its primary clinical purpose in the setting of MDS, MPN, and leukemias is to quantify blasts in the peripheral blood or bone marrow, or to identify unique cell populations through immunophenotyping. Flow cytometry assessment may also be referred to as "MRD" or minimal residual disease testing.

Indicate if flow cytometry was performed on peripheral blood and/or bone marrow sample immediately prior to the start of the preparative regimen.

If flow cytometry was performed, select “yes” and continue with question 148.

If flow cytometry was not performed or it is unknown if flow cytometry was performed, indicate “no” or “unknown” and continue with question 154.

**Questions 148-149: Blood**

Indicate if flow cytometry was performed on peripheral blood immediately prior to the start of the preparative regimen.

If flow cytometry was performed on a peripheral blood sample, select “yes” and report the date the sample was collected in question 149.

If flow cytometry was not performed on peripheral blood, indicate “no” and continue with question 151.

**Question 150: Was disease detected:**

Indicate if evidence of disease was detected in the peripheral blood sample sent for flow cytometry analysis. Evidence of disease may include the presence of blasts or an immunophenotype known to characterize the patient’s disease.

If flow cytometry results were not consistent with continued evidence of disease, select “no.”

**Questions 151-152: Bone marrow:**

Indicate if flow cytometry was performed on bone marrow immediately prior to the start of the preparative regimen.

If flow cytometry was performed on a bone marrow sample, select “yes” and report the date the sample was collected in question 152.
If flow cytometry was not performed, indicate “no” and continue with question 154.

**Question 153: Was disease detected:**

Indicate if evidence of disease was detected in the bone marrow sample sent for flow cytometry analysis. Evidence of disease may include the presence of blasts or an immunophenotype known to characterize the patient’s disease.

If flow cytometry results were not consistent with continued evidence of disease, select “no.”
Q154-161: Disease Assessment at the Last Evaluation Prior to the Preparative Regimen

Questions 154-156 refer to MPN subtypes only; if the diagnosis is other than MPN, continue with question 157.

**Question 154: Were systemic symptoms (B symptoms) present (unexplained fever > 38°C; or night sweats; unexplained weight loss > 10% body weight in six months before last evaluation prior to the start of the preparative regimen)?**

Indicate if systemic symptoms were present at the last evaluation prior to the preparative regimen. Systemic symptoms are often called “B” symptoms and include unexplained fever greater than 38°C (100.4°F), night sweats, or unexplained weight loss in the six months prior to diagnosis. Indicate “yes” if any systemic symptoms were present at the last evaluation before the preparative regimen. Indicate “no” if systemic symptoms were not present at the last evaluation prior to the preparative regimen. Indicate “unknown” if it is not possible to determine the presence or absence of systemic symptoms at the last evaluation prior to the start of the preparative regimen.

**Question 155: Did the recipient have splenomegaly (spleen palpable > 3 cm below left costal margin)?**

Indicate if the spleen was palpable greater than 3 centimeters below the left costal margin at the last evaluation prior to the preparative regimen. Splenomegaly is often documented during the physician’s physical assessment of the patient and represents an abnormal finding. Indicate “yes” if splenomegaly was present at the last evaluation prior to the preparative regimen. Indicate “no” if splenomegaly was not present at the last evaluation prior to the preparative regimen. Indicate “unknown” if it is not possible to determine the presence or absence of splenomegaly at the last evaluation prior to the preparative regimen.

**Question 156: Did the recipient have hepatomegaly (liver edge palpable > 3 cm below right costal margin)?**

Indicate if the edge of the liver was palpable greater than 3 centimeters below the right costal margin at the time of last evaluation prior to the preparative regimen. Hepatomegaly is often documented during the physician’s physical assessment of the patient and represents an abnormal finding. Indicate “yes” if hepatomegaly was present at the time of the last evaluation prior to the preparative regimen. Indicate “no” if hepatomegaly was not present at the last evaluation prior to the preparative regimen. Indicate “unknown” if it is not possible to determine the presence or absence of hepatomegaly at the last evaluation prior to the preparative regimen.
Question 157: What was the disease status?

“Never Treated” is not an option choice on revision three of the Myelodysplasia / Myeloproliferative Disorders Pre-HSCT Data (MDS) Form. When completing revision three of this form, centers should report “No Response (NR) / Stable Disease (SD)” for recipients who have only received supportive care prior to transplant.

Indicate the disease status of MDS/MPN at the last evaluation prior the start of the preparative regimen using the definitions found in the text or on FormsNet. These definitions are also located in the MDS/MPN Response Criteria.

If the recipient’s disease status was “Complete remission (CR),” or “No response (NR)/stable disease (SD)” prior the start of the preparative regimen, continue with question 161.

If the recipient’s disease status was “Hematologic improvement (HI)” prior to the start of the preparative regimen, continue with question 158.

If the recipient’s disease status was “Progression from hematologic improvement (Prog from HI)” prior the start of the preparative regimen, continue with question 159.

If the recipient’s disease status was “Relapse from a complete remission (Rel from CR)” prior the start of the preparative regimen, continue with question 160.

If the disease status was “not assessed” prior the start of the preparative regimen, continue with the signature lines at the bottom of the form.

Question 158: Specify the cell line examined to determine HI status:

Indicate the cell line examined to determine hematologic improvement. Review the Hematologic Improvement criteria shown above to determine the cell line.

Question 159: Date of progression:

Enter the assessment date that progression from hematologic improvement was established prior to the start of the preparative regimen. Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations. If extramedullary disease is detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place.

If the exact date is not known, use the process for reporting partial or unknown dates as described in
General Instructions, Guidelines for Completing Forms.

**Question 160: Date of relapse:**

Enter the date of the assessment that established relapse from complete remission prior to the start of the preparative regimen. Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations. If extramedullary disease was detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 161: Date assessed:**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant work-up period (approximately 30 days prior to transplant). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
2114: MDS/MPN Post-HCT

This form must be completed for all recipients who are randomized to the Comprehensive Report Form (CRF) track and whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as “Myelodysplastic (MDS)/myeloproliferative (MPN) diseases (50) (Please classify all preleukemias)” The Myelodysplasia/Myeloproliferative Neoplasms (MDS/MPN) Post-HCT Data (Form 2114) must be completed in conjunction with each Post-HCT follow-up form completed (Forms 2100, 2200, and 2300). The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200, between the date of contact for the six-month follow up and the date of contact for the one-year follow up for Form 2200, etc.).

For recipients who had a MDS/MPN that transformed to AML prior to transplant, only Form 2110 (Acute Myelogenous Leukemia Post-HCT Data) must be completed. Form 2014 (Myelodysplasia/Myeloproliferative Disorders Pre-HCT Data) is required to obtain MDS/MPN data pre-HCT, but Form 2114 (Myelodysplasia/Myeloproliferative Disorders Post-HCT Data) is not required for these recipients.

Q1-20: Disease Assessment at the Time of Best Response to HCT
Q21-31: Relapse or Progression Post-HCT
Q32-37: Most Recent Laboratory Studies
Q38-41: Disease Status at the Time of Evaluation for this Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
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</thead>
</table>
| 3/19/18    | Comprehensive Disease Specific Manuals      | Add               | Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119). The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical
<table>
<thead>
<tr>
<th>Date</th>
<th>Update Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/17</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
<tr>
<td>6/26/15</td>
<td>Modify</td>
<td>Modified text of Question 30 to include the following concept: Progression to AML: ≥ 20% blasts in the blood or bone marrow</td>
</tr>
</tbody>
</table>
Best response is based on response to the HCT, but does not include response to any therapy given for disease relapse or progression post-HCT. When determining the best response to HCT, compare the post-HCT disease status to the status immediately prior to the preparative regimen, regardless of time since HCT. This comparison is meant to capture the best disease status in response to HCT that occurred during the same reporting interval. If a recipient achieved their best response in a previous reporting interval, confirm the best response and check the box to indicate “date previously reported.”

**Question 1:** Compared to the disease status prior to the preparative regimen, what was the best response to HCT since the date of the last report? (Include response to any therapy given for post-HCT maintenance or consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease)

The intent of this question is to determine the best response to HCT overall. This is assessed in each reporting period. When evaluating the best response, determine the disease status within the reporting period and compare it to all previous post-HCT reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status.

Any specified therapy administered post-HCT to prolong remission or for minimal residual disease, is considered part of the HCT and should be included when assessing the recipient’s response to transplant. Treatment given post-HCT for relapsed or persistent disease is not considered part of the HCT and should be excluded when assessing the response to HCT. If treatment was given post-HCT for relapsed or persistent disease, assess the patient’s best response prior to the start of therapy. If therapy was given for reasons other than relapsed or persistent disease, assess the patient’s best response throughout the entire duration of the reporting period.

If the recipient was in remission at the start of the preparative regimen, indicate “continued complete remission” and continue with question 21. For all other responses, continue with question 2. See MDS/MPN Response Criteria for disease status definitions.

**Question 2:** Was the date of best response previously reported?

If the recipient achieved their best response in the current reporting period, indicate “no” and continue with question 3.
If the recipient achieved their best response in a previous reporting period (applicable on the 6-month follow-up forms and beyond), indicate “yes” and continue with question 21.

**Question 3: Date assessed:**

Indicate the date the best response was achieved. Report the date of the pathological evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations.

If the exact date is not known, use the process for reporting partial or unknown dates as described in [General Instructions, Guidelines for Completing Forms](#).

**Question 4: Was the disease status assessed by molecular testing (e.g., PCR)?**

Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient’s disease. Molecular assessments are the most sensitive test for genetic abnormalities and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control.

Indicate if molecular studies were obtained at the time the recipient achieved their best response.

If molecular studies were obtained, select “yes” and continue with question 5.

If molecular studies were not obtained, the sample for molecular studies was inadequate, or it is unknown if molecular studies were performed, select “no” and continue with question 8.

**Question 5: Date assessed:**

Report the date the sample was collected for molecular testing.

If the exact date is not known, use the process for reporting partial or unknown dates as described in [General Instructions, Guidelines for Completing Forms](#).

**Question 6: Was there evidence of disease?**

Indicate if molecular studies showed abnormalities consistent with the recipient’s disease. If there are molecular abnormalities consistent with evidence of disease, check “yes” and continue with question 7.

If molecular study results were not consistent with evidence of disease, check “no” and continue with
question 8.

**Question 7: Was the status considered a disease relapse or progressive disease?**

Indicate if the molecular abnormalities were considered to be relapsed or progressive disease. Criteria for molecular relapse or progression are established by clinical judgment, and should reflect the clinical decision of the transplant physician. A recipient may be reported to have molecular relapse or progression even in the setting of hematologic CR; criteria for complete remission are based on hematologic and pathologic characteristics and are independent of molecular markers of disease.

If the recipient has molecular abnormalities that the physician considers to be consistent with molecular relapse or progression, select “yes.” Also report relapse or progression under the “Disease Relapse or Progression Post-HCT” section of this form.

If the recipient has molecular abnormalities that the physician does not consider to be consistent with molecular relapse or progression, select “no.”

**Question 8: Was the disease status assessed via flow cytometry?**

Flow cytometry assessment is a method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics; its primary clinical purpose in the setting of MDS, MPN, and leukemias is to quantify blasts in the peripheral blood or bone marrow, or to identify unique cell populations through immunophenotyping. Flow cytometry assessment may also be referred to as “MRD” or minimal residual disease testing.

Indicate if flow cytometry was performed on peripheral blood and/or bone marrow sample at the time the recipient achieved their best response post-HCT.

If flow cytometry was performed, select “yes” and continue with question 9.

If flow cytometry was not performed, flow cytometry sample was inadequate, or it is unknown if flow cytometry was performed, select “no” and continue with question 12.

**Question 9: Date assessed:**

Report the date peripheral blood or bone marrow sample was collected for flow cytometry analysis.

If the exact date is not known, use the process for reporting partial or unknown dates as described in [General Instructions, Guidelines for Completing Forms](https://www.cibmtr.org/forms-instructions-guidelines-for-completing-forms).
**Question 10: Was there evidence of disease?**

Indicate if evidence of disease was detected in the sample sent for flow cytometry analysis. Evidence of disease may include the presence of blasts or an immunophenotype known to characterize the patient's disease. If flow cytometry results are consistent with evidence of disease, select “yes” and continue with question 11.

If flow cytometry results were not consistent with evidence of disease, check “no” and continue with question 12.

**Question 11: Was the status considered a disease relapse or progressive disease?**

Indicate if the flow cytometry results were considered consistent with relapsed or progressive disease. Criteria for flow cytometric relapse or progression are established by clinical judgment. If the recipient has abnormalities by flow cytometry that the physician considers to be consistent with flow cytometric relapse or progression, select “yes.” Also report relapse or progression under the “Disease Relapse or Progression Post-HCT” section of this form.

If the recipient has residual disease by flow cytometry that the physician does not consider to be consistent with relapse or progression, select “no.”

**Question 12: Was the disease status assessed by cytogenetic testing (conventional or FISH)?**

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease. Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at the time the recipient achieved their best response post-transplant.

If cytogenetic studies were obtained, select “yes” and continue with question 13.

If cytogenetic studies were not obtained, cytogenetic samples were inadequate, or it is unknown if chromosome studies were performed, select “no” and continue with question 21.

**Question 13: Was the disease status assessed via FISH?**

FISH, fluorescence in situ hybridization, is a sensitive technique that assesses a large number of cells. This technique utilizes special probes that recognize and bind to fragments of DNA commonly found in MDS/MPN. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to
visualize the binding of the probe to the diseased cells.

FISH testing for sex chromosomes after sex-mismatched allogeneic HCT should not be considered disease assessment, as the purpose is to determine donor chimerism. Additionally, the FISH probe panel should reflect the patient’s current disease; FISH may be used as surveillance for changes associated with post-therapy malignancy.

If FISH studies were obtained, select “yes” and continue with question 14.

If FISH studies were not obtained, FISH sample was inadequate, or it is unknown if FISH studies were performed, indicate “no” and continue with question 17.

**Question 14: Date assessed:**

Report the date the sample was collected for FISH assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 15: Was there evidence of disease?**

Indicate if evidence of disease was detected in the sample sent for FISH assessment. If FISH results were consistent with evidence of disease, check “yes” and continue with question 16.

If FISH results were not consistent with evidence of disease, check “no” and continue with question 17.

**Question 16: Was the status considered a disease relapse or progressive disease?**

Indicate if the FISH abnormalities were considered to be relapsed or progressive disease. Criteria for cytogenetic relapse or progression are established by clinical judgment, and should reflect the clinical decision of the transplant physician. A recipient may be reported to have cytogenetic relapse or progression even in the setting of hematologic CR; criteria for complete remission are based on hematologic and pathologic characteristics and are independent of cytogenetic markers of disease.

If the recipient has FISH abnormalities that the physician considers to be consistent with cytogenetic relapse or progression, check “yes.” Also report relapse or progression under the “Disease Relapse or Progression Post-HCT” section of this form.

If the recipient has FISH abnormalities that the physician does not consider to be consistent with relapse or progression, check “no.”
Question 17: Was the disease status assessed via conventional cytogenetics?

Conventional cytogenetics are performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. This is called karyotyping. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

If conventional cytogenetic studies were obtained, check “yes” and continue with question 18.

If conventional cytogenetic studies were not obtained, if the culture failed, or if it is unknown if conventional cytogenetic studies were performed, indicate “no” and continue with question 21.

Question 18: Date assessed:

Report the date the sample was collected for conventional cytogenetic assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 19: Was there evidence of disease?

Indicate if evidence of disease was detected in the sample sent for conventional cytogenetic assessment. If conventional cytogenetic results were consistent with evidence of disease, check “yes” and continue with question 20.

If conventional cytogenetic results were not consistent with evidence of disease, check “no” and continue with question 21.

Question 20: Was the status considered a disease relapse or progressive disease?

Indicate if the conventional cytogenetic abnormalities were considered to be relapsed or progressive disease. Criteria for cytogenetic relapse or progression are established by clinical judgment, and should reflect the clinical decision of the transplant physician. A recipient may be reported to have cytogenetic relapse or progression even in the setting of hematologic CR; criteria for complete remission are based on hematologic and pathologic characteristics and are independent of cytogenetic markers of disease.

If the recipient has conventional cytogenetic abnormalities that the physician considers to be consistent with cytogenetic relapse or progression, select “yes.” Also report relapse under the “Disease Relapse or Progression Post-HCT” section of this form.

If the recipient has conventional cytogenetic abnormalities that the physician does not consider to be
consistent with cytogenetic relapse or progression, check “no.”
Q21-31: Relapse or Progression Post-HCT

Question 21: Was a disease relapse or progression detected by molecular testing (e.g., PCR)?

Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient’s disease. Molecular assessments are the most sensitive test for genetic abnormalities and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control.

If molecular studies were obtained and consistent with relapse or progression at any point in the reporting period, check “yes” and continue with question 22.

If molecular studies were not consistent with relapse or progression during the reporting period, indicate “no” and continue with question 23. Examples include no molecular studies obtained, sample for molecular studies was inadequate, it is unknown if molecular studies were performed, or molecular studies were obtained and were not consistent with relapse or progression.

Question 22: Date assessed:

Report the date the sample was collected for molecular testing.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 23: Was a disease relapse or progression detected via flow cytometry?

Flow cytometry assessment is a method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics. Its primary clinical purpose in the setting of MDS, MPN, or leukemias is to quantify blasts in the peripheral blood or bone marrow, or to identify unique cell populations through immunophenotyping. Flow cytometry assessment may also be referred to as “MRD” or minimal residual disease testing.

If flow cytometry was performed and results were consistent with relapse or progression at any point in the reporting period, check “yes” and continue with question 24.

If flow cytometry results were not consistent with relapse or progression during the reporting period, indicate “no” and continue with question 25. Examples include no flow cytometry assessment performed, flow
cytometry sample was inadequate, it is unknown if flow cytometry was performed, or flow cytometry studies were obtained and were not consistent with relapse or progression.

**Question 24: Date assessed:**

Report the date the peripheral blood or bone marrow sample was collected for flow cytometry analysis.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 25: Was a disease relapse or progression detected by cytogenetic testing (conventional or FISH)?**

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient’s disease. Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

If cytogenetic studies were performed and the results were consistent with relapse or progression at any point in the reporting period, check “yes” and continue with question 26.

If cytogenetic studies were not consistent with relapse or progression during the reporting period, indicate “no” and continue with question 30. Examples include no karyotype or FISH study performed, karyotype or FISH sample was inadequate, it is unknown if karyotype or FISH study was performed, or karyotype or FISH studies were performed and results were not consistent with relapse or progression.

**Question 26: Was a disease relapse or progression detected via FISH?**

FISH, fluorescence *in situ* hybridization, is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in MDS/MPN. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells.

FISH testing for sex chromosomes after sex-mismatched allogeneic HCT should not be considered disease assessment, as the purpose is to determine donor chimerism. Additionally, the FISH probe panel should reflect the patient’s current disease; FISH may be used as surveillance for changes associated with post-therapy malignancy.

If FISH studies were performed and consistent with relapse or progression at any point in the reporting period, check “yes” and continue with question 27.
If FISH studies were not consistent with relapse or progression during the reporting period, indicate “no” and continue with question 28. Examples include no FISH study was performed, FISH sample was inadequate, it is unknown if FISH study was performed, or FISH studies were obtained and were not consistent with relapse or progression.

**Question 27: Date assessed:**

Report the date the sample was collected for FISH assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 28: Was a disease relapse or progression detected via conventional cytogenetics?**

Conventional cytogenetics are performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. This is called karyotyping. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

If conventional cytogenetic studies were performed and results were consistent with relapse or progression at any point in the reporting period, check “yes” and continue with question 29.

If conventional cytogenetic studies were not consistent with relapse or progression during the reporting period, indicate “no” and continue with question 30. Examples include no conventional cytogenetics performed, conventional cytogenetic culture failed, it is unknown if conventional cytogenetic studies were performed, or conventional cytogenetics were obtained and were not consistent with relapse or progression.

**Question 29: Date assessed:**

Report the date the sample was collected for conventional cytogenetic assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 30: Was a disease relapse or progression detected via clinical/hematologic assessment?**

Clinical and hematologic assessments are the least sensitive methods of establishing a patient’s disease status. Examples include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), laboratory assessment (e.g., CBC, peripheral blood smear), and clinician evaluation and physical examination.
The following criteria are used to determine if a clinical/hematologic relapse or progression was detected:

**Progression from Hematologic Improvement (Prog from HI)**

Requires at least one of the following in the absence of another explanation (e.g., infection, bleeding, ongoing chemotherapy, etc.):

- ≥ 50% reduction from maximum response levels in granulocytes or platelets
- Reduction in hemoglobin by ≥ 1.5 g/dL
- Transfusion dependence

*Note: declining donor chimerism does not meet the criteria for progression.*

**Relapse from Complete Remission (Rel from CR)**

Requires at least one of the following:

- Return to pre-treatment bone marrow blast percentage
- Decrease of ≥ 50% from maximum response levels in granulocytes or platelets
- Transfusion dependence, or hemoglobin level ≥ 1.5 g/dL lower than prior to therapy

*Note: declining donor chimerism does not meet the criteria for relapse.*

**Progression to AML**

≥ 20% blasts in the blood or bone marrow

If clinical and/or hematologic assessments were performed and consistent with relapse or progression at any point in the reporting period, check “yes” and continue with question 31.

If clinical and/or hematologic assessments were not consistent with relapse or progression during the reporting period, indicate “no” and continue with question 32. Examples include if it is unknown if clinical and/or hematologic assessments were performed, or clinical and/or hematologic assessments were not consistent with relapse or progression.

**Question 31: Date assessed:**

Report the date of clinical or hematologic assessment. Indicate the date the sample was collected for pathological and laboratory evaluations, the date the imaging took place for radiographic assessments, or the date of physical examination.

If the exact date is not known, use the process for reporting partial or unknown dates as described in...
Q32-37: Most Recent Laboratory Studies

Questions 32-33: Was the bone marrow examined (post-HCT) since the date of last report?

Indicate if a bone marrow examination was performed during the current reporting period. If “yes,” indicate the date sample was collected in question 33. If “no” or “unknown,” continue with question 38.

Questions 34-35: Blasts in bone marrow:

Indicate whether the percentage of blasts in the bone marrow was “known” or “unknown.” If “known,” report the percentage documented on the laboratory report during the current reporting period in question 35. If “unknown,” continue with question 36.

If multiple marrow examinations were performed, report the most recent evaluation.

Question 36: Did the recipient have myelofibrosis since the date of last report?

Myelofibrosis describes the replacement of bone marrow by fibrous (scar) tissue. Indicate if the recipient’s bone marrow showed myelofibrosis since the date of the last report. If there was evidence of myelofibrosis since the date of the last report, indicate “yes” and continue with question 37. If there was no evidence of myelofibrosis or the presence of myelofibrosis is unknown, select “no” or “unknown” and continue with question 38.

If multiple marrow examinations were performed, report the most recent evaluation.

Question 37: Specify the status of marrow fibrosis since the date of last report.

Compared to the status of the marrow fibrosis since the last report, indicate if the fibrosis is “unchanged,” “worse,” “improved,” “resolved,” or “unknown.”

If multiple marrow examinations were performed, report the most recent evaluation.

If this comprehensive report form is for the 100-day post-HCT reporting period, compare the fibrosis in the most recent bone marrow examination during the 100-day reporting period to the fibrosis in the bone marrow examination just prior to the start of the preparative regimen for the HCT.
Q38-41: Disease Status at the Time of Evaluation for this Reporting Period

Question 38: What is the current disease status?

Report the disease status at the time of evaluation for this reporting period. Some judgment is required when evaluating if the recipient meets all specified CR criteria, specifically ANC and platelet criteria. If the recipient does not meet these parameters, the underlying cause should be assessed. If the cause for a low ANC or a low platelet count is related to MDS/MPN, the disease status should not be reported as “complete remission.” If the cause for not meeting one of these parameters is due to something other than underlying hematologic disease, such as renal insufficiency, hemolysis, or drug-related causes, the disease status may still be reported as “complete remission.” See MDS/MPN Response Criteria for disease status definitions.

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

Question 39: Was the recipient in molecular remission?

Molecular assessment involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection and can indicate known genetic abnormalities. RFLP testing (with PCR amplification) is an example of a molecular testing method.

Molecular remission is a treatment response in which no molecular abnormalities are detected in the blood and/or marrow following a previously identified molecular abnormality associated with the recipient's disease. If molecular abnormalities associated with the recipient's disease were identified previously and were absent at the time of evaluation for the reporting period, indicate “yes.”

If molecular abnormalities associated with the recipient's disease were identified at the time of evaluation for the reporting period, indicate “no.”

Indicate “unknown” if no molecular assessments were performed during the reporting period and the recipient has a history of molecular abnormalities associated with their disease.

Indicate “Not applicable” if the recipient has never had evidence of molecular abnormalities associated with their disease.
Question 40: Was the recipient in cytogenetic remission?

Cytogenetic assessment involves testing blood or bone marrow for the presence of known cytogenetic abnormalities that reflect the recipient’s disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

Cytogenetic remission is a treatment response where both of the following criteria are met:

- The karyotype reverts to normal, and
- There are no clonal chromosomal abnormalities detected in the blood and/or marrow.

If cytogenetic abnormalities associated with the recipient’s disease were identified previously and the criteria above were met at the time of evaluation for the reporting period, indicate "yes."

If cytogenetic abnormalities associated with the recipient’s disease were identified at the time of evaluation for the reporting period, indicate "no."

Indicate “unknown” if no cytogenetic assessments were performed during the reporting period and the recipient has a history of cytogenetic abnormalities associated with their disease.

Indicate “Not applicable” if the recipient has never had evidence of cytogenetic abnormalities associated with their disease.

Question 41: Date assessed:

Enter the date of the most recent assessment establishing disease status within the reporting period. The date reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), laboratory assessment (e.g., CBC, peripheral blood smear), and clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluations, the date the imaging took place for radiographic assessments, or the date of physical examination.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
Juvenile Myelomonocytic Leukemia (JMML) is a cancer of the white blood cells. It is characterized by overproduction of myelocytes and monocytes; this chronic proliferation of myelocytes and monocytes in the bone marrow prevents the formation of healthy red blood cells, white blood cells, and/or platelets. Since JMML is characterized both by dysregulation and excessive proliferation of the bone marrow, it is classified as a mixed myelodysplastic-myeloproliferative disorder. The pathologic features of JMML are believed to primarily be the result of a clonal abnormality leading to activation of Ras signaling; this inappropriate activation of Ras leads to over-proliferation of certain cell types. Approximately 75% of all JMML patients carry one of three mutually exclusive mutations associated with inappropriate Ras activation: direct RAS mutations; NF1 -inactivating mutations; or protein tyrosine phosphatase, non-receptor type 11 (PTPN11) mutations.\(^1\)

Clinically, JMML presents as hepatosplenomegaly with or without lymphadenopathy, pallor, fever, and rash. Due to the broad differential diagnosis associated with this presentation, a diagnosis of JMML may require a very extensive workup. JMML most commonly affects children less than six years of age, with most patients diagnosed at less than two years of age. It comprises less than 2% of all childhood leukemias, and has historically carried a grim prognosis, with less than 10% survival with a chemotherapy-only approach.\(^1\) With HCT, survival approaches 50%.\(^2\)

Accessibility verified August 8, 2013.

JMML Response Criteria

Complete Remission (CR)
Normalization of WBC and resolution of organomegaly.

Partial Remission (PR)
≥ 50% reduction of WBC from maximum pre-treatment value and/or ≥ 50% reduction of organomegaly from pre-treatment maximum

Marginal Response (MR)
25-50% reduction of WBC from maximum pre-treatment value and 25-50% reduction of organomegaly from pre-treatment maximum

or

≥ 50% reduction of WBC from maximum pre-treatment value and no change in organomegaly

or

≥ 50% reduction of organomegaly from pre-treatment maximum and no change in WBC

Stable Disease (SD)
≤ 25% reduction of WBC from maximum pre-treatment value and/or ≤ 25% reduction of organomegaly from pre-treatment maximum

Progressive Disease (PD)
Increase in WBC and/or organomegaly

Relapse
Reappearance of disease characteristics such as leukocytosis, absolute monocytosis, and organomegaly after complete remission (CR)

Not assessed
No assessment of leukocytosis or organomegaly was done at any time after therapy. If the patient was not treated, no assessment of leukocytosis or organomegaly was done at any time after diagnosis.
2015: JMML Pre-HCT

The Juvenile Myelomonocytic Leukemia Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures JMML-specific pre-HCT data such as: the recipient’s hematologic and cytogenetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HCT treatments administered, and disease status prior to the start of the preparative regimen.

This form must be complete for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Myelodysplastic (MDS)/myeloproliferative (MPN) diseases and the subtype is reported as Juvenile Myelomonocytic Leukemia (JMML/JCML); also for all recipients with AML whose disease transformed from JMML.

**Subsequent Transplant**

If this is a report of a second or subsequent transplant for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1.

If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than Juvenile Myelomonocytic Leukemia), begin at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, check the indicator box and continue with question 63.

**Q1-6: Clinical Features at Diagnosis**
**Q7-48: Laboratory Values at Diagnosis**
**Q49-62: Pre-HCT Therapy**
**Q63-64: Transformation**
**Q65-91: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen**
**Q92-93: Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen**

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove</th>
<th>Description</th>
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</tr>
<tr>
<td>Date</td>
<td>Description</td>
<td>Action</td>
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</tr>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
<tr>
<td>6/26/15</td>
<td>2015: JMML Pre-HCT</td>
<td>Modify</td>
<td>Modified text of Questions 63 to include the following concept: Progression to AML: ≥ 20% blasts in the <strong>blood or bone marrow</strong></td>
</tr>
</tbody>
</table>
Q1-6: Clinical Features at Diagnosis

Question 1: What was the date of diagnosis?

Juvenile myelomonocytic leukemia (JMML) is characterized by multiple clinical and laboratory features, rather than distinct pathological characteristics. As such, the date of diagnosis should be the date of the last assessment used to establish a diagnosis of JMML.

Table 1. Diagnostic Criteria for JMML

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| **Category 1**<br>All Category 1 criteria plus additional Category 2 or Category 3 criteria are required to establish a diagnosis of JMML. | • Absence of BCR/ABL fusion gene  
• Peripheral blood with >1 × 10⁹/L monocytes  
• Bone marrow with <20% blasts  
• Splenomegaly |
| **Category 2**<br>All Category 1 traits plus at least one Category 2 trait can establish a diagnosis of JMML. | • Somatic mutation in RAS or PTPN11  
• Clinical diagnosis of Neurofibromatosis 1 (NF1) or presence of NF1 gene mutation  
• Monosomy 7 |
| **Category 3**<br>All Category 1 traits plus at least two Category 3 traits can establish a diagnosis of JMML in the absence of any Category 2 traits. | • WBC >10 × 10⁹/L  
• Circulating myeloblasts  
• Increased hemoglobin F (HbF) for age  
• Clonal cytogenetic abnormality (excluding monosomy 7, which is Category 2 criteria)  
• GM-CSF hypersensitivity |

In order to establish a diagnosis of JMML, all of the category 1 criteria must be met. In addition, the patient must meet at least one category 2 criterion or at least two category 3 criteria. Report the date of sample collection for the last required assessment used to establish the diagnosis for JMML.

**Example:** Patient has absolute peripheral monocytosis of 3.2 × 10⁹/L with palpable splenomegaly. On April 19, 2007, patient has a bone marrow biopsy and aspirate that show 2% blasts. On May 12, 2007, a
peripheral blood sample is drawn and sent for BCR/ABL and PTPN11 molecular studies. On May 27, 2007, the lab results come back showing no BCR/ABL gene fusion but the presence of a PTPN11 gene mutation. The physician meets with the family to explain the diagnosis of Juvenile Myelomonocytic Leukemia (JMML) on June 7, 2007.

The reported date of diagnosis would be **May 12, 2007**.

**Specify whether the recipient expressed the following clinical features at diagnosis:**

For questions 2-6, report the patient’s status at diagnosis or prior to first therapy. Include supportive measures such as leukapheresis and 13-cis-retinoic acid as first therapy for the purposes of establishing clinical features at diagnosis.

**Question 2: Adenopathy**

Indicate if the patient had clinical adenopathy at diagnosis or prior to first therapy. Adenopathy refers to enlargement of lymph nodes and may be established by physical examination or imaging.

**Question 3: Hepatomegaly**

Indicate if the patient had palpable hepatomegaly at diagnosis or prior to first therapy. Hepatomegaly refers to enlargement of the liver and should be established on physical exam; hepatomegaly is defined as the liver edge being palpable more than three centimeters below the right costal margin. Hepatomegaly may be confirmed by imaging.

**Question 4: Neurofibromatosis**

Indicate if the patient had neurofibromatosis of any type at diagnosis or prior to first therapy. Neurofibromatosis refers to the abnormal proliferation of neural crest cells that form tumors. The most common type of neurofibromatosis is type 1, also known as von Recklinghausen disease, which is an autosomal dominant genetic disorder characterized by neurofibromas, skeletal abnormalities, café au lait spots, Lisch nodules, freckling in the axilla or groin, and/or optic nerve glioma.

**Question 5: Skin involvement**

Indicate if the patient had skin involvement at diagnosis or prior to first therapy. Skin involvement may clinically be characterized by edematous or erythematous lesions, or generalized rash. Do not report petechiae or pallor as skin involvement.

**Question 6: Splenomegaly**

Indicate if the patient had palpable splenomegaly at diagnosis or prior to first therapy. Splenomegaly refers
to enlargement of the spleen and should be established on physical exam; splenomegaly is defined as the spleen being palpable more than three centimeters below the left costal margin. Splenomegaly may be confirmed by imaging.
Q7-48: Laboratory Values at Diagnosis

Report findings at the time of diagnosis; if multiple studies were performed prior to the institution of therapy, report the latest values prior to first therapy.

Questions 7-8: WBC

Indicate whether the white blood count (WBC) was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the cell count and unit of measure documented on the laboratory report in question 8. If “unknown,” continue with question 9.

Questions 9-10: Hemoglobin

Indicate whether the hemoglobin was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the cell count and unit of measure documented on the laboratory report in question 10. If “unknown,” continue with question 12.

Question 11: Were RBC transfused < 30 days before date of test?

Packed red blood cell transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support their counts.

Indicate if red blood cells were transfused less than 30 days prior to the testing.

Questions 12-13: Platelets

Indicate whether the platelet count was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the cell count and unit of measure documented on the laboratory report in question 13. If “unknown,” continue with question 15.

Question 14: Were platelets transfused < 7 days before date of test?

Platelet transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support their counts.

Indicate if platelets were transfused less than 7 days prior to the testing.
Questions 15-16: Monocytes

Indicate whether the percentage of monocytes in the peripheral blood was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the percentage documented on the laboratory report in question 16. If “unknown,” continue with question 17.

Questions 17-18: Absolute monocyte count

Indicate whether the absolute monocyte count was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the cell count and unit of measure documented on the laboratory report in question 18. If “unknown,” continue with question 19.

Questions 19-20: Blasts in blood

Indicate whether the percentage of blasts in the peripheral blood was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the percentage documented on the laboratory report in question 20. If “unknown,” continue with question 21.

If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.

Questions 21-23: LDH

Indicate whether LDH (lactate dehydrogenase) was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report in question 22; also report the LDH upper limit of normal from the laboratory report in question 23. If “unknown,” continue with question 24.

Questions 24-25: Fetal hemoglobin (HbF)

Fetal hemoglobin is elevated in nearly 2/3 of patients with JMML and nearly all patients without monosomy 7. Greater elevation of fetal hemoglobin is associated with worse prognosis. Indicate whether fetal hemoglobin percentage was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the percentage documented on the laboratory report in question 25. If “unknown,” continue with question 26.

Question 26: Was testing performed for hypersensitivity to GM-CSF?

Indicate whether testing was performed to establish if the patient was hypersensitive to GM-CSF. If “yes,” report the result as positive (hypersensitive) or negative (normosensitive) in question 27. If “no” or “unknown,” continue with question 28.
**Question 28: Was the recipient's bone marrow examined?**

Indicate whether the recipient had a pathologic examination of their bone marrow. If “yes,” continue with question 29. If “no” or “unknown,” continue with question 32.

**Question 29: Blasts in bone marrow**

Specify the percentage of blasts in the bone marrow as documented on the pathology report. This should be taken from the aspirate differential.

**Question 30: Monocytes in bone marrow**

Specify the percentage of monocytes in the bone marrow as documented on the pathology report. This should be taken from the aspirate differential.

**Question 31: Was documentation submitted to the CIBMTR (e.g., examination report)?**

Indicate if a copy of the bone marrow pathology report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the bone marrow pathology report. Attaching a copy of the report may prevent additional queries.

**Question 32: Were cytogenetics tested (conventional or FISH)?**

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH).

Indicate if cytogenetic studies were obtained at diagnosis or prior to first therapy.

If cytogenetic studies were obtained, check “yes” and continue with question 33.

If cytogenetic studies were not obtained or it is unknown if chromosome studies were performed, indicate “no” or “unknown” and continue with question 42.

**Question 33: Results of test**

If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), report “abnormalities identified” and continue with question 34.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, report this and continue with question 42.
Questions 34-40: Specify cytogenetic abnormalities identified at diagnosis

If question 33 indicates that abnormalities were identified, each of questions 34-39 must be answered as “yes” or “no.” Do not leave any response blank. Indicate “yes” for each cytogenetic abnormality identified at diagnosis or prior to first therapy in questions 34-39; indicate “no” for all options not identified on cytogenetic assessment at diagnosis or prior to first therapy. If at least one abnormality is best classified as “other abnormality,” specify in question 40.

Question 41: Was documentation submitted to the CIBMTR? (e.g., cytogenetic or FISH report)

Indicate if a copy of the cytogenetic or FISH report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the cytogenetic or FISH report. Attaching a copy of the report may prevent additional queries.

Question 42: Were tests for molecular markers performed (e.g., PCR)?

Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient’s disease. Molecular assessment is the most sensitive test for genetic abnormalities and involves amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically utilizing RNA to generate complementary DNA through reverse transcription (RT-PCR).

Indicate if molecular studies were obtained at the time the recipient was diagnosed with JMML or prior to first therapy.

If molecular studies were obtained, check “yes” and continue with question 43.

If molecular studies were not obtained or it is unknown if molecular studies were performed, indicate “no” or “unknown” and continue with question 49.

Questions 43-47: Specify abnormalities

If question 42 indicates that molecular markers were identified, then each of questions 43-47 must be answered as “positive,” “negative,” or “not done.” Do not leave any response blank.

Table 2. Common Molecular Markers Associated with JMML

<table>
<thead>
<tr>
<th>Molecular Abnormality</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCR-ABL</td>
<td>BCR-ABL, aka Philadelphia chromosome, refers to the tyrosine kinase gene fusion resulting from the translocation of material from chromosome 9 (ABL) onto chromosome 22 (BCR). Molecular weight varies depending on exact location of the translocation. BCR-ABL fusion cannot be present in patients diagnosed with JMML.1</td>
</tr>
<tr>
<td>Gene</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>-------------</td>
</tr>
<tr>
<td>CBL</td>
<td>Genes encode for CBL proteins that are involved in protein ubiquitination, which has an effect of moderating protein tyrosine kinase signaling. Mutations to the CBL genes, particularly c-Cbl mutations, are therefore believed to be involved in a severe myeloproliferative presentation.(^2)</td>
</tr>
<tr>
<td>K-Ras</td>
<td>K-Ras is one of many Ras proteins, which belong to a larger group of proteins known as GTPases. GTPases are enzymes that bind and hydrolyze GTP. Mutant K-Ras is believed to target hematopoietic progenitor cells, inducing lineage-specific malignancies.(^3)</td>
</tr>
<tr>
<td>N-Ras</td>
<td>N-Ras is one of many Ras proteins, which belong to a larger group of proteins known as GTPases. GTPases are enzymes that bind and hydrolyze GTP. Mutant N-Ras is associated with increased sensitivity to GM-CSF.(^4)</td>
</tr>
<tr>
<td>PTPN11</td>
<td>The \textit{PTPN11} gene encodes SHP-2, a protein tyrosine phosphatase involved with signal transduction and hematopoiesis; specifically, it relays signals from activated growth factor signals to Ras proteins, leading to cell proliferation. Mutations in the \textit{PTPN11} gene are associated with Noonan syndrome and myeloproliferative disorders, including JMML.(^5)</td>
</tr>
</tbody>
</table>


**Question 48: Was documentation submitted to the CIBMTR?**

Indicate if a copy of the molecular report(s) is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the molecular report. Attaching a copy of the report may prevent additional queries.
Q49-62: Pre-HCT Therapy

**Question 49: Was therapy given?**

Indicate if the recipient received treatment for JMML after the time of diagnosis and before the start of the preparative regimen. If “yes,” continue with question 50. If “no,” continue with question 63.

**Questions 50-58: Specify therapy given**

Indicate “yes” or “no” for each therapeutic agent or intervention listed. Do not leave any response blank. If the recipient received a chemotherapy agent that is not listed, check “yes” for “other therapy” and specify the treatment in question 58.

**Question 59: Was a complete remission achieved?**

Complete hematologic response (CR) is a treatment response where white blood cell count normalizes and organomegaly resolves.

Indicate if the patient achieved complete remission as a response to therapy and prior to the start of the preparative regimen.

**Question 60: Date of complete remission**

Enter the date complete remission was established. Report the date of the pathological evaluation (e.g., bone marrow biopsy); if no pathologic evaluation was reported, report the date of blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for examination for pathological and/or laboratory evaluations. If the recipient was treated for extramedullary disease and a radiological assessment (e.g., X-ray, CT scan, MRI scan, PET scan) was performed to assess disease response, enter the date the imaging took place for radiologic assessments. If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit at which the physician clinically assessed the recipient’s response.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 61: Was there a disease relapse?**

Relapse is the recurrence of disease after CR. JMML relapse is demonstrated by the reappearance of disease characteristics such as leukocytosis, absolute monocytosis, and organomegaly.
Indicate if relapse occurred at any point after therapy but prior to the start of the preparative regimen. If no relapse occurred, report “no” and continue with question 63.

**Question 62: Date of disease relapse**

Enter the assessment date that relapse was established following the line of therapy. Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations. If extramedullary disease was detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place. If the physician determined cytogenetic or molecular relapse occurred, enter the date the sample was collected for cytogenetic or molecular evaluation. If the physician determined evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](http://CIBMTR.org/forms manuals).
Q63-64: Transformation

**Question 63: Did transformation to acute myelogenous leukemia (AML) occur?**

Indicate if the recipient’s disease transformed to AML between initial diagnosis and the start of the preparative regimen. Approximately 10-15% of JMML cases will transform to AML. Progression to AML is generally defined by an increase in blood or bone marrow blasts (≥ 20%). If the patient’s disease transformed to AML, also complete AML Pre-HCT Data, Form 2010.

**Question 64: Date of transformation**

Enter the date of the assessment that determined the disease transformation. Report the date of the first pathological diagnosis (i.e., bone marrow biopsy) of AML. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.

If the exact date is not known, use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](#).
Q65-91: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen

These questions are intended to determine the hematological status of the recipient prior to the preparative regimen. Testing may be performed multiple times within the pre-transplant work-up period (approximately 30 days) prior to the start of the preparative regimen; report the most recent laboratory values. Laboratory values obtained on the first day of the preparative regimen may be reported as long as the sample was taken before any radiation or systemic therapy was administered.

Questions 65-66: Fetal hemoglobin (HbF)

Fetal hemoglobin is elevated in nearly 2/3 of patients with JMML and nearly all patients without monosomy 7. Greater elevation of fetal hemoglobin is associated with worse prognosis. Indicate whether fetal hemoglobin percentage immediately prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the percentage documented on the laboratory report in question 66. If “unknown,” continue with question 67.

Questions 67-68: Monocytes

Indicate whether the percentage of monocytes in the peripheral blood immediately prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the percentage documented on the laboratory report in question 68. If “unknown,” continue with question 69.

Questions 69-70: Absolute monocyte count

Indicate whether the absolute monocyte count immediately prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 70. If “unknown,” continue with question 71.

Questions 71-72: Blasts in blood

Indicate whether the percentage of blasts in the peripheral blood immediately prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the percentage documented on the laboratory report in question 72. If “unknown,” continue with question 73.

* If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.
Question 73: Were cytogenetics tested (conventional or FISH)?

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH).

Indicate if cytogenetic studies were obtained immediately prior to the start of the preparative regimen.

If cytogenetic studies were obtained, check “yes” and continue with question 74.

If cytogenetic studies were not obtained or it is unknown if they were performed, indicate “no” or “unknown” and continue with question 82.

Question 74: Results of test

If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), indicate “abnormalities identified” and continued with question 75.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate such and continue with question 82.

Questions 75-81: Specify cytogenetic abnormalities identified at diagnosis

If question 74 indicates that abnormalities were identified, each of questions 75-80 must be answered as “yes” or “no.” Do not leave any response blank. Indicate “yes” for each cytogenetic abnormality identified at diagnosis or prior to first therapy in questions 75-80; indicate “no” for all options not identified on cytogenetic assessment at diagnosis or prior to first therapy. If one or more abnormalities are best classified as “other abnormality,” specify in question 81.

Question 82: Were tests for molecular markers performed (e.g., PCR)?

Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient’s disease. Molecular assessment is the most sensitive test for genetic abnormalities and involves amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically utilizing RNA to generate complementary DNA through reverse transcription (RT-PCR).

Indicate if molecular studies were obtained immediately prior to the start of the preparative regimen.

If molecular studies were obtained, check “yes” and continue with question 83.

If molecular studies were not obtained or it is unknown if molecular studies were performed, indicate “no” or “unknown” and continue with question 88.
Questions 83-87: Specify abnormalities

If question 82 indicates that molecular markers were identified, then each of questions 83-87 must be answered as “positive,” “negative,” or “not done.” Do not leave any response blank.

See Table 2 in this manual for additional information on common molecular markers associated with JMML.

Question 88: Was the recipient's bone marrow examined just prior to the preparative regimen?

Indicate whether the recipient had a pathologic examination of their bone marrow. If “yes,” continue with question 89. If “no” or “unknown,” continue with question 92.

Question 89: Date sample collected

Report the date the bone marrow specimen was collected for analysis.

Question 90: Blasts in bone marrow

Specify the percentage of blasts in the bone marrow as documented on the pathology report. This should be taken from the aspirate differential.

Question 91: Monocytes in bone marrow

Specify the percentage of monocytes in the bone marrow as documented on the pathology report. This should be taken from the aspirate differential.
Q92-93: Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen

Question 92: What was the disease status?

Indicate the disease status of JMML at the last evaluation prior to the start of the preparative regimen.

If the patient’s disease transformed to AML, do not complete questions 92-93 and continue with the signature section.

See JMML Response Criteria for disease status definitions.

Question 93: Date assessed

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant work-up period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for examination for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.
2115: JMML Post HCT

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Myelodysplastic (MDS)/myeloproliferative (MPN) diseases and question 480 as Juvenile Myelomonocytic Leukemia (JMML/JCML). The Juvenile Myelomonocytic Leukemia Post-HCT Data (Form 2115) must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, 2300) completed. The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200, between the date of contact for the six-month follow up and the date of contact for the one-year follow up for Form 2200, etc.).

For recipients who had JMML that transformed to AML prior to transplant, it is only necessary to complete Form 2110 (Acute Myelogenous Leukemia Post-HCT Data). Although form 2015 (Juvenile Myelomonocytic Leukemia Pre-HCT Data) is required to obtain JMML data pre-HCT, Form 2115 (Juvenile Myelomonocytic Leukemia Post-HCT Data) is not required for these recipients.

Q1-3: Disease Assessment at the Time of Best Response to HCT
Q4-10: Relapse or Progression Post-HCT
Q11-19: Post-HCT Therapy
Q21-22: Disease Status at the Time of Evaluation for This Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/19/18</td>
<td>Comprehensive Disease Specific Manuals</td>
<td>Add</td>
<td>Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119). The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.</td>
</tr>
<tr>
<td>2/24/</td>
<td>Comprehensive Disease-</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402)</td>
</tr>
<tr>
<td>17</td>
<td>Specific Manuals</td>
<td>instead of the Pre-TED Form (Form 2400)</td>
<td></td>
</tr>
</tbody>
</table>
Q1-3: Disease Assessment at the Time of Best Response to HCT

**Question 1:** Compared to the disease status prior to the preparative regimen, what was the best response to HCT since the date of the last report? (Include response to any therapy given for post-HCT maintenance or consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease.)

Any specified therapy administered post-HCT to prolong remission or for minimal residual disease is considered part of the HCT and should be included when assessing the recipient's response to transplant. Treatment given post-HCT for relapsed or persistent disease is not considered part of the HCT and should be excluded when assessing the response to HCT. If treatment was given post-HCT for relapsed or persistent disease, assess the patient's best response prior to the start of that treatment. If therapy was only given for reasons other than relapsed or persistent disease, assess the patient's best response throughout the entire duration of the reporting period.

If the recipient was in remission at the start of the preparative regimen, indicate “continued complete remission” and continue with question 4.

If the recipient did not achieve CR prior to the start of the preparative regimen, specify their best response following transplant and continue with question 2.

See [JMML Response Criteria](https://www.jmml-research.org) for disease status definitions.

**Question 2:** Was the date of best response previously reported?

If the patient achieved their best response in the current reporting period, indicate “no” and continue with question 3.

If the recipient achieved their best response during a previous reporting period, indicate “yes” and continue with question 4.

**Question 3: Date assessed**

Indicate the date best response was achieved. Report the date of the pathological evaluation (e.g., bone marrow biopsy), blood/serum assessment (e.g., CBC, peripheral blood smear), radiographic evaluation (e.g., abdominal CT), or physical examination (e.g., organomegaly on palpation). Enter the date the sample was collected for pathological and/or laboratory evaluations.
Question 4: Has the disease relapsed or progressed since the date of last report?

Report if the recipient had a hematologic or clinical relapse at any time during the reporting period. Progression is defined as an increase in WBC and/or organomegaly or transformation to AML. Relapse is defined as the reappearance of disease characteristics after a complete remission. Do not report relapse or progression for the reappearance of molecular or cytogenetic abnormalities associated with the patient’s disease in the absence of clinical evidence of disease.

If no assessments were consistent with relapse or progression during the reporting period, indicate “no” and continue with question 11.

Question 5: Date of disease relapse/progression

Report the date of the assessment consistent with relapse or progression. If relapse or progression was identified by hematologic assessment, report the date the specimen was collected.

Questions 6-10: Specify site(s) of disease relapse/progression

Indicate “yes” or “no” for each site specified in questions 6-9. Do not leave any responses blank. Specify only the sites of clinical or hematologic disease; cytogenetic and molecular evidence of disease does not need to be specified. If “yes” is indicated for “other site,” specify the site in question 10. At least one of questions 6-9 must be answered “yes.”
Q11-19: Post-HCT Therapy

Question 11: Was any therapy given for relapsed, persistent, or progressive disease since the date of last report?

Indicate if the recipient received treatment for relapsed JMML during the current reporting period. Do not report therapy given for maintenance (to prolong remission or for minimal residual disease). If the patient received therapy for relapsed, persistent, or progressive disease, check “yes” and continue with question 12. If the patient did not receive therapy, or only received therapy for maintenance, check “no” and continue with question 21.

Question 12: Systemic therapy

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body.

Indicate “yes” if the patient received systemic and continue with question 12. If the patient did not receive systemic therapy, indicate “no” and continue with question 17.

Questions 13-16: Specify systemic therapy agent(s)

Indicate “yes” or “no” for each drug administered for therapy during the current reporting period for reasons relapse, progressive, or persistent disease. Do not leave any responses blank. If the recipient received an agent that is not listed, check “yes” for “other systemic therapy” and specify the treatment in question 16.

Question 17: Donor cellular infusion

A donor cellular infusion, or DCI, is a form of immunotherapy that is commonly used for a variety of purposes, including the treatment of refractory or recurrent disease. In the setting of relapsed, persistent, or progressive disease, the DCI is used to create a graft-versus-leukemia/tumor (GVL/GVT) effect. In general, the recipient does not receive a preparative regimen prior to receiving the additional donor cells since replacement of the marrow is not the goal.

Indicate “yes” if the patient received one or more donor cellular infusion(s); also report the DCI on the corresponding Form 2100, 2200, or 2300. If the patient did not receive a donor cellular infusion, check “no.”

Question 18: Subsequent HCT

An HCT is an infusion of a product (i.e., bone marrow, peripheral blood stem cells, cord blood, etc.) that contains CD34+ cells. Refer to Appendix D for further clarification on defining a subsequent HCT.
The intention of an HCT is to restore hematopoiesis and immunity. It is usually preceded by a preparative regimen used to both reduce disease burden and prevent rejection of the new stem cells by killing normal and malignant cells, if present. In some cases, a preparative regimen might not be used prior to the infusion of CD34+ cells, but this would still be considered an HCT.

A subsequent HCT may be administered to replace or repopulate the recipient’s marrow and reconstitute the immune system. If the recipient receives a subsequent HCT as treatment for relapsed disease, check “yes” and continue with question 19. Only report a subsequent HCT given for relapsed, persistent, or progressive disease. If a subsequent HCT is reported in question 18, it must also be reported on the corresponding Form 2100, 2200, or 2300.

If a recipient receives a subsequent HCT between the HCT follow-up time points (100 day, six months, annually), the comprehensive report form sequence will start over with another Pre-TED Form (2400), Recipient Baseline Data Form (2000), and Juvenile Myelomonocytic Leukemia Pre-HCT Data Form (2015). However, if the recipient receives an autologous HCT as a result of a poor graft or graft failure, the comprehensive report form sequence will not start over if the preceding HCT was also autologous. Generally this type of infusion (autologous rescue) is used to treat the recipient’s poor graft response, rather than to treat the recipient’s disease.

**Question 19: Other therapy**

If the patient received a therapy that is not listed, indicate “yes” and specify the therapy in question 20. If the patient did not receive another therapy not listed, check “no.”
Q21-22: Disease Status at the Time of Evaluation for this Reporting Period

Question 21: What was the disease status?

Indicate the disease status of JMML as of the last evaluation during the reporting period.

See JMML Response Criteria for disease status definitions.

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

Question 22: Date assessed

Enter the date of the most recent assessment establishing disease status within the reporting period. The date reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and/or laboratory evaluations, the date the imaging took place for radiographic assessments, or the date of physical examination.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
2016/2116: Plasma Cell Disorders (PCD)

The blood is composed of platelets, red blood cells, and several kinds of white blood cells. One kind of white blood cells, the plasma cells (also called plasma B cells, plasmocytes, or effector B cells) produce proteins called antibodies or immunoglobulins (Igs) that are part of our defense system against foreign substances (called antigens). Antibodies are produced in response to such things as viruses, bacteria, and other infectious agents.

Multiple myeloma is a cancer that leads to the proliferation of malignant plasma cells (myeloma cells). Myeloma cells usually proliferate in the bone marrow. When myeloma cells grow into isolated masses in other sites, these masses are called plasmacytomas. Health problems caused by multiple myeloma can affect the bones, immune system, kidneys, and red blood cell count.

The immunoglobulins (antibodies) produced by healthy plasma cells are composed of pairs of heavy chains and light chains (see Graphic 1 below). Healthy plasma cells create many different kinds of immunoglobulins that are classified by their heavy chain type into five categories (IgG, IgA, IgM, IgD, or IgE). The light chain types are designated kappa (κ) or lambda (λ). The whole Ig molecule is then labeled IgG kappa, IgG lambda, IgA kappa, IgA lambda, etc. These protein levels can be measured in blood serum and/or urine.

**Graphic 1: Structure of an Immunoglobulin (Antibody)**

Secretory Multiple Myeloma:
Healthy plasma cells make immunoglobulins (antibodies) of all types. With the proliferation of malignant plasma cells, the level of one immunoglobulin type increases in the blood and/or urine. This abnormal immunoglobulin type is called the monoclonal immunoglobulin, monoclonal protein (M-protein/M-spike/M-component), or paraprotein. In most cases, the normal immunoglobulins are reciprocally depressed.
Patients with this condition are said to have *secretory myeloma*.

Some myeloma patients make only an excess of the light chain portion of the immunoglobulin molecule (i.e., only monoclonal kappa or lambda light chains). The light chain is also called Bence Jones protein. In most patients whose myeloma cells only make light chains, this paraprotein may not be detectable in the blood, but only in the urine. These patients are said to have *light chain only* disease. Ninety-seven percent of patients diagnosed with multiple myeloma have a detectable paraprotein in the blood serum and/or urine.

**Table 1. Distribution of Monoclonal Proteins in Secretory Multiple Myeloma**¹²

<table>
<thead>
<tr>
<th>Monoclonal Proteins at Diagnosis</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source of monoclonal proteins</td>
<td></td>
</tr>
<tr>
<td>Serum monoclonal proteins</td>
<td>80%</td>
</tr>
<tr>
<td>Urine monoclonal proteins</td>
<td>75%</td>
</tr>
<tr>
<td>Type of monoclonal proteins</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>50-54%</td>
</tr>
<tr>
<td>IgA</td>
<td>20%</td>
</tr>
<tr>
<td>Monoclonal light chain (light-chain-only disease)</td>
<td>20%</td>
</tr>
<tr>
<td>IgD</td>
<td>2%</td>
</tr>
</tbody>
</table>


**Nonsecretory Multiple Myeloma:**

In some myeloma patients, the malignant plasma cells do not produce an excess of the heavy chain or light chain portion of the immunoglobulin molecule; therefore, a paraprotein is not detectable in the serum or urine. These patients are said to have *nonsecretory myeloma* (i.e., the absence of a paraprotein on immunofixation). Immunofixation detects the specific immunoglobulins after separating the proteins into bands on an electrophoresis gel. Nonsecretory myeloma accounts for 3% of myeloma cases.

**Table 2. Epidemiology of Multiple Myeloma in the United States**¹

<table>
<thead>
<tr>
<th>Cases diagnosed per year</th>
<th>~21,700</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age at Diagnosis</td>
<td>69 yrs</td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Sex</td>
<td>Higher incidence in men</td>
</tr>
<tr>
<td>Race</td>
<td>Higher incidence in African Americans</td>
</tr>
<tr>
<td>5-year survival rate</td>
<td>40%</td>
</tr>
</tbody>
</table>


**Amyloidosis:**

Amyloidosis is a disease in which abnormally folded proteins build up in different tissues of the body. In the most common amyloidosis, AL amyloidosis, the abnormally folded protein is the light chain component of an immunoglobulin. These light chains may build up in a variety of tissues, but the most common sites of build-up are the heart, kidneys, liver, and nerves. According to the Amyloidosis Foundation, AL Amyloidosis is a relatively rare disorder, with 1200-3200 new cases reported each year in the United States. The disease mostly impacts men over 40.1


Multiple Myeloma Response Criteria
Amyloidosis Response Criteria
2016: PCD Pre-HCT
2116: PCD Post-HCT
Multiple Myeloma Response Criteria

General Reporting Guidelines

• Use the multiple myeloma response criteria when determining the disease status for multiple myeloma and solitary plasmacytoma.
• At any response level, if some but not all criteria are met, the disease status should be downgraded to next lower level of response.
• The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).
• Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR. Electrophoresis (SPEP and UPEP) are, however, different assessments.
• Review Appendix G for examples of how to determine disease status for Multiple Myeloma.

Urine Studies

In order to report a Stringent Complete Remission (sCR) or Complete Remission (CR), urine studies MUST be performed and agree with the international myeloma working group (IMWG) criteria provided above. As long as the negative serum electrophoresis and immunofixation studies have been confirmed, only one set of negative urine studies needs to be documented to report sCR or CR.

Stringent Complete Remission (sCR)

Follows criteria for CR as defined below, plus all of the following:

• Normal free light chain ratio,
• Absence of clonal cells in the bone marrow by immunohistochemistry or immunofluorescence (confirmation with repeat bone marrow biopsy not needed). (Presence and/or absence of clonal cells is based upon the κ/λ ratio. An abnormal κ/λ ratio by immunohistochemistry and/or immunofluorescence requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting the presence of an abnormal clone is κ/λ of > 4:1 or < 1:2.)

sCR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy sCR requirements.
Complete Remission (CR)

A treatment response where all of the following criteria are met:

- Negative immunofixation on serum and urine samples
- Disappearance of any soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

For recipients with light chain only myeloma, all of the following criteria must be met:

- Normal serum free light chain ratio
- Negative immunofixation on urine samples
- Disappearance of any soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

For recipients with non-secretory myeloma, all of the following criteria must be met:

- Disappearance of all soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

CR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy CR requirements.

The method of the two consecutive assessments may be any of the biochemical tests (urine/serum testing) listed in the disease status criteria available in the manual. Though it is preferable the biochemical confirmatory testing include both the urine & serum, this disease status does not require two consecutive assessments by each method. As an example:

A recipient with IgG kappa myeloma receives therapy and has assessments performed on April 1, which appear to show resolution of disease. These include negative serum and urine immunofixations, a bone survey and PET/CT without evidence of active disease, and a negative bone marrow with 2% plasma cells. On May 1, the recipient has another negative serum immunofixation prior to proceeding with transplant on May 12. This recipient would be in complete remission at transplant, as they meet all specified CR criteria and have two consecutive negative serum immunofixation studies; additional imaging and bone marrow studies are not required.
**Near Complete Remission (nCR)**

A treatment where all of the following criteria met:

- Serum and urine M-protein detectable by immunoelectrophoresis\(^1\) (immunofixation, IFE) but not on electrophoresis (SPEP and UPEP)
- < 5% plasma cells in bone marrow (confirmation with repeat bone marrow biopsy not needed).

nCR requires two consecutive assessments (by the same method) made at any time prior to the initiation of any new therapy, and no known evidence of new or progressive bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy nCR requirements.

**Very Good Partial Response (VGPR)**

One or more of the following must be present:

- Serum and urine M-protein detectable by immunofixation but not on electrophoresis
- ≥ 90% reduction in serum M-protein and urine M-protein level < 100 mg/24 hours.

If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):

- Serum M-protein ≥ 1 g/dL
- Urine M-protein ≥ 200 mg/24 hours;

then a ≥ 90% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level > 10 mg/dL and the serum free light chain is abnormal).
VGPR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy VGPR requirements.

**Partial Response (PR)**

**Both** of the following must be present:

- $\geq 50\%$ reduction in serum M-protein
- Reduction in 24-hour urinary M-protein by $\geq 90\%$ or to $< 200$ mg/24 hours.

If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):

- Serum M-protein $\geq 1$ g/dL
- Urine M-protein $\geq 200$ mg/24 hours;

then a $\geq 50\%$ decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level $> 10$ mg/dL and the serum free light chain is abnormal).

If serum and urine M-protein and serum-free light assay are not measurable, a $\geq 50\%$ reduction in bone marrow plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was $\geq 30\%$.

In addition to the above-listed criteria, if soft tissue plasmacytomas were present at baseline, a $\geq 50\%$ reduction in their size is also required.

PR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy PR requirements.

**Stable Disease (SD)**

Does not meet the criteria for CR, VGPR, PR, or PD.

SD requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy SD requirements.
Progressive Disease (PD)

Requires **one or more** of the following:
Increase of ≥ 25% from the lowest response value achieved in:

- Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); and/or
- Urine M-component with an absolute increase ≥ 200 mg/24 hours; and/or
- For recipients without measurable serum and urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL; and/or
- Bone marrow plasma cell percentage with absolute percentage ≥ 10%; and/or
- Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas (≥ 50% increase from nadir in size of >1 lesion, or a ≥ 50% increase in the longest diameter of a previous lesion >1 cm in short axis); and/or
- Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol) that can be attributed solely to the plasma cell proliferative disorder.

PD requires two consecutive assessments (by the same method) made at any time before classification as disease progression, and/or the start of any new therapy.

Relapse from CR

Requires one or more of the following:

- Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or
- Development of ≥ 5% plasma cells in the bone marrow; and/or
- Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia).

Relapse requires two consecutive assessments (by the same method) made at any time before classification as relapse, and/or the start of any new therapy.

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.
If you need to reference the historical Manual Change History for this form, please [click here](#) or reference the retired manual section on the [Retired Forms Manuals](#) webpage.

<table>
<thead>
<tr>
<th>Date</th>
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<th>Add/Remove/Modify</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>12/3/18</td>
<td><a href="#">Multiple Myeloma Response Criteria</a></td>
<td>Modify</td>
<td>Separated the blue note box regarding urine studies to better reflect requirements needed for sCR and CR versus requirements needed for nCR, VGPR, and PR.</td>
</tr>
<tr>
<td>11/20/18</td>
<td><a href="#">Multiple Myeloma Response Criteria</a></td>
<td>Add</td>
<td>Added the following (in red) to the Near Complete Remission (nCR) response criteria: &lt; 5% plasma cells in bone marrow (confirmation with repeat bone marrow biopsy not needed).</td>
</tr>
<tr>
<td>3/19/18</td>
<td><a href="#">Multiple Myeloma Response Criteria</a></td>
<td>Add</td>
<td>Added in Progressive Disease (PD) response criteria (red) with regards to plasmacytomas: <em>Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas (≥ 50% increase from nadir in size of &gt;1 lesion, or a ≥ 50% increase in the longest diameter of a previous lesion &gt;1 cm in short axis).</em></td>
</tr>
<tr>
<td>10/14/17</td>
<td><a href="#">Multiple Myeloma Response Criteria</a></td>
<td>Add</td>
<td>Added the bullet points below to General Reporting Guidelines. Note, the second bullet point above was previously available in this section as a footnote.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• <em>Use the multiple myeloma response criteria when determining the disease status for multiple myeloma and solitary plasmacytoma.</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• <em>Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR.</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Electrophoresis (SPEP and UPEP) are, however, different assessments.</em></td>
</tr>
<tr>
<td>5/1/17</td>
<td><a href="#">Multiple Myeloma Response Criteria</a></td>
<td>Modify</td>
<td>Corrected an error in the criteria for Near Complete Remission. A treatment where all of the following criteria met:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• <em>Serum and Urine M-protein detectable by immunoelectrophoresis</em> (immunofixation, IFE) but not on electrophoresis (SPEP and UPEP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ≤ &lt; 5% plasma cells in bone marrow.</td>
</tr>
<tr>
<td>1/23/17</td>
<td><a href="#">Multiple Myeloma Response Criteria</a></td>
<td>Add</td>
<td>Added General Reporting Guidelines. This information was previously available in Pre-TED and Multiple Myeloma Response Criteria sections of the Forms Instructions Manual.</td>
</tr>
<tr>
<td>8/26/16</td>
<td><a href="#">Multiple Myeloma Response Criteria</a></td>
<td>Modify</td>
<td>Updated PR criteria: If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):</td>
</tr>
<tr>
<td>Date</td>
<td>Type</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>------------</td>
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<td>-------------</td>
<td></td>
</tr>
<tr>
<td>6/27/16</td>
<td>Modify</td>
<td>Changed text in information box regarding <strong>Urine Studies</strong>: In order to report a Stringent Complete Remission (sCR) or Complete Remission (CR), urine studies MUST be performed and agree with the international myeloma working group (IMWG) criteria provided above. As long as the negative serum electrophoresis and immunofixation studies have been confirmed, only one set of negative urine studies needs to be documented to report sCR or CR. Urine electrophoresis and immunofixation studies may not be performed in all cases. The disease response options below (Near Complete Remission, Very Good Partial Response, and Partial Response) may still be reported even if urine studies were never obtained or were only obtained at diagnosis. If urine studies were performed following the most recent line of therapy, the results must agree with the international working group IMWG criteria for the disease status being reported. In any case, serum studies MUST be performed and agree with the international working group criteria for the disease status being reported (excluding non-secretory myeloma).</td>
<td></td>
</tr>
<tr>
<td>6/24/16</td>
<td>Add</td>
<td>Added information box: <strong>Urine Studies</strong> In order to report a Stringent Complete Remission or Complete Remission, urine studies MUST be performed and agree with the international working group criteria provided above. Urine electrophoresis and immunofixation studies may not be performed in all cases. The disease response options below (Near Complete Remission, Very Good Partial Response, and Partial Response) may still be reported even if urine studies were never obtained or were only obtained at diagnosis. If urine studies were performed following the most recent line of therapy, the results must agree with the international working group criteria for the disease status being reported. In any case, serum studies MUST be performed and agree with the international working group criteria for the disease status being reported.</td>
<td></td>
</tr>
<tr>
<td>6/24/16</td>
<td>Add</td>
<td>Added link to Appendix W below disease status criteria.</td>
<td></td>
</tr>
<tr>
<td>1/19/16</td>
<td>Add</td>
<td>Added the following text to CR: The method of the two consecutive assessments may be any of the biochemical tests (urine/serum testing) listed in the disease status criteria available in the manual. Though it is preferable the biochemical confirmatory testing include both the urine &amp; serum, this disease status does not require two consecutive assessments by each method. As an example: [see in text]</td>
<td></td>
</tr>
<tr>
<td>9/27/15</td>
<td>Add</td>
<td>Added a footnote: Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR. Electrophoresis (SPEP and UPEP) are, however, different assessments.</td>
<td></td>
</tr>
</tbody>
</table>
| 5/29/15    | Add    | Added the following text to **VGPR**: … then a ≥ 90% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria.
Plasma Cell Leukemia Response Criteria

General Reporting Guidelines

- At any response level, if some but not all criteria are met, the disease status should be downgraded to the next lower level of response.
- The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).
- Immunofixation (IFE) and immunoelectrophoresis (IEP) are essentially measuring the same thing and either may be used to determine CR. Electrophoresis (SPEP and UPEP) are, however, different assessments.

Stringent Complete Remission (sCR)

Follows criteria for CR as defined below, plus all of the following:

- No malignant plasma cells in the bone marrow and peripheral blood by flow cytometry; and
- Normal serum free light chain (FLC) ratio

sCR by biochemical testing requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy.

Complete Remission (CR)

A treatment response where all of the following criteria are met:

- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed); and
- Absence of extramedullary disease; and
- No plasma cells in peripheral blood; and
- Negative immunofixation on serum and urine samples.

If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):

- Serum M-protein ≥ 1 g / dL
- Urine M-protein ≥ 200 mg / 24 hours
then a normal serum free light chain (FLC) ratio is required in place of the M-protein criteria (provided the serum FLC assay showed an involved level > 10 mg / dL and an abnormal serum FLC ratio at diagnosis).

CR by biochemical testing requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy.

**Very Good Partial Response (VGPR)**

A treatment response where all the following criteria are met:

- Bone marrow plasma cells <5% (confirmation not required); and
- No plasma cells in the peripheral blood; and
- Absence of extramedullary disease; and
- Serum and urine M-protein detectable by immunofixation but not on electrophoresis or a ≥ 90% reduction in serum M-protein and urine M-protein level < 100 mg / 24 hours.

If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):

- Serum M-protein ≥ 1 g / dL
- Urine M-protein ≥ 200 mg / 24 hours

then a ≥ 90% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria (provided the serum FLC assay showed an involved FLC level > 10 mg / dL and an abnormal serum FLC ratio at diagnosis).

VGPR by biochemical testing requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy.

**Partial Response (PR)**

A treatment response where all the following criteria are met:

- 5% to 25% plasma cells in the bone marrow; and
- 1% to 5% plasma cells in peripheral blood; and
- ≥ 50% reduction in the size of extramedullary disease; and
- ≥ 50% reduction in serum M-protein; and
• ≥ 90% reduction in 24-hour urinary M-protein and < 200 mg / 24 hours.

If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):

• Serum M-protein ≥ 1 g / dL
• Urine M-protein ≥ 200 mg / 24 hours

then a ≥ 50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria (provided the serum FLC assay showed an involved level > 10 mg / dL and an abnormal serum FLC ratio at diagnosis).

PR by biochemical testing requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy.

**Stable Disease (SD)**

Does not meet the criteria for PR or PD.

**Progressive Disease (PD)**

Requires one or more of the following:

• Increase of ≥ 25% from the lowest response value achieved in:
  ◦ Bone marrow plasma cell percentage (in aspirate) or absolute percentage ≥ 10%; and / or
  ◦ Serum M-component with an absolute increase ≥ 0.5 g / dL (or 5 g / L) (for progressive disease, serum M-component increases of ≥ 1 g / dL are sufficient if the starting M-component is ≥ 5 g / dL); and / or
  ◦ Urine M-component with an absolute increase ≥ 200 mg / 24 hours; and / or
• >5% absolute increase in peripheral blood plasma cells; and / or
• Definite development of new bone lesions or extramedullary disease, or definite increase in the size of any existing bone lesions or extramedullary disease; and / or
• Development of hypercalcemia (corrected serum calcium > 11.5 mg / dL or 2.65 mmol) that can be attributed solely to the PCL.

PD by biochemical testing requires two consecutive assessments (by the same method) made at any time before classification as disease progression, and / or the start of any new therapy.
**Relapse from CR**

Requires **one or more** of the following:

- Development of ≥ 10% plasma cells in the bone marrow; *and/or*
- Reappearance of peripheral blood plasma cells at any level; *and/or*
- Appearance of any extramedullary disease; *and/or*
- Reappearance of original serum or urine M-protein by immunofixation.

Relapse by biochemical testing requires two consecutive assessments (by the same method) made at any time before classification as relapse, and/or the start of any new therapy.

**Manual Updates:**
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Amyloidosis Response Criteria

Hematologic Response

**Complete Response**

Requires all of the following:

- Serum and urine negative for monoclonal proteins by immunofixation
- Normal free light chain ratio
- Plasma cells in marrow < 5%

**Partial Response (PR)**

Requires any of the following:

- ≥ 50% reduction in current serum monoclonal protein levels > 0.5 g/dL
- ≥ 50% reduction in current urine light chain levels > 100 mg/day with a visible peak
- ≥ 50% reduction in current free light chain levels > 10mg/dL

**No Response (NR)/Stable Disease (SD)**

Does not meet the criteria for CR, PR, or progressive disease.

**Progressive Disease (PD)**

Requires any of the following:

- If progressing from CR, any detectable monoclonal protein or abnormal free light chain ratio (light chain must double)
- If progressive from PR or SD, ≥ 50% increase in the serum M protein to > 0.5 g/dL, or ≥ 50% increase in urine M protein to > 200mg/day with visible peak present.
- Free light chain increase of ≥ 50% to > 10 mg/dL (100 mg/L)
**Cardiac Response**

**Cardiac Response**

Requires any of the following:

- ≥ 2 mm decrease in mean intraventricular septal wall thickness by echocardiogram
- ≥ 20% increase in left ventricular ejection fraction
- ≥ 2 grade decrease in New York Heart Association functional class without an increase in diuretic use and no increase in wall thickness
- Reduction (≥ 30% and ≥ 300ng/L) of NT-proBNP in patients whom the eGFR is ≥ 45 ml/minute/1.73m²

**No Response/Stable Disease**

Does not meet the criteria for cardiac response or progressive disease

**Progressive Disease**

Requires any of the following:

- ≥ 2 mm increase from baseline in the intraventricular wall thickness by echocardiogram
- ≥ 10% decrease in the left ventricular ejection fraction.
- ≥ 1 grade increase in New York Heart Association functional class

**Hepatic Response**

**Hepatic Response**

Requires all of the following:

- ≥ 2 cm decrease in liver span if hepatomegaly present (liver > 15 cm)
- ≥ 50% decrease and/or normalization of serum alkaline phosphatase (ALP) level

**No Response/Stable Disease**

Does not meet the criteria for hepatic response or progressive disease
Progressive Disease

Requires the following:

- ≥ 50% increase in the serum alkaline phosphatase (ALP) level

**Autonomic Neuropathy Response**

Autonomic Neuropathy Response

Resolution of symptomatic orthostatic hypotension

No Response/Stable Disease

Does not meet the criteria for autonomic neuropathy response or progressive disease

Progressive Disease

Worsening of symptomatic orthostatic hypotension

**Peripheral Neuropathy Response**

Peripheral Neuropathy Response

Requires any of the following:

- Resolution of abnormal physical findings
- Resolution or improvement of abnormal electromyography (EMG) and/or Nerve Conduction Velocity (NCV) findings

No Response/Stable Disease

Does not meet the criteria for peripheral neuropathy response or progressive disease

Progressive Disease

Requires any of the following:

- Worsening of physical findings
- Worsening of EMG and/or NCV findings
Renal Response

Renal Response

• ≥ 50% decrease of at least 0.5 g/day (500mg/24hr) in 24-hour urine protein of > 0.5 g/day (500mg/24hr) pre-treatment and
• Creatinine clearance must not have worsened by ≥ 25% over baseline

No Response/Stable Disease

Does not meet the criteria for renal response or progressive disease

Progressive Disease

Requires any of the following:

• ≥ 50% increase of at least 1 g/day (1000mg/24hr) for urine protein to > 1g/day (1000mg/24hr)
• 25% worsening of serum creatinine or creatinine clearance

Manual Updates:
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<tr>
<td>12/3/18</td>
<td>Amyloidosis</td>
<td>Add</td>
<td>Added further clarification for the Renal Response criteria (indicated in red below):</td>
</tr>
<tr>
<td></td>
<td>Response Criteria</td>
<td></td>
<td>• ≥ 50% decrease of at least 0.5 g/day (500mg/24hr) in 24-hour urine protein of &gt; 0.5 g/day (500mg/24hr) pre-treatment and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Creatinine clearance must not have worsened by ≥ 25% over baseline</td>
</tr>
</tbody>
</table>
New York Heart Association Function Classifications

**Class I**
Able to perform ordinary activities without symptoms; no limitation of physical activity

**Class II**
Ordinary physical activity produces symptoms; slight limitation of physical activity

**Class III**
Less-than-ordinary physical activity produces symptoms; moderate limitation of physical activity

**Class IV**
Symptoms present even at rest; severe limitation of physical activity
The Plasma Cell Disorder Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures plasma cell disorder pre-HCT data such as: disease status at diagnosis, laboratory studies at diagnosis, amyloidosis organ involvement at diagnosis, pre-HCT therapy, laboratory studies at last evaluation prior to the start of the preparative regimen, amyloidosis organ involvement at last evaluation prior to the start of the preparative regimen, and disease status at the last evaluation prior to the start of the preparative regimen. This form must be completed for all recipients whose primary disease reported on the Pre-TED Disease Classification Form (Form 2402) is “Multiple myeloma/plasma cell disorder (PCD).”

**Subsequent Transplant**

If this is a report of a second or subsequent transplant for the same disease subtype and **this baseline insert was not completed for the previous transplant** (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent), begin at question 1.

If this is a report of a second or subsequent transplant for a **different disease** (e.g., patient was previously transplanted for a disease other than Plasma Cell Disorder/Multiple Myeloma), select “no” and begin at question 1.

If this is a report for a second or subsequent transplant for **relapse or progression of the same disease**, select “yes” and continue with question 188. Beginning with question 188 allows for the capture of data related to treatment given for relapsed or progressed disease.

If this is a report for the **same disease, but not for relapsed or progressive disease** (i.e., a planned subsequent transplant), select “no” and continue with question 233.

**Q1-8: Disease Assessment at Diagnosis**

**Q9-118: Laboratory Studies at Diagnosis**

**Q119-187: Amyloidosis Organ Involvement at Diagnosis**

**Q188-232: Pre-HCT Therapy**

**Q233-325: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen**

**Q326-362: Amyloidosis Organ Involvement at Last Evaluation Prior to the Start of the Preparative Regimen**

**Q363-364: Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen**

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.
Currently there is an issue on Form 2400 regarding the ISS Staging. Stage I requires albumin greater or equal to 3.5 g/dL.

<table>
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<tr>
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<td>2/13/18</td>
<td>2016: PCD Pre-HCT</td>
<td>Add</td>
<td>Added Daratumumab note box to the instructions for questions 196-222.</td>
</tr>
<tr>
<td>1/23/18</td>
<td>2016: PCD Pre-HCT</td>
<td>Remove</td>
<td>Removed text (struck out below) from the instructions for questions 229 and 363. If the recipient had amyloidosis or POEMS syndrome, but no evidence of myeloma, select “Not Applicable (POEMS or Amyloidosis with no evidence of myeloma)” and continue with …</td>
</tr>
<tr>
<td>1/23/18</td>
<td>2016: PCD Pre-HCT</td>
<td>Add</td>
<td>Added Amyloidosis note box to the instructions for questions 229 and 363.</td>
</tr>
<tr>
<td>2/27/17</td>
<td>2016: PCD Pre-HCT</td>
<td>Remove</td>
<td>Removed the following warning box from the instructions for questions 237-239: Currently there is an issue on Form 2400 regarding the ISS Staging. Stage I requires albumin greater or equal to 3.5 g/dL. This question was removed from the Form 2400 and included in the Form 2402 during the Winter Forms Revision 2017 (January 31, 2017). The ISS staging criteria are correct on the Form 2402.</td>
</tr>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400).</td>
</tr>
<tr>
<td>2/20/17</td>
<td>2016: PCD Pre-HCT</td>
<td>Modify</td>
<td>Updated the multiple myeloma diagnostic criteria provided in the instructions for question 1 to match the IMWG criteria released October 2015.</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2016: PCD Pre-HCT</td>
<td>Add</td>
<td>Added information box to question 188: If this form is being completed for a second or subsequent transplant for relapse or progression of the same disease, report all therapy given for relapse or progression of disease. Do not report maintenance therapy given after the prior transplant, as this will be captured on the post-transplant disease inserts associated with the prior transplant.</td>
</tr>
<tr>
<td>3/31/16</td>
<td>2016: PCD Pre-HCT</td>
<td>Modify</td>
<td>Changed disease characteristics for plasma cell leukemia in question 1 to: more than $\geq 20%$ plasma cells in the peripheral differential white blood cell count.</td>
</tr>
<tr>
<td>Date</td>
<td>Version</td>
<td>Action</td>
<td>Text</td>
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</tr>
<tr>
<td>5/29/15</td>
<td>2016: PCD Pre-HCT</td>
<td>Modify</td>
<td>Added text for clarification in questions 42 and 249: (total in g/dL of monoclonal protein) x (total urine volume) = urinary M-protein/24 hours (0.145 g/dL of monoclonal protein) x (1500 mL total urine) x (1 dL/100 mL) = 2.175 g/24 hours</td>
</tr>
<tr>
<td>5/29/15</td>
<td>2016: PCD Pre-HCT</td>
<td>Modify</td>
<td>Modified the text in question 363 for clarity: <strong>Example 1:</strong> A 62-year-old man is diagnosed with IgG Kappa multiple myeloma. He receives initial therapy with 6 cycles of bortezomib and lenalidomide/dexamethasone; and achieves a near complete remission (nCR). The values used to determine disease status at transplant are the values obtained at diagnosis. The comparison values used to determine disease status at transplant are the values obtained at diagnosis.</td>
</tr>
<tr>
<td>5/29/15</td>
<td>2016: PCD Pre-HCT</td>
<td>Modify</td>
<td>Modified the explanatory text for questions 229 and 363: If the recipient had amyloidosis or POEMS syndrome, but no evidence of myeloma, select “Not Applicable (POEMS or Amyloidosis with no evidence of myeloma)”</td>
</tr>
<tr>
<td>5/29/15</td>
<td>2016: PCD Pre-HCT</td>
<td>Modify</td>
<td>Added the following text to the subsequent transplant text: If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than Plasma Cell Disorder/Multiple Myeloma), select “no” and begin at question 1.</td>
</tr>
</tbody>
</table>
Q1-8: Disease Assessment at Diagnosis

Questions 1-2: What is the diagnosis?

Specify the indication for transplant. See below for characteristics of each disease.

If the diagnosis at transplant was Multiple Myeloma (symptomatic), plasma cell leukemia, amyloidosis, osteosclerotic myeloma/POEMS syndrome, or light chain deposition disease, continue with question 4.

If the recipient had a solitary plasmacytoma without diagnosis of multiple myeloma or plasma cell leukemia, continue with question 3.

If the transplant is for a plasma cell disorder not listed above, select “other plasma cell disorder (PCD)” and specify the disorder in question 2.

Plasma Cell Disorders and Characteristics

**Multiple Myeloma (symptomatic)**

Diagnostic criteria for symptomatic multiple myeloma requires clonal bone marrow plasma cells in ≥ 10% or biopsy proven bony or extramedullary plasmacytoma and any one or more of the following myeloma-defining events:

1. Evidence of end organ damage (i.e., CRAB features) that can be attributed to the underlying plasma cell proliferative disorder, specifically:
   - Hypercalcemia: serum calcium >1 mg/dL (> 0.25 mmol/L) higher than the ULN or > 11 mg/dL (> 2.75 mmol/L)
   - Renal insufficiency: creatinine clearance < 40 ml/min or serum creat > 2 mg/dL (> 177 μmol/L)
   - Anemia: hemoglobin > 2 g/dL (> 20 g/L) below the LLN or a hemoglobin < 10 g/dL (< 100 g/dL)
   - Bone lesions: one or more osteolytic lesions on skeletal x-ray, CT or PET-CT

2. Any one or more of the following biomarkers of malignancy:
   - Clonal bone marrow plasma cell percentage ≥ 60%
   - Involved : uninvolved serum free light chain ratio ≥ 100
   - > 1 focal lesion on MRI studies (each lesion must be ≥ 5 mm in size)
Plasma Cell Leukemia

- Peripheral blood absolute plasma cell count of at least $2.0 \times 10^9/L$ (2,000 cells/mm$^3$)
- ≥ 20% plasma cells in the peripheral differential white blood cell count.$^1$

Solitary Plasmacytoma (in absence of bone marrow findings diagnostic for Multiple Myeloma or Plasma Cell Leukemia)

Extramedullary:

- No M-protein in serum and/or urine
- Extramedullary tumor of clonal plasma cells
- Normal bone marrow
- Normal skeletal survey
- No related organ or tissue impairment (end organ damage including bone lesions)

Bone Derived:

- No M-protein in serum and/or urine
- Single area of bone destruction due to clonal plasma cells
- Bone marrow not consistent with multiple myeloma
- Normal skeletal survey (and MRI of spine and pelvis if done)
- No related organ or tissue impairment (no end organ damage other than solitary bone lesion)$^1$

Note: if the recipient has greater than one plasmacytoma, but has not been diagnosed with another plasma cell disorder, select “other plasma cell disorder” and specify how many plasmacytomases are present and if each is bone derived or extramedullary.

Amyloidosis

Amyloidosis is the buildup of abnormally folded proteins in various tissues of the body. Affected tissues may include the kidneys, heart, liver, gastrointestinal tract, etc. In the most common type of amyloidosis, “AL amyloidosis,” light chains from antibodies function as the amyloid protein, building up within organs and disrupting organ function. Serum and urine tests are useful for evaluating amyloidosis, but a tissue biopsy is
the best way to diagnose the condition.

Osteosclerotic Myeloma/ POEMS Syndrome

POEMS syndrome is poorly understood, but generally refers to p olyneuropathy, o rganomegaly, e ndocrinopathy, M protein, and s kin changes. Diagnosis may be made using the presence of the major criteria and one minor criteria below:

Major Criteria (both of the following):

- Polyneuropathy
- Monoclonal plasmaproliferative disorder

Minor Criteria (at least one of the following):

- Sclerotic bone lesions†
- Castleman disease†
- Organomegaly (splenomegaly, hepatomegaly, lymphadenopathy)
- Edema (edema, pleural effusion, or ascites)
- Endocrinopathy (adrenal, thyroid‡, pituitary, gonadal, parathyroid, pancreatic‡)
- Skin changes (hyperpigmentation, hypertrichosis, plethora, hemangiomata, white nails)
- Papilledema

† Osteosclerotic lesion or Castleman disease is usually present.
‡ Because of the high prevalence of diabetes mellitus and thyroid abnormalities, this diagnosis alone is not sufficient to meet this minor criterion.  

Light Chain Deposition Disease

Similar to amyloidosis, light chain deposition disease is characterized by the overproduction and deposition of light chains in organs throughout the body; however, the organ most often affected is the kidneys. Under microscopy, the pattern of deposition and the use of staining techniques help pathologists differentiate between amyloidosis and light chain deposition disease.  


Question 3: Solitary plasmacytoma was:

Indicate if the solitary plasmacytoma was “bone derived” or “extramedullary.” Refer to the Plasma Cell Characteristics above for additional information regarding the characteristics of each type.

Question 4: What was the date of diagnosis?

Report the date the recipient was first diagnosed with the plasma cell disorder indicated for transplant. Enter the date the blood/urine was collected for the laboratory evaluations (e.g., serum/urine protein electrophoresis [SPEP/UPEP, respectively], or serum/urine immunofixation) or enter the date of the first pathological diagnosis (e.g., bone marrow biopsy, plasmacytoma). Enter the date the sample was collected for examination.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 5: Did the recipient have a preceding or concurrent plasma cell disorder?

Indicate if the recipient had a concurrent or preceding plasma cell disorder. Many recipients progress to symptomatic myeloma from a preceding condition or have a concurrent plasma cell disorder, such as amyloidosis.

Example 1. If a recipient has smoldering myeloma (asymptomatic) and then develops symptomatic multiple myeloma, “multiple myeloma (symptomatic)” should be reported as the primary diagnosis in question 1 and “smoldering myeloma (asymptomatic)” should be reported in question 6.

Example 2. If a recipient has smoldering myeloma (asymptomatic) and amyloidosis, “amyloidosis” should be reported as the primary diagnosis in question 1 and “smoldering myeloma (asymptomatic)” should be reported in question 6.

Example 3. If the recipient has symptomatic multiple myeloma and amyloidosis, “multiple myeloma (symptomatic)” should be reported as the primary diagnosis in question 1 and “amyloidosis” should be reported as a concurrent diagnosis is question 6.
Questions 6-7: Specify preceding/concurrent disorder:

Indicate the preceding or concurrent disorder. See the Plasma Cell Characteristics information above for descriptions of disease and the previous question for examples of situations with preceding or concurrent disorders. If the recipient has a preceding or concurrent plasma cell disorder that is not listed, select “other plasma cell disorder (PCD)” and specify the type in question 7.

Question 8: Date of diagnosis of preceding/concurrent disorder:

Report the date the recipient was first diagnosed with the preceding or concurrent plasma cell disorder. Enter the date the blood/urine was collected for the laboratory evaluations (e.g., serum/urine protein electrophoresis [SPEP/UPEP, respectively], or serum/urine immunofixation) or enter the date of the first pathological diagnosis (e.g., bone marrow biopsy, plasmacytoma, tissue). Enter the date the sample was collected for examination.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Copy questions 6-8 to report more than one concurrent or preceding disorder.
Q9-118: Laboratory Studies at Diagnosis

For questions 9-118, report values obtained at diagnosis or prior to the first treatment for the plasma cell disorder for which the transplant was performed. If testing is performed multiple times prior to the start of the first treatment, report the last test before the start of treatment. If the recipient has a plasma cells disorder other than plasma cell leukemia, do not answer questions 15-18, as they apply only to the diagnosis of PCL.

Questions 9-10: WBC:

Indicate if the WBC was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 10. If “unknown,” continue with question 11.

Questions 11-12: Hemoglobin:

Indicate whether the hemoglobin was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 12. If “unknown” continue with question 13.

Question 13-14: Platelets:

Indicate whether the platelet count was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “unknown” continue with question 15.

Questions 15-16: Absolute number of plasma cells in blood: (for PCL only)

Indicate if the absolute number of plasma cells in the blood was “known” or “unknown” at the time of plasma cell leukemia (PCL) diagnosis. If “known,” report the absolute number of plasma cells in the blood documented on the laboratory report in question 16. If “unknown” continue with question 17.

If only the percentage of plasma cells is available, multiply the percentage of plasma cells by the white blood cell count (WBC) to determine the absolute number of plasma cells.

Questions 17-18: Plasma cells in blood: (for PCL only)

Indicate if the percentage of plasma cells in the blood was “known” or “unknown” at the time of PCL diagnosis. If “known,” report the percentage documented on the laboratory report in question 18. If “unknown” continue with question 19.
Questions 19-20: Serum albumin:
Indicate whether the serum albumin was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report. If “unknown,” continue with question 21.

Questions 21-22: Serum calcium:
Indicate whether the serum calcium was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 22. If “unknown,” continue with question 23.

Questions 23-24: Serum creatinine:
Indicate whether the serum creatinine was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report in question 24 and continue with question 25. If “unknown,” continue with question 26.

Question 25: Upper limit of serum creatinine:
Indicate the upper limit of normal for serum creatinine value used at your institution.

Questions 26-27: LDH:
Indicate whether the LDH (lactate dehydrogenase) level was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 27 and continue with question 28. If “unknown,” continue with question 29.

Question 28: Upper limit of normal for LDH:
Indicate the upper limit of normal for LDH value and the unit of measure used at your institution.

Questions 29-30: Serum β2 microglobulin:
At the time of plasma cell disorder diagnosis, an elevated serum β2 microglobulin protein may indicate a poorer prognosis. If this value was “known,” report the value and unit of measure documented on the laboratory report in question 30. If “unknown,” continue with question 31.

Question 31: What was the Durie-Salmon staging?
Indicate the Durie-Salmon staging at diagnosis and continue with question 32. If the Durie-Salmon stage is not documented in the medical record, use Table 4 below to determine the appropriate stage.
If the Durie-Salmon stage is unknown and cannot be determined using the table below, select “unknown” and continue with question 33.

**Table 1. Durie-Salmon Staging System for Multiple Myeloma**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| I     | All of the following:  
• Hemoglobin > 10 g/dL  
• Serum calcium normal (< 10.5 mg/dL)  
• On radiograph, normal bone structure or solitary bone plasmacytoma only  
• Low M-component production rate (IgG < 5 g/dL, IgA < 3 g/dL), Urinary light chain M-component on electrophoresis (< 4 g/24 hr) |
| II    | Fitting neither stage I nor stage III |
| III   | One or more of the following:  
• Hemoglobin < 8.5 g/dL  
• Serum calcium > 12 mg/dL  
• Advanced lytic bone lesions (three or more lytic lesions)  
• High M-component production rate (IgG > 7 g/dL, IgA > 5 g/dL), Urinary light chain M-component on electrophoresis (> 12 g/24 hr) |

1 Adapted from Durie BG, Salmon SE. A clinical staging system for multiple myeloma: Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. *Cancer*. 1975;36(3):842-854.

**Question 32: What was the Durie-Salmon sub classification?**

Indicate the Durie-Salmon sub classification at diagnosis and continue with question 33. If the Durie-Salmon sub classification is not documented in the medical record, use the criteria below to determine the appropriate sub classification.

- **A**: Relatively normal renal function (serum creatinine < 2.0 mg/dL)

- **B**: Abnormal renal function (serum creatinine ≥ 2.0 mg/dL)

**Question 33: Immunochromical type:**

Indicate whether the plasma cell disorder is secretory or non-secretory. Secretory plasma cell disorders are characterized by the presence of clonal paraproteins (M-protein) in the blood and serum, detected by immunofixation. Non-secretory refers to the absence of clonal paraprotein (M-protein) in the serum or urine.

If the plasma cell disorder is secretory, continue with question 34. If the plasma cell disorder is non-secretory, continue with question 54.
Questions 34-35: Serum heavy chain:

Indicate the involved heavy chain(s) in the plasma cell disorder detected on serum immunofixation. The involved heavy chain, also called M-spike or monoclonal protein, can be identified but not quantified using this test. If only one heavy chain is involved, select “IgG,” “IgA,” “IgM,” “IgD,” or “IgE” and continue with question 36. If the heavy chain is IgM, ensure that the disease subtype is not Waldenstrom’s Macroglobulinemia. If the disease subtype is Waldenstrom’s Macroglobulinemia, complete Form 2019 and update the Pre-TED form to indicate that Waldenstrom’s is the transplant indication. If two heavy chains are involved in the plasma cell disorder, select “Biclonal” and specify which two heavy chains in question 35. If the recipient has light chain only disease, meaning that no monoclonal heavy chain was present at any time during the disease history, select “Not applicable (light chain only disease)” and continue with question 36.

Table 2. Concept of Clonality in Multiple Myeloma

<table>
<thead>
<tr>
<th>Type of Myeloma</th>
<th>M-proteins Expressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Cell Myeloma</td>
<td>One heavy chain (IgG, IgA, etc.) and one light chain (either kappa or lambda)</td>
</tr>
<tr>
<td>Biclonal Myeloma</td>
<td>Two different M-proteins (e.g., IgG Kappa and IgA Lambda)</td>
</tr>
</tbody>
</table>

Question 36: Serum light chain:

Indicate the involved light chain in the plasma cell disorder detected on serum immunofixation. The involved light chain can be identified, but not quantified, using this test. Select “κ” if the kappa light chain is involved or “λ” if the lambda light chain is involved.

Questions 37-38: Urine heavy chain:

Indicate the involved heavy chain(s) in the plasma cell disorder detected on urine immunofixation. The involved heavy chain, also called M-spike or monoclonal protein, can be identified but not quantified using this test. If only one heavy chain is involved, select “IgG,” “IgA,” “IgM,” “IgD,” or “IgE” and continue with question 39. If the heavy chain is IgM, ensure that the disease subtype is not Waldenstrom’s Macroglobulinemia. If the disease subtype is Waldenstrom’s Macroglobulinemia, complete Form 2019 and update the Pre-TED form to indicate that Waldenstrom’s is the transplant indication. If two heavy chains were involved in the plasma cell disorder, select “Biclonal” and specify which two heavy chains in question
38. If the recipient has light chain only disease, meaning that no monoclonal heavy chain was present at any time during the disease history, select “Not applicable (light chain only disease)” and continue with question 39.

**Question 39: Urine light chain:**

Indicate the involved light chain in the plasma cell disorder detected on urine immunofixation. The involved light chain can be identified, but not quantified, using this test. Select “κ” if the kappa light chain is involved or “λ” if the lambda light chain is involved.

**Questions 40-41: Serum monoclonal protein (M-spike): (only from electrophoresis)**

Monoclonal gammopathy is defined as the increased production of abnormal immunoglobulins. The abnormal protein produced is called paraprotein or M-protein. Indicate whether the serum monoclonal immunoglobulin was “known” or “unknown” at the time of the plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 41. If “unknown,” continue with question 42.

For recipients with biclonal myeloma, report the serum monoclonal immunoglobulin with the largest quantity. Do not report immunofixation results here.

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**Urinary Monoclonal Protein**

Questions 42-43 are intended to capture the 24-hour urine monoclonal protein results, not the 24-hour protein excretion (questions 44-45 capture the total protein secretion/24 hours). The results will be reported as XX g or XX g/dL. If the value is reported in XX g/dL, it can be multiplied by the volume of the urine to determine the 24-hour urine monoclonal protein. Do not report immunofixation results here.

**Example:**

(0.145 g/dL of monoclonal protein) x (1500 mL total urine) = \( \text{urinary M-protein/24 hours} \)

(0.145 g/dL of monoclonal protein) x (1500 mL total urine) x (1 dL/100 mL) = 2.175 g/24 hours

**Questions 42-43: Urinary monoclonal protein (M-spike):**

Indicate whether the amount of urinary monoclonal protein was “known” or “unknown” at the time of plasma cell disorder diagnosis. The value reported here should be based on a 24 hour urine collection. If “known,” report the laboratory value in question 43. If “unknown,” continue with question 44.

**Questions 44-45: Total urinary protein secretion:**

Indicate whether the amount of urinary protein was “known” or “unknown” at the time of plasma cell disorder
Questions 46-47: 24-hour creatinine clearance:

Indicate whether the amount of urinary protein was “known” or “unknown” at the time of plasma cell disorder diagnosis. The value reported here should be based on a 24-hour urine collection in milliliters per minute (mL/minute). If “known,” report the laboratory value in question 47. If “unknown,” continue with question 48.

Questions 48-49: Serum free light chains – κ (kappa):

Indicate whether the serum κ (kappa) free light chain level was “known” or “unknown” at the time of plasma cell disorder diagnosis. This value should reflect the quantity of serum free light chains, not a quantification of total light chains. If “known,” report the value and unit of measure documented on the laboratory report in question 49 and continue with question 50. If “unknown,” continue with question 51.

Question 50: Upper limit of normal for κ free light chain:

Indicate the upper limit of normal for κ (kappa) free light chain value and the unit of measure used at your institution.

Questions 51-52: Serum free light chains – λ (lambda):

Indicate whether the serum λ (lambda) free light chain level was “known” or “unknown” at the time of plasma cell disorder diagnosis. This value should reflect the quantity of serum free light chains, not a quantification of total light chains. If “known,” report the value and unit of measure documented on the laboratory report in question 52 and continue with question 53. If “unknown,” continue with question 54.

Question 53: Upper limit of normal for λ free light chains:

Indicate the upper limit of normal for λ (lambda) free light chain value and the unit of measure used at your institution.

Questions 54-55: IgG:

Indicate whether the IgG level was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 55 and continue with question 56. If “unknown,” continue with question 57.

Question 56: Upper limit of normal for IgG:

Indicate the upper limit of normal for IgG value used at your institution.
**Questions 57-58: IgA:**

Indicate whether the IgA level was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 58 and continue with question 59. If “unknown,” continue with question 60.

**Question 59: Upper limit of normal for IgA:**

Indicate the upper limit of normal for IgA value used at your institution.

**Questions 60-61: IgM:**

Indicate whether the IgM level was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 61 and continue with question 62. If “unknown,” continue with question 63.

**Question 62: Upper limit of normal for IgM:**

Indicate the upper limit of normal for IgM value used at your institution.

**Questions 63-64: IgD:**

Indicate whether the IgD level was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 64 and continue with question 65. If “unknown,” continue with question 66.

**Question 65: Upper limit of normal for IgD:**

Indicate the upper limit of normal for IgD value used at your institution.

**Questions 66-67: IgE:**

Indicate whether the IgE level was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the value and unit of measure documented on the laboratory report in question 67 and continue with question 68. If “unknown,” continue with question 69.

**Question 68: Upper limit of normal for IgE:**

Indicate the upper limit of normal for IgE value used at your institution.
Questions 69-70: Plasma cells in bone marrow aspirate:

Under normal circumstances, a marrow aspirate is used to obtain the differential cell count, review morphology of the cells, and perform cytogenetic studies, flow cytometry, etc. A biopsy is obtained to evaluate the overall cellularity of the marrow. In the case of myeloma, the marrow plasma cells tend to be a patchy infiltrate rather than a diffuse infiltrate as in the case of acute leukemia. Therefore, it is possible that the plasma cell numbers may vary between the aspirate and the biopsy.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used as source documentation when reporting the data for questions 69-72.

• If the bone marrow pathology report states a range for plasma cells, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
• If the report states > 90% plasma cells, enter 91% on the form.
• If the report states a marrow packed with plasma cells or sheets of plasma cells, report 99% on the form.
• If the report states < 5% plasma cells, enter 4% on the form.

Indicate whether the percentage of plasma cells in the bone marrow aspirate was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the percentage of plasma cells in the bone marrow aspirate documented on the pathology report in question 70. If “unknown,” continue with question 71.

Questions 71-72: Plasma cells in bone marrow biopsy:

Indicate whether the percentage of plasma cells in the bone marrow biopsy was “known” or “unknown” at the time of plasma cell disorder diagnosis. If “known,” report the percentage of plasma cells in the bone marrow biopsy documented on the pathology report in question 72. If “unknown,” continue with question 73.

Question 73: Were conventional cytogenetics tested?

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Cytogenetics may also be referred to as karyotyping or g-banding.

Indicate if cytogenetic studies were obtained at the time the recipient was diagnosed with a plasma cell disorder or prior to the start of treatment. If cytogenetic studies were obtained, select “yes” and continue
with question 74.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select “no” or “unknown” and continue with question 96.

**Question 74: Results of test:**

If cytogenetic studies identified abnormalities, indicate “abnormalities identified” and continue with question 75.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 96.

**Questions 75-94: Specify cytogenetic abnormalities identified via conventional cytogenetics at diagnosis:**

Report all abnormalities identified by all methods of cytogenetic assessment prior to the start of first therapy by selecting “yes” or “no” for each question. Do not leave any responses blank. If one or more abnormality is best classified as “other abnormality,” select “yes” in question 93 and specify in question 94.

**Question 95: Was documentation submitted to the CIBMTR (e.g., cytogenetic report)?**

Indicate if a copy of the cytogenetic report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the cytogenetic report. Attaching a copy of the report may prevent additional queries.

**Question 96: Were cytogenetics tested via FISH?**

FISH, fluorescence in situ hybridization, is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in plasma cell disorders. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells.

Indicate if FISH studies were obtained at the time the recipient was diagnosed with a plasma cell disorder or prior to the start of treatment. If FISH studies were obtained, select “yes” and continue with question 97.

If no FISH studies were obtained or it is unknown if FISH studies were performed, select “no” or “unknown” and continue with question 117.

**Question 97: Results of test:**

If FISH studies identified abnormalities, indicate “abnormalities identified” and continue with question 98.

If there were no abnormalities identified, indicate “no abnormalities” and continue with question 117.
Questions 98-115: Specify cytogenetic abnormalities identified via FISH at diagnosis:

Report all abnormalities identified by all methods of FISH assessment prior to the start of first therapy by selecting “yes” or “no” for each question. Do not leave any responses blank. If one or more abnormality is best classified as “other abnormality,” select “yes” in question 114 and specify in question 115.

Question 116: Was documentation submitted to the CIBMTR (e.g., FISH report)?

Indicate if a copy of the FISH report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the FISH report. Attaching a copy of the report may prevent additional queries.

Question 117: Was a gene expression profile performed?

Gene expression profiling (GEP) allows for the analysis of thousands of genes at once, creating a global picture of cell function. GEP can distinguish cells that are actively dividing and show how cells react to specific treatments.²

If gene expression profiling was performed at the time of plasma cell disorder diagnosis or prior to the start of first therapy, indicate “yes” and continue with question 118. If gene expression was not performed, select “no” and continue with question 119.


Question 118: Were results considered high-risk myeloma?

Based on the opinion of a physician, indicate if the results of the gene expression profile are considered high-risk myeloma. Indicate “yes” or “no.”
**Q119-187: Amyloidosis Organ Involvement at Diagnosis**

Complete questions 119-187 for amyloidosis patients only. If diagnosis was other than amyloidosis (question 1), or there is no evidence or history of it (question 6), skip to question 188.

**Question 119: Was an abdominal fat aspirate performed?**

Abdominal fat is the most common initial biopsy site when amyloidosis is suspected. A sample of abdominal fat is taken by needle aspiration and stained with Congo red dye. Indicate if an abdominal fat biopsy was performed at diagnosis or prior to the first therapy. If “yes,” continue with question 120. If “no,” continue with question 121.

**Question 120: Specify the aspirate results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the abdominal fat aspirate. Select “positive (for amyloid involvement)” if the aspirate showed characteristics of amyloid involvement. Select “negative” if the aspirate was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 121.

**Question 121: Was a renal biopsy performed?**

Kidney involvement in amyloidosis is common, and evaluation of renal tissue may be necessary to determine the extent of the disease. Indicate if a renal biopsy was performed at diagnosis or prior to the first therapy. If “yes,” continue with question 122. If “no,” continue with question 123.

**Question 122: Specify the renal biopsy results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the renal biopsy. Select “positive (for amyloid involvement)” if the biopsy showed characteristics of amyloid involvement. Select “negative” if the biopsy was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 123.
**Question 123: Was a cardiographic imaging procedure performed?**

Cardiographic imaging may show amyloid infiltration in heart tissue. Cardiac MRI, echocardiogram [(sometimes referred to as an echo) (do not report an ECG or EKG, which refer to electrocardiogram)], or Multiple Gate Acquisition (MUGA) scans may be performed to assess heart involvement. Indicate if cardiographic imaging was performed at diagnosis or prior to the first therapy. If “yes,” continue with question 124. If “no,” continue with question 130.

**Question 124: Was a cardiac MRI done?**

Cardiac MRI may be used to differentiate amyloid involvement from other cardiopathologies. Indicate if a cardiac MRI was performed at diagnosis or prior to the first therapy. If “yes,” continue with question 125. If “no,” continue with question 126.

**Question 125: Specify cardiac MRI results:**

Characteristics of amyloid involvement in cardiac tissue include impaired ventricular systolic function, thickened valves, increased atrial septal thickness and left ventricular mass, pleural and pericardial effusions, and subendocardial hyperenhancement.\(^1\) Indicate if the results of cardiac MRI were “normal,” “abnormal,” or “unknown,” and continue with question 126.


**Question 126: Was the left ventricular ejection fraction measured?**

The left ventricular ejection fraction (LVEF) is a percentage that represents the volume of blood pumped from the left ventricle into the aorta (also known as stroke volume) compared to the volume of blood in the ventricle just prior to the heart contraction (also known as end diastolic volume). Indicate if the left ventricular ejection fraction (LVEF) was measured. If “yes,” continue with question 127. If “no,” continue with question 129.

**Question 127: Specify the left ventricular ejection fraction:**

Indicate the left ventricular ejection fraction at diagnosis or prior to the first therapy. Most imaging reports will report the LVEF, but if not, the LVEF may be determined by dividing the stroke volume (SV, the volume of blood pumped into the aorta from the left ventricle) by the end diastolic volume (EDV, the volume of blood in the left ventricle just prior to contraction) of the left ventricle. For example, if the stroke volume was 75 ml and the end diastolic volume was 150ml, the ejection fraction would be 50%.

If the recipient had multiple assessments using different methods, report the most recent assessment prior
to the initiation of treatment.

**Question 128: Specify the method used to determine the left ventricular ejection fraction:**

Indicate the method used to determine the LVEF reported in question 127.

**Question 129: Was diastolic dysfunction present?**

Diastole is the period in which chambers of the heart fill with blood. Diastolic dysfunction may be characterized by the difficulty of the ventricles to expand and contract appropriately due to stiffening of the heart walls by amyloid deposits. Indicate if diastolic dysfunction was present. Specify “yes,” “no,” or “unknown,” and continue with question 130.

**Questions 130-131: Specify the intraventricular septal wall thickness measured by echocardiogram:**

The heart is divided into the right and left sides by the septum. The area between the left and right ventricles is the intraventricular septum. Indicate if the intraventricular septal thickness is “known” or “unknown.” If known, based on evaluation by echocardiogram, indicate the thickness of the intraventricular septal wall in question 131. If unknown or not measured by echocardiogram, continue with question 132.

**Question 132: Was a cardiac biopsy performed?**

Heart involvement in amyloidosis is common and evaluation of cardiac tissue may be necessary to determine the extent of the disease. Indicate if a cardiac biopsy was performed at diagnosis or prior to the first therapy. If “yes,” continue with question 133. If “no,” continue with question 134.

**Question 133: Specify the cardiac biopsy results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the cardiac biopsy. Select “positive (for amyloid involvement)” if the biopsy showed characteristics of amyloid involvement. Select “negative” if the biopsy was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 134.

**Question 134: Were any serum cardiac biomarkers assessed?**

Assessment of cardiac biomarkers helps determine if injury to cardiac tissue has occurred. Cardiac biomarkers include brain natriuretic peptide (BNP), N-terminal prohormone brain natriuretic peptide (NT-proBNP), troponin I, troponin T, and high-sensitivity troponin T. Indicate if serum cardiac biomarkers were assessed at diagnosis or prior to first therapy. If “yes,” continue with question 135. If “no” or “unknown” continue with question 150.
Questions 135-136: Brain natriuretic peptide (BNP):

Indicate if the BNP was assessed at the time of amyloidosis diagnosis. If “yes,” report the value and unit of measure documented on the laboratory report in question 136 and continue with question 137. If “no,” continue with question 138.

Question 137: Upper limit of normal for BNP:

Indicate the upper limit of normal for BNP used at your institution.

Questions 138-139: N-terminal prohormone brain natriuretic peptide (NT-proBNP):

Indicate if the NT-proBNP was assessed at the time of amyloidosis diagnosis. If “yes,” report the value and unit of measure documented on the laboratory report in question 139 and continue with question 140. If “no,” continue with question 141.

Question 140: Upper limit of normal for NT-proBNP:

Indicate the upper limit of normal for NT-proBNP used at your institution.

Questions 141-142: Troponin I:

Indicate if the Troponin I was assessed at the time of amyloidosis diagnosis. If “yes,” report the value and unit of measure documented on the laboratory report in question 142 and continue with question 143. If “no,” continue with question 144.

Question 143: Upper limit of normal for troponin I:

Indicate the upper limit of normal for Troponin I used at your institution.

Questions 144-145: Troponin T:

Indicate if the Troponin T was assessed at the time of amyloidosis diagnosis. If “yes,” report the value and unit of measure documented on the laboratory report in question 145 and continue with question 146. If “no,” continue with question 147.

Question 146: Upper limit of normal for Troponin T:

Indicate the upper limit of normal for Troponin T used at your institution.

Questions 147-148: High-sensitivity troponin T:

Indicate if the high-sensitivity troponin T was assessed at the time of amyloidosis diagnosis. If “yes,” report
the value and unit of measure documented on the laboratory report in question 145 and continue with question 146. If “no,” continue with question 147.

**Question 149: Upper limit of normal for high-sensitivity troponin T:**

Indicate the upper limit of normal for high-sensitivity troponin T used at your institution.

**Question 150: Specify the recipient’s New York Heart Association functional classification of heart failure:** (Symptoms may include dyspnea, chest pain, fatigue, and palpitations; activity level should be assessed with consideration for patient’s age group)

Indicate the recipient’s New York Heart Association (NYHA) functional classification. If the recipient’s NYHA functional classification is not known, select “unknown.”

**Question 151: Was there clinical suspicion of gastrointestinal (GI) involvement?**

GI involvement by amyloidosis is usually proven by biopsy; however, clinical symptoms of gastrointestinal involvement may include esophageal reflux, constipation, nausea and abdominal pain, diarrhea, weight loss, or early satiety (fullness). Indicate if there was any clinical suspicion of GI involvement at diagnosis or prior to the first therapy. If “yes,” continue with question 152. If “no” or “unknown,” continue with question 154.


**Question 152: Upper GI tract:**

Symptoms of upper GI tract involvement may include esophageal reflux, nausea, and abdominal pain. Indicate if the recipient had upper GI involvement. Select “yes” or “no” and continue with question 153.

**Question 153: Lower GI tract:**

Symptoms of lower GI tract involvement may include abdominal pain, nausea, weight loss, constipation, or diarrhea. Indicate if there was any suspicion of lower GI involvement. Select “yes” or “no” and continue with question 154.

**Question 154: Was a gastrointestinal biopsy performed?**

GI involvement in amyloidosis is less common than cardiac or renal involvement, and evaluation of GI tissue may be necessary to determine the extent of the disease. Indicate if a GI biopsy was performed at diagnosis or prior to the first therapy. If “yes,” continue with question 155. If “no,” continue with question 160.
**Question 155: Rectal**

Indicate if the recipient had a rectal biopsy to confirm amyloid involvement at the time of diagnosis or before first therapy. If “yes,” continue with question 156. If “no,” continue with question 157.

**Question 156: Specify the biopsy results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the rectal biopsy. Select “positive (for amyloid involvement)” if the biopsy showed characteristics of amyloid involvement. Select “negative” if the biopsy was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 157.

**Questions 157-158: Other site:**

Indicate if the recipient had a gastrointestinal site other than the rectum biopsied at diagnosis or prior to the first therapy. If “yes,” specify the site in question 158 and continue with question 159. If “no,” continue with question 160.

**Question 159: Specify the biopsy results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the GI biopsy. Select “positive (for amyloid involvement)” if the biopsy showed characteristics of amyloid involvement. Select “negative” if the biopsy was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 160.

**Question 160: Was hepatomegaly present on radiographic imaging (liver span > 15 cm) or on examination (liver edge palpable > 3 cm below right costal margin)?**

At the time of diagnosis or prior to first therapy, indicate if the liver spanned more than 15 cm or the edge of the liver was palpable more than 3 cm below the right costal margin by radiographic imaging. Indicate “yes” if hepatomegaly was present at diagnosis or prior to first therapy. Indicate “no” if hepatomegaly was not present at diagnosis or prior to first therapy. Indicate “unknown” if it was not possible to determine the presence or absence of hepatomegaly at diagnosis or prior to first therapy.

**Questions 161-162: Specify the level of serum alkaline phosphatase:**

Indicate whether the alkaline phosphatase (ALP) level at the time of amyloidosis diagnosis or prior to first treatment is “known” or “unknown.” If “known,” report the laboratory count and unit of measure documented
on the laboratory report in question 162 and continue with question 163. If “unknown,” continue with question 164.

**Question 163: Upper limit of normal for alkaline phosphatase:**

Report the upper limit of normal for ALP at your institution.

**Question 164: Was a liver biopsy performed?**

Evaluation of liver tissue may be necessary to determine the extent of the disease. Indicate if a liver biopsy was performed at diagnosis or prior to the first therapy. If “yes,” continue with question 165. If “no,” continue with question 166.

**Question 165: Specify the liver biopsy results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the liver biopsy. Select “positive (for amyloid involvement)” if the biopsy showed characteristics of amyloid involvement. Select “negative” if the biopsy was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 166.

**Question 166: Was a sensory/motor exam performed?**

Indicate if a sensory/motor exam was performed. This exam evaluates the neurological status of the recipient and consists of assessing the recipient’s body positioning, involuntary movements, muscle tone, muscle strength, ability to sense pain and light touch, position sense (proprioception), stereognosis (ability to discern an object with eyes closed, such as a coin), graphesthesia (ability to identify number of letter drawn on skin with eyes closed), and extinction (ability to discern multiple simultaneous stimuli). If a sensory/motor exam was performed, indicate “yes,” and continue with question 167. If “no” or “unknown,” continue with question 168.

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**Question 167: Specify the exam results:**

Indicate the results of the sensory/motor exam. If the recipient’s sensory/motor exam was within normal limits, select “normal.” If the recipient displayed neurologic impairment, select “abnormal.” If the results of the test are unknown or inconclusive, select “unknown.” Continue with question 168.
**Question 168: Was a nerve biopsy performed?**

Evaluation of nerve tissue may be necessary to determine the extent of the disease. Indicate if a nerve biopsy was performed at diagnosis or prior to the first therapy. If “yes,” continue with question 169. If “no,” continue with question 174.

**Question 169: Sural**

The most common site for a nerve biopsy is the sural nerve in the ankle. Indicate if the nerve biopsy was taken from the sural nerve. If “yes,” continue with question 170. If “no,” continue with question 171.

**Question 170: Specify the sural nerve biopsy results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the nerve biopsy. Select “positive (for amyloid involvement)” if the biopsy showed characteristics of amyloid involvement. Select “negative” if the biopsy was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 171.

**Questions 171-172: Other site**

Indicate if a nerve biopsy was taken from a site other than the sural nerve. If “yes,” specify the nerve biopsy site in question 172 and continue with question 173. If “no,” continue with question 174.

**Question 173: Specify other nerve biopsy results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the nerve biopsy. Select “positive (for amyloid involvement)” if the biopsy showed characteristics of amyloid involvement. Select “negative” if the biopsy was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 174.

Copy questions 172-173 to report more than one other site.

**Questions 174-175: Did the recipient display any other evidence of peripheral nerve involvement for amyloidosis?**

Indicate if the recipient displayed any other evidence of peripheral nerve involvement (other than displayed on sensory/motor examination and nerve biopsy). If “yes,” specify the other evidence in question 175 and continue with question 176. If “no,” continue with question 176.
Question 176: Did the recipient display symptomatic orthostatic hypotension (not attributable to medications or volume depletion)?

Orthostatic hypotension is a decrease in blood pressure (systolic by 20 mmHg or diastolic by 10 mmHg) within 3 minutes of standing from a sitting or lying down position. Symptoms include “dizziness, lightheadedness, blurred vision, weakness, fatigue, nausea, palpitation and headache.” Indicate if the recipient had evidence of orthostatic hypotension that was not attributable to medications or volume depletion.


Questions 177-178: Did the recipient display any other evidence of autonomic neuropathy (e.g., pseudo-obstruction or intractable diarrhea)?

Pseudo-obstruction is a condition in which food does not pass through the intestines as if the intestines were blocked; however, rather than a blockage, it is caused by nerve damage within the intestinal tract.

Intractable diarrhea is diarrhea that cannot be stopped by medication.

Indicate if the recipient had any other evidence of autonomic neuropathy, such as pseudo-obstruction or intractable diarrhea, at the time of diagnosis or prior to first therapy. If “yes,” specify the other evidence in question 178. If “no,” continue with question 179.

Question 179: Did the recipient display any other clinical involvement?

Indicate if the recipient displayed any other clinical manifestations at the time of diagnosis or prior to first therapy. Please review the preceding section starting from question 119 and ensure that any manifestations reported here do not already have a specific place for reporting. If the recipient displayed clinical involvement not already reported elsewhere, select “yes” and continue with question 180. If “no,” continue with question 188.

Questions 180-185: Specify the evidence of other organ involvement:

For each option, indicate if there was evidence of other organ involvement. Select “yes” or “no” for each, and do not leave any questions blank. If there was other organ involvement not listed in this section, select “yes” in question 184 and specify the other organ in question 185.

Arthropathy is a disease of the joints. An example of a common arthropathy in patients with amyloidosis is carpal tunnel-like symptoms.

Amyloid deposits may be found in the lung, impairing their function. Examples of lung involvement may be
alveolar-septal disease, nodular disease, intra- and extra-thoracic adenopathy, pleural disease, and diaphragm deposition.\textsuperscript{5}

Soft tissue involvement, other than those already listed, may include glandular involvement (such as submandibular glands).

Involvement of the tongue by amyloidosis is characterized by macroglossia, or the enlargement of the tongue.


**Question 186: Was a biopsy performed?**

Indicate if a biopsy was performed on one of the sites above. If “yes,” continue with question 187. If “no,” continue with question 188.

**Question 187: Specify the biopsy results:**

Samples that are positive have their normal architecture disrupted by amyloid deposits, which appear red under microscopy due to Congo red stain. Under polarized light microscopy, amyloid deposits stained with Congo red appear green (birefringence). Indicate the results of the biopsy. Select “positive (for amyloid involvement)” if the biopsy showed characteristics of amyloid involvement. Select “negative” if the biopsy was negative. Select “unknown” if the results of the evaluation were unknown or inconclusive. Continue with question 188.
Q188-232: Pre-HCT Therapy

Question 188: Was therapy given?

If this form is being completed for a second or subsequent transplant for relapse or progression of the same disease, report all therapy given for relapse or progression of disease. Do not report maintenance therapy given after the prior transplant, as this will be captured on the post-transplant disease inserts associated with the prior transplant.

Indicate if the recipient received treatment for the plasma cell disorder between the time of diagnosis and the preparative regimen. If “yes,” continue with question 189. If “no,” continue with question 233.

Copy questions 189-232 to report more than one line of therapy

Question 189: Systemic therapy:

Systemic therapy (e.g., chemotherapy) may be injected into a vein or given orally and is delivered to the whole body via the bloodstream. If “yes,” continue with question 190. If “no,” continue with question 224.

Questions 190-191: Date therapy started:

Indicate if the therapy start date is “known” or “unknown.” If the therapy start date is known, enter the date the recipient began this line of therapy in question 191. If the start date is partially known (i.e., the recipient started treatment in mid-July 2010), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Questions 192-193: Date therapy stopped:

Indicate if therapy stop date is “known” or “unknown.” If the therapy stop date is known and the recipient received therapy administered in cycles, report the date the recipient started the last cycle for this line of therapy in question 193.

If the recipient received therapy administered on a daily basis (e.g., lenalidomide therapy at 10 mg/day) report the last date the recipient received the line of therapy.

Questions 194-195: Number of cycles:

Systemic therapy (e.g., chemotherapy, monoclonal Abs) is usually administered in cycles with rest periods between the cycles. This enables cancer cells to be attacked at vulnerable times and provides healthy cells...
adequate time to recover from the damage. A cycle can last one or more days and may repeat weekly, bi-weekly, or monthly. A systemic therapy course may consist of multiple cycles. Indicate if the number of cycles is “known” or “unknown.” If “unknown,” enter the number of cycles the recipient received during the line of therapy being reported in question 195. If “unknown,” continue with question 196.

**Question 196-222: Treatment:**

**Daratumumab**
If the recipient received Daratumumab (Darzalex) as part of the line of therapy, report this drug in “Other systemic therapy.”

Systemic treatments vary based on protocol and in most cases are administered in the outpatient setting. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. Indicate “yes” or “no” for each chemotherapy treatment regimen or drug administered for the line of therapy being reported. Do not leave any yes/no responses blank. If the recipient received a chemotherapy treatment that is not listed, check “yes” for “other systemic therapy” and specify the treatment in question 222. Report the generic name of the agent, not the brand name.

Common regimens such as VCD (Bortezomib [Velcade], cyclophosphamide, and dexamethasone) and RD (Lenalidomide [Revlimed] and dexamethasone) are combined options available for selection. Select the appropriate regimen option, if applicable. If a regimen (such as RD) is selected, the individual drugs (corticosteroids and lenalidomide) should not be selected. However, if a drug is given in addition to a common regimen, specify both the regimen and the individual drug.

**Question 223: Was this line of therapy given for stem cell priming?**

Indicate “yes” if this line of therapy was given for stem cell priming. For example, high dose cyclophosphamide (Cytoxan) may be used in a myeloma patient to collect their peripheral blood stem cells (PBSCs) as they recover their white blood count. Answer “no” if this line of therapy was not given for stem cell priming.

**Question 224: Radiation therapy:**

Radiation therapy uses high-energy radiation to kill cancer cells. For multiple myeloma, external beam radiation is the type of radiation used most frequently. In this method, a beam of radiation is delivered to a specific part of the body, such as a lytic lesion or plasmacytoma. Indicate if the recipient received radiation therapy between the time of diagnosis and the start of the preparative regimen. If “yes,” continue with question 225. If “no,” continue with question 229.
Questions 225-226: Date therapy started:

Indicate if the start date for radiation therapy is “known” or “unknown.” If known, enter the date the line of radiation therapy began in question 226. If unknown, continue with question 227.

Questions 227-228: Date therapy stopped:

Indicate if the stop date for radiation therapy is “known” or “unknown.” If known, enter the date the line of radiation therapy ended in question 228. If unknown, continue with question 229.

Question 229: Best response to line of therapy:

Amyloidosis

If the recipient’s primary disease is Amyloidosis (without evidence of myeloma), report Complete Remission (CR) if the CR criteria for all involved organs are met (see Amyloidosis Response Criteria). If the disease status is anything other than CR, report “Not applicable” for question 229. This is a change from the previous instruction which asked centers to report “Not applicable” for all amyloidosis cases, regardless of disease response.

Indicate the best response to the line of therapy. See the Multiple Myeloma Response Criteria section for multiple myeloma and solitary plasmacytoma disease status definitions. See Plasma Cell Leukemia Response Criteria for plasma cell leukemia disease status definitions. For more information on determining what baseline values to use to establish best response, see Appendix G.

Currently there is an issue on Form 2016 regarding the number of plasma cells required for CR. CR requires less than (but not equal to) 5% plasma cells in the bone marrow.

If, at any response level, some but not all criteria are met, the best response should be downgraded to next lower level of response.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).

If the disease response to this line of therapy is unknown, select “unknown” and continue with question 231.

If the recipient had POEMS syndrome, but no evidence of myeloma, select “Not Applicable” and continue with question 231.
**Question 230: Date assessed:**

Enter the date the best response was assessed. Report the date of the first assessment, not the date of the second confirmatory assessment. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathologic examination.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 231: Did disease relapse/progress following this line of therapy?**

Indicate “yes” if a relapse or progression occurred following the line of therapy being reported and continue with question 232. Indicate “no” if the recipient did not relapse or progress following this line of therapy and continue with question 233.

See Multiple Myeloma Response Criteria for progressive disease and Relapse from CR disease status definitions.

**Question 232: Date of relapse/progression:**

Enter the date the relapse or progression was established following the line of therapy. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathologic evaluation. However, if there was not a second assessment obtained prior to the start of the new therapy, report the date the new therapy started as the date of relapse/progression.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.
Q233-325: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen

Questions 233-234: Absolute number of plasma cells in blood: (for PCL only)

Indicate if the absolute number of plasma cells in the blood at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the absolute number of plasma cells in the blood as documented on the laboratory report in question 234. If “unknown” continue with question 235.

If only the percentage of plasma cells is available, multiply the percentage of plasma cells by the white blood cell count (WBC) to determine the absolute number of plasma cells.

Questions 235-236: Plasma cells in blood: (for PCL only)

Indicate if the percentage of plasma cells in the blood at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the percentage as documented on the laboratory report in question 236. If “unknown” continue with question 237.

Questions 237-238: Serum albumin:

Indicate whether the serum albumin at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the value and unit of measure documented on the laboratory report in question 238. If “unknown,” continue with question 239.

Question 239-240: Serum calcium:

Indicate whether the serum calcium at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the value and unit of measure documented on the laboratory report in question 240. If “unknown,” continue with question 241.

Questions 241-242: Serum β2 microglobulin:

An elevated serum β2 microglobulin protein at the last evaluation prior to the start of the preparative regimen may indicate a poorer prognosis. If this value is “known,” report the value and unit of measure documented on the laboratory report in question 242. If “unknown,” continue with question 243.
Questions 243-244: Serum monoclonal protein (M-spike): (only from electrophoresis)

Monoclonal gammopathy is defined as the increased production of abnormal immunoglobulins. The abnormal protein produced is called paraprotein or M-protein. Indicate whether the quantity serum monoclonal immunoglobulin at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the value and unit of measure documented on the laboratory report in question 244. If “unknown,” continue with question 245.

For recipients with biclonal myeloma, report the serum monoclonal immunoglobulin with the largest quantity.

Question 245: Serum immunofixation:

Serum immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the blood. If “known,” continue with question 246. If “unknown,” continue with question 249.

Question 246: Specify monoclonal immunoglobulin result:

If monoclonal immunoglobulin was “present,” continue with question 247. If “absent,” continue with question 249.

Question 247: Original monoclonal bands:

Indicate “yes” if the original monoclonal band was present or “no” if it was not present.

Question 248: New monoclonal (or oligoclonal) bands:

Indicate “yes” if a new monoclonal band (or oligoclonal) was present or “no” if it was not present.

Questions 249-250: Urinary monoclonal protein (M-spike):

Indicate whether the amount of urinary monoclonal protein at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” The value reported here should be based on a 24-hour urine collection. If “known,” report the laboratory value in question 250. If “unknown,” continue with question 251. Do not report immunofixation results here.

Urinary Monoclonal Protein

Questions 249-250 are intended to capture the 24-hour urine monoclonal protein results, not the 24-hour protein excretion. The results will be reported as XX g or XX g/dL. If the value is reported in XX g/dL, it can be multiplied by the volume of the urine to determine the 24-hour urine monoclonal protein. Do not report immunofixation results here.
Example:

\[(\text{total in g/dL of monoclonal protein}) \times (\text{total urine volume}) = \underline{\text{urinary M-protein/24 hours}}\]

\[(0.145 \text{ g/dL of monoclonal protein}) \times (1500 \text{ mL total urine}) \times (1 \text{ dL/100 mL}) = 2.175 \text{ g/24 hours}\]

Question 251: Urinary immunofixation

Urine immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the urine. Indicate if the results of urinary immunofixation at the last evaluation prior to the start of the preparative regimen are “known” or “unknown.” If “known,” continue with question 252. If “unknown,” continue with question 255.

Question 252: Specify monoclonal immunoglobulin result:

If monoclonal immunoglobulin was “present,” continue with question 253. If “absent,” continue with question 255.

Question 253: Original monoclonal bands:

Indicate “yes” if the original monoclonal band was present or “no” if it was not present.

Question 254: New monoclonal (or oligoclonal) bands:

Indicate “yes” if a new monoclonal (or oligoclonal) band was present or “no” if it was not present.

Questions 255-256: Total urinary protein excretion:

Indicate whether the amount of urinary protein at the last evaluation prior to the start of the preparative regimen was “known” or “unknown.” The value reported here should be based on a 24-hour urine collection. If “known,” report the laboratory value in question 256. If “unknown,” continue with question 257.

Questions 257-258: 24-hour creatinine clearance:

Indicate whether the amount of urinary protein at the last evaluation prior to the start of the preparative regimen was “known” or “unknown.” The value reported here should be based on a 24-hour urine collection in milliliters per minute (mL/minute). If “known,” report the laboratory value in question 258. If “unknown,” continue with question 259.

Questions 259-260: Serum free light chains – κ (kappa):

Indicate whether the serum κ (kappa) free light chain level at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” This value should reflect the quantity of serum free light chains, not a quantification of total light chains. If “known,” report the value and unit of measure documented
on the laboratory report in question 260 and continue with question 261. If “unknown,” continue with question 262.

**Question 261: Upper limit of normal for κ free light chain:**

Indicate the upper limit of normal for κ (kappa) free light chains value and the unit of measure used at your institution.

**Questions 262-263: Serum free light chains – λ (lambda):**

Indicate whether the serum λ (lambda) free light chain level at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” This value should reflect the quantity of serum free light chains, not a quantification of total light chains. If “known,” use question 263 to record the value and unit of measure documented on the laboratory report and continue with question 264. If “unknown,” continue with question 265.

**Question 264: Upper limit of normal for λ free light chains:**

Indicate the upper limit of normal for λ (lambda) free light chains value and the unit of measure used at your institution.

**Questions 265-266: IgG:**

Indicate whether the IgG level at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the value and unit of measure documented on the laboratory report in question 266 and continue with question 267. If “unknown,” continue with question 268.

**Question 267: Upper limit of normal for IgG:**

Indicate the upper limit of normal for IgG value used at your institution.

**Questions 268-269: IgA:**

Indicate whether the IgA level at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” use question 269 to record the value and unit of measure documented on the laboratory report and continue with question 270. If “unknown,” continue with question 271.

**Question 270: Upper limit of normal for IgA:**

Indicate the upper limit of normal for IgA value used at your institution.
Questions 271-272: IgM:

Indicate whether the IgM level at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the value and unit of measure documented on the laboratory report in question 272 and continue with question 273. If “unknown,” continue with question 274.

Question 273: Upper limit of normal for IgM:

Indicate the upper limit of normal for IgM value used at your institution.

Questions 274-275: IgD:

Indicate whether the IgD level at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the value and unit of measure documented on the laboratory report in question 275 and continue with question 276. If “unknown,” continue with question 277.

Question 276: Upper limit of normal for IgD:

Indicate the upper limit of normal for IgD value used at your institution.

Questions 277-278: IgE:

Indicate whether the IgE level at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the value and unit of measure documented on the laboratory report in question 278 and continue with question 279. If “unknown,” continue with question 280.

Question 279: Upper limit of normal for IgE:

Indicate the upper limit of normal for IgE value used at your institution.

Questions 280-281: Plasma cells in bone marrow aspirate:

* Under normal circumstances, the marrow aspirate is used to obtain the differential cell count, review morphology of the cells, and perform cytogenetic studies, flow cytometry, etc. The biopsy is obtained to evaluate the overall cellularity of the marrow. In the case of myeloma, the marrow plasma cells tend to be a patchy infiltrate rather than a diffuse infiltrate as in the case of acute leukemia. Therefore, it is possible that the plasma cell numbers may vary between the aspirate and biopsy.

⚠️ The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used as source
Indicate whether the percentage of plasma cells in the bone marrow aspirate at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the percentage of plasma cells in the bone marrow aspirate documented on the pathology report in question 281. If “unknown,” continue with question 282.

Questions 282-283: Plasma cells in bone marrow biopsy:

Indicate whether the percentage of plasma cells in the bone marrow biopsy at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the percentage of plasma cells in the bone marrow biopsy documented on the pathology report in question 283. If “unknown,” continue with question 284.

Question 284: Were conventional cytogenetics tested?

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Cytogenetics may also be referred to as karyotyping or g-banding.

Indicate if cytogenetic studies were obtained at the last evaluation prior to the start of the preparative regimen. If cytogenetic studies were obtained, select “yes” and continue with question 285.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select “no” or “unknown” and continue with question 306.

Question 285: Results of test:

If cytogenetic studies identified abnormalities, indicate “abnormalities identified” and continue with question 286.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate
this and continue with question 306.

**Questions 286-305: Specify cytogenetic abnormalities identified via conventional cytogenetics at the last evaluation prior to the start of the preparative regimen:**

Report all abnormalities identified by all methods of cytogenetic assessment at the last evaluation prior to the start of the preparative regimen by selecting “yes” or “no” for each question. Do not leave any responses blank. If one or more abnormality is best classified as “other abnormality,” select “yes” in question 304 and specify in question 305.

**Question 306: Were cytogenetics tested via FISH?**

FISH, fluorescence in situ hybridization, is a sensitive technique that assesses a large number of cells. This technique utilizes special probes that recognize and bind to fragments of DNA commonly found in plasma cell disorders. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells.

Indicate if FISH studies were obtained at the last evaluation prior to the start of the preparative regimen. If FISH studies were obtained, select “yes” and continue with question 307.

If no FISH studies were obtained or it is unknown if FISH studies were performed, select “no” or “unknown” and continue with question 326.

**Question 307: Results of test:**

If FISH studies identified abnormalities, indicate “abnormalities identified” and continue with question 308.

If there were no abnormalities identified, indicate this and continue with question 326.

**Questions 308-325: Specify cytogenetic abnormalities identified via FISH at last evaluation prior to the start of the preparative regimen:**

Report all abnormalities identified by all methods of FISH assessment at the last evaluation prior to the start of the preparative regimen by selecting “yes” or “no” for each question. Do not leave any responses blank. If one or more abnormality is best classified as “other abnormality,” select “yes” in question 324 and specify in question 325.
**Q326-362: Amyloidosis Organ Involvement at Last Evaluation Prior to the Start of the Preparative Regimen**

Questions 326–362 are for amyloid patients only. If diagnosis was other than amyloidosis (question 1), or there is no evidence or history of it (question 6), skip to question 363.

**Question 326: Was a cardiographic imaging procedure performed?**

Cardiographic imaging may show amyloid infiltration in heart tissue. Cardiac MRI, echocardiogram [(sometimes referred to as an echo) (do not report an ECG or EKG, which refer to electrocardiogram)], or Multiple Gate Acquisition (MUGA) scans may be performed to assess heart involvement. Indicate if cardiographic imaging was performed at the last evaluation prior to the start of the preparative regimen. If “yes,” continue with question 327. If “no” or “unknown,” continue with question 333.

**Question 327: Was a cardiac MRI done?**

Cardiac MRI may be used to differentiate amyloid involvement from other cardiopathologies. Indicate if a cardiac MRI was performed at the last evaluation prior to the start of the preparative regimen. If “yes,” continue with question 328. If “no,” continue with question 329.

**Question 328: Specify cardiac MRI results:**

Characteristics of amyloid involvement in cardiac tissue include impaired ventricular systolic function, thickened valves, increased atrial septal thickness, and left ventricular mass, pleural and pericardial effusions, and subendocardial hyperenhancement\(^1\). Indicate if the results of cardiac MRI were “normal,” “abnormal,” or “unknown,” and continue with question 329.


**Question 329: Was the left ventricular ejection fraction measured?**

The left ventricular ejection fraction (LVEF) is a percentage that represents the volume of blood pumped from the left ventricle into the aorta (also known as stroke volume) compared to the volume of blood in the ventricle just prior to the heart contraction (also known as end diastolic volume). Indicate if the left ventricular ejection fraction (LVEF) was measured at the last evaluation prior to the start of the preparative regimen. If “yes,” continue with question 330. If “no,” continue with question 332.
Question 330: Specify results of left ventricular fraction:

Indicate the left ventricular ejection fraction at the last evaluation prior to the start of the preparative regimen. Most imaging reports will report the LVEF, but if not, the LVEF may be determined by dividing the stroke volume (SV, the volume of blood pumped into the aorta from the left ventricle) by the end diastolic volume (EDV, the volume of blood in the left ventricle just prior to contraction) of the left ventricle. For example, if the stroke volume was 75 ml and the end diastolic volume was 150 ml, the ejection fraction would be 50%.

Question 331: Specify the method used to determine the left ventricular ejection fraction:

Indicate the method used to determine the LVEF reported in question 330.

Question 332: Was diastolic dysfunction present?

Diastole is the period in which chambers of the heart fill with blood. Diastolic dysfunction may be characterized by the difficulty of the ventricles to expand and contract appropriately due to stiffening of the heart walls by amyloid deposits. Indicate if diastolic dysfunction was present at the last evaluation prior to the start of the preparative regimen. Specify “yes,” “no,” or “unknown,” and continue with question 333.

Questions 333-334: Specify the intraventricular septal wall thickness measured by echocardiogram:

The heart is divided into the right and left sides by the septum. The area between the left and right ventricles is the intraventricular septum. Indicate if the intraventricular septal thickness is “known” or “unknown.” If “known,” based on evaluation by echocardiogram, indicate the thickness of the intraventricular septal wall in question 334. If unknown or not measured by echocardiogram, continue with question 335.

Question 335: Were any serum cardiac biomarkers assessed?

Assessment of cardiac biomarkers helps determine if injury to cardiac tissue has occurred. Cardiac biomarkers include brain natriuretic peptide (BNP), N-terminal prohormone brain natriuretic peptide (NT-proBNP), Troponin I, and Troponin T. Indicate if serum cardiac biomarkers were assessed at the last evaluation prior to the start of the preparative regimen. If “yes,” continue with question 336. If “no” or “unknown” continue with question 335.

Questions 336-350: Specify the cardiac biomarkers assessed:

Indicate if each biomarker was assessed, and if so, specify the biomarker level and the upper limit of normal for the assessment. Do not leave any yes/no responses blank.

Question 351: Specify the recipient’s New York Heart Association functional classification of heart failure: (Symptoms may include dyspnea, chest pain, fatigue, and palpitations; activity level should be
assessed with consideration for patient’s age group)

Indicate the recipient’s **New York Heart Association functional classification** at the last evaluation prior to the start of the preparative regimen. If the recipient’s NYHA functional classification it not known, select “unknown.”

**Question 352: Was hepatomegaly present on radiographic imaging (liver span > 15 cm) or on examination (liver edge palpable > 3 cm below right costal margin)?**

At the last evaluation prior to the start of the preparative regimen, indicate if the liver spanned more than 15 cm or the edge of the liver was palpable more than 3 cm below the right costal margin by radiographic imaging. Indicate “yes” if hepatomegaly was present. Indicate “no” if hepatomegaly was not present. Indicate “unknown” if it was not possible to determine the presence or absence of hepatomegaly.

**Questions 353-354: Specify the level of serum alkaline phosphatase:**

Indicate whether the alkaline phosphatase (ALP) level at the last evaluation prior to the start of the preparative regimen is “known” or “unknown.” If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 354 and continue with question 355. If “unknown,” continue with question 356.

**Question 355: Upper limit of normal for alkaline phosphatase:**

Report the upper limit of normal for ALP for the evaluation.

**Question 356: Was a sensory/motor exam performed?**

Indicate if a sensory/motor exam was performed. This exam evaluates the neurological status of the recipient and assesses the recipient’s body positioning, involuntary movements, muscle tone, muscle strength, ability to sense pain and light touch, position sense (proprioception), stereognosis (ability to discern an object with eyes closed, such as a coin), graphesthesia (ability to identify number of letter drawn on skin with eyes closed), and extinction (ability to discern multiple simultaneous stimuli). If a sensory/motor exam was performed, indicate “yes,” and continue with question 357. If “no” or “unknown,” continue with question 358.

**Question 357: Specify the exam results:**

Indicate the results of the sensory/motor exam. If the recipient’s results were within normal limits, select “normal.” If the recipient displayed neurologic impairment, select “abnormal.” If the results of the test are
unknown or inconclusive, select “unknown.” Continue with question 358.

**Questions 358-359: Did the recipient display any other evidence of peripheral nerve involvement for amyloidosis?**

Indicate if the recipient displayed any other evidence of peripheral nerve involvement (other than displayed on sensory/motor examination). If “yes,” specify the other evidence in question 359 and continue with question 360. If “no” or “unknown,” continue with question 360.

**Question 360: Did the recipient display symptomatic orthostatic hypotension (not attributable to medications or volume depletion)?**

Orthostatic hypotension is 1) a decrease in systolic blood pressure of 20 mmHg or diastolic blood pressure of 10 mmHg within 3 minutes of standing, compared to sitting or laying down. Symptoms include “dizziness, lightheadedness, blurred vision, weakness, fatigue, nausea, palpitation and headache.” Indicate if the recipient had evidence of orthostatic hypotension that was not attributable to medications or volume depletion.


**Questions 361-362: Did the recipient display any other evidence of autonomic neuropathy (e.g., pseudo-obstruction or intractable diarrhea)?**

Pseudo-obstruction is a condition in which food does not pass through the intestines as if the intestines were blocked; however, rather than a blockage, it is caused by nerve damage within the intestinal tract. Intractable diarrhea is diarrhea that cannot be stopped by medication.

Indicate if the recipient had any other evidence of autonomic neuropathy, such as pseudo-obstruction or intractable diarrhea, at the time prior to the start of the preparative regimen. If “yes,” specify the other evidence in question 362. If “no” or “unknown,” continue with question 363.
**Q363-364: Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen**

**Question 363:** What was the disease status? (Report the most recent assessment prior to the preparative regimen)

* Amyloidosis
  If the recipient’s primary disease is Amyloidosis (without evidence of myeloma), report Complete Remission (CR) if the CR criteria for all involved organs are met (see Amyloidosis Response Criteria). If the disease status is anything other than CR, report “Not applicable” for question 229. This is a change from the previous instruction which asked centers to report “Not applicable” for all amyloidosis cases, regardless of disease response.

Indicate the disease status of the plasma cell disorder (PCD) at the last evaluation prior to the start of the preparative regimen. See the Multiple Myeloma Response Criteria section for multiple myeloma and solitary plasmacytoma disease status definitions. See Plasma Cell Leukemia Response Criteria for plasma cell leukemia disease status definitions.

Currently there is an issue on Form 2016 regarding the number of plasma cells required for CR. CR requires less than (but not equal to) 5% plasma cells in the bone marrow.

At any response level, if some but not all criteria are met, the disease status should be downgraded to next lower level of response.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).

For more information on determining how to report disease status prior to the preparative regimen, see Appendix G.

If the disease response prior to transplant is unknown, select “unknown” and continue with the signature lines.

If the recipient had POEMS syndrome, but no evidence of myeloma, select “Not Applicable (POEMS or Amyloidosis with no evidence of myeloma)” and continue with the signature lines.
**Example 1:** A 62-year-old man is diagnosed with IgG Kappa multiple myeloma. He receives initial therapy with 6 cycles of bortezomib and lenalidomide/dexamethasone; and achieves a near complete remission (nCR). The comparison values used to determine disease status at transplant are the values obtained at diagnosis.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>BMBX</th>
<th>SPEP</th>
<th>SIFE</th>
<th>UPEP</th>
<th>UIFE</th>
<th>Skeletal Survey</th>
<th>Treatment</th>
<th>Disease Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/31/08</td>
<td>27% plasma cells</td>
<td>3.3 g/dL</td>
<td>+</td>
<td>336 mg/24 hours</td>
<td>+</td>
<td>Negative</td>
<td>Bortezomib/ Lenalidomide/ Dexamethasone</td>
<td>Diagnosis: IgG Kappa</td>
</tr>
<tr>
<td>4/3/09</td>
<td>3% plasma cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/17/09</td>
<td>Negative</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td>nCR</td>
</tr>
<tr>
<td>5/13/09</td>
<td>Negative</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td>nCR (confirmatory)</td>
</tr>
<tr>
<td>5/17/09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Autologous HCT</td>
</tr>
</tbody>
</table>

**Example 2:** A 59-year-old woman is diagnosed with IgA Lambda multiple myeloma. She receives bortezomib and thalidomide/dexamethasone as initial treatment and achieves a CR. A few months later she has evidence of relapse. She is then treated with lenalidomide/dexamethasone and achieves a PR. The patient receives high-dose cyclophosphamide as part of an autologous stem cell harvest. The values used to determine disease status at transplant would be the values obtained at the time of relapse.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>BMBX</th>
<th>SPEP</th>
<th>SIFE</th>
<th>UPEP</th>
<th>UIFE</th>
<th>Skeletal Survey</th>
<th>Treatment</th>
<th>Disease Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/27/10</td>
<td>4.5 g/dL</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/01/10</td>
<td>Aspirate=18% plasma cells; biopsy= sheets of plasma cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Diagnosis: IgA lambda</td>
</tr>
<tr>
<td>2/05/10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/05/10</td>
<td>2.6 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/5/10</td>
<td>1.7 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date</td>
<td>Hemoglobin</td>
<td>Plasma Cells</td>
<td>Bence Jones</td>
<td>Pathological Status</td>
<td>Therapies</td>
<td></td>
<td></td>
<td></td>
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<td>---------------------</td>
<td>-----------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/5/10</td>
<td>0.5 g/dL</td>
<td>+</td>
<td></td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/4/10</td>
<td>0.03 g/dL</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/18/10</td>
<td>1% plasma cells</td>
<td>0.01 g/dL</td>
<td>+</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/15/10</td>
<td>Not detected</td>
<td>+</td>
<td></td>
<td>CR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/15/10</td>
<td>Not detected</td>
<td>Negative</td>
<td></td>
<td>CR (confirmatory)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11/15/10</td>
<td>Not detected</td>
<td>Negative</td>
<td></td>
<td>(no treatment given)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12/15/11</td>
<td>Not detected</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/15/11</td>
<td>1.9 g/dL</td>
<td>+</td>
<td>Negative</td>
<td>Relapse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/15/11</td>
<td>7% plasma cells</td>
<td>2.2 g/dL</td>
<td>+</td>
<td>Negative</td>
<td>Lenalidomide/ Dexamethasone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/15/11</td>
<td>1.4 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td>Relapse (confirmatory)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/15/11</td>
<td>0.9 g/dL</td>
<td>+</td>
<td></td>
<td>PR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/15/11</td>
<td>0.7 g/dL</td>
<td>+</td>
<td></td>
<td>PR</td>
<td>(confirmatory)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/15/11</td>
<td>3% plasma cells</td>
<td>0.5 g/dL</td>
<td>+</td>
<td></td>
<td>Autologous HCT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7/31/11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Question 364: Date Assessed:**

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. A PET scan may be used if a previous PET scan had been obtained and only in limited circumstances (e.g., plasmacytomas, lytic lesions).

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.
2116: PCD Post-HCT

The Plasma Cell Disorder Post-HCT Data Form is one of the Comprehensive Report Forms. This form captures plasma cell disorder post-HCT data such as: disease assessment at the time of best response, hematologic and organ parameters at the time of best response, post-HCT therapy, disease status at the time of evaluation for this reporting period, and current status of amyloidosis for this reporting period.

This form must be completed for all recipients whose primary disease reported on the Pre-TED Disease Classification Form (Form 2402) is “Multiple myeloma/plasma cell disorder (PCD).” The Post-HCT Plasma Cell Disorder form must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, and 2300). This form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100; between day 100 and the six-month date of contact for six-month follow-up for Form 2200; and between the date of contact for the six-month follow-up and the date of contact for the one-year follow-up for Form 2200, etc.).

Q1-2: Disease Specificity
Q3-34: Disease Assessment at the Time of Best Response to HCT
Q35-60: Hematologic and Organ Parameters at the Time of Best Response
Q61-101: Post-HCT Therapy
Q102-136: Disease Status at the Time of Evaluation for this Reporting Period
Q137-162: Current Status of Amyloidosis for this Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/27/19</td>
<td>2116: PCD Post-HCT</td>
<td>Add</td>
<td>Added (in red below) additional instruction for question 61: However, bisphosphonate therapy (e.g., Zometa) should not be reported as planned therapy since it is universally administered to myeloma patients. Additionally, supportive care such as Denosumab (e.g., Prolia) should not be reported as planned therapy.</td>
</tr>
<tr>
<td>12/</td>
<td>2116: PCD</td>
<td>Remove</td>
<td>Removed the following blue note box instruction (struck out below) for</td>
</tr>
<tr>
<td>Date</td>
<td>Section</td>
<td>Action</td>
<td>Details</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------</td>
<td>----------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>21/2018</td>
<td>Post-HCT</td>
<td>Add</td>
<td>Questions 30 and 126 regarding Flow Cytometry reporting for Myeloma. These assessments can now be reported in the same way as all other disease assessments. An exception of the note above applies to multiple myeloma if the flow cytometry assessment has &lt; 5% malignant plasma cells, this result should not be reported because the result is not reliable; if no other cytogenetic or FISH assessments were performed, report “no.” However, if the flow cytometry assessment found ≥ 5% malignant plasma cells, this should be reported as evidence of disease.</td>
</tr>
<tr>
<td>3/19/18</td>
<td>2116: PCD</td>
<td>Add</td>
<td>Added Current Disease Status note box above the instructions for question 137.</td>
</tr>
<tr>
<td>3/19/18</td>
<td>Comprehensive Disease Specific Manuals</td>
<td>Add</td>
<td>Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119). The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.</td>
</tr>
<tr>
<td>2/13/18</td>
<td>2116: PCD</td>
<td>Add</td>
<td>Added Daratumumab note box to the instructions for questions 69-90.</td>
</tr>
<tr>
<td>1/24/18</td>
<td>2116: PCD</td>
<td>Add</td>
<td>Added Not Applicable Amyloidosis note box to the instructions for question 135.</td>
</tr>
<tr>
<td>1/24/18</td>
<td>2116: PCD</td>
<td>Remove</td>
<td>Removed text (struck out below) from the instructions for question 96. If the recipient had amyloidosis or POEMS syndrome, but no evidence of myeloma, select “Not Applicable (Amyloidosis with no evidence of myeloma)”</td>
</tr>
<tr>
<td>1/24/18</td>
<td>2116: PCD</td>
<td>Add</td>
<td>Added Amyloidosis note box to the instructions for questions 96.</td>
</tr>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400).</td>
</tr>
<tr>
<td>6/12/15</td>
<td>2116: PCD</td>
<td>Add</td>
<td>Added instruction for METHOD and DATE reporting in the Q102-136: Disease Status at the Time of Evaluation for this Reporting Period section just prior to question 126. See text for full detail.</td>
</tr>
</tbody>
</table>
| 5/29/15    | 2116: PCD       | Modify   | Added text for clarification in questions 18 and 114: (total in g/dL of monoclonal protein) x (total urine volume) = urinary M-protein/24 hours  
(0.145 g/dL of monoclonal protein) x (1500 mL total urine) x (1 dL/100 mL) = 2.175 g/24 hours |
| 5/29/15    | 2116: PCD       | Add      | Added an informational bubble in questions 30 and 126: Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be
quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in question 31 [or 127]. An exception to the note above applies to multiple myeloma. If the flow cytometry assessment has < 5% malignant plasma cells, this result should not be reported because the result is not reliable; if no other cytogenetic or FISH assessments were performed, report "no." However, if the flow cytometry assessment found ≥ 5% malignant plasma cells, this should be reported as evidence of disease.

<table>
<thead>
<tr>
<th>Date</th>
<th>Code</th>
<th>Action</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/29/15</td>
<td>2116: PCD Post-HCT</td>
<td>Add</td>
<td>Added text to questions 67-68: Indicate if the number of cycles is “known” or “unknown.” If known, report the number of cycles the recipient received during the reporting period for the line of therapy being reported in question 68. If the therapy is not given in cycles or the number of cycles is not known, select “unknown” and continue with question 69.</td>
</tr>
<tr>
<td>5/29/15</td>
<td>2116: PCD Post-HCT</td>
<td>Modify</td>
<td>Modified explanatory text for questions 96 and 135: If the recipient had amyloidosis or POEMS syndrome, but no evidence of myeloma, select “Not Applicable (POEMS or Amyloidosis with no evidence of myeloma)”</td>
</tr>
</tbody>
</table>
Q1-2: Disease Specificity

Question 1: Was the recipient transplanted for or do they have a history of amyloidosis?

This form is designed to best capture data related to the recipient’s specific plasma cell disorder. Select “yes” to indicate that the recipient was transplanted for or has a history of amyloidosis and continue with question 2. Questions appropriate for amyloidosis will became active if completing the form electronically. Select “no” to indicate that the recipient was not transplanted for and does not have a history of amyloidosis and continue with question 3. When completing the form electronically, selecting no will prevent questions specific to amyloidosis from becoming active and only questions relating to non-amyloidosis plasma cell disorders will be shown.

Question 2: Did the recipient have features of multiple myeloma?

If the recipient had multiple myeloma in addition to amyloidosis, select “yes” & continue with question 3. If the recipient did not have multiple myeloma in addition to amyloidosis, select “no” and continue with question 4.
Q3-34: Disease Assessment at the Time of Best Response to HCT

Best response is based on response to the HCT and does NOT include response to therapy given for disease relapse or progression post-HCT.

- If the HCT was planned as part of initial therapy for a recipient with no disease progression or relapse at any time prior to HCT, determine the best response by comparing to the disease assessment at time of original diagnosis.
- If the HCT was performed later in the disease course for a patient who has not received any chemotherapy within 6 months of HCT or has untreated relapse or progression, determine the best response to HCT by comparing the disease status immediately prior to the start of the preparative regimen.
- If the patient had a disease progression or relapse of disease at any time prior to HCT, and was treated to reduce the myeloma burden prior to the start of the preparative regimen, determine the best response to HCT by comparing to the disease evaluation at the time of relapse or progression. In other words, the baseline is reset to the time of relapse or progression.

This comparison is meant to capture the best disease status in response to HCT that occurred in the reporting interval, even if a subsequent disease relapse or progression occurred during the same reporting interval. If a recipient already achieved their best response in a previous interval, confirm the best response and check the box to indicate “date previously reported.” This option is only applicable on report forms for the six-month reporting interval and beyond.

Question 3: Compared to the disease status prior to the preparative regimen, what was the best response to HCT since the date of last report? (Include response to any therapy given for post-HCT maintenance or consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease):

The intent of this question is to determine the best overall response to HCT, which could include any response to planned therapy post-HCT, or to therapy given for maintenance or prophylaxis. (DO NOT include any response to treatment given for relapsed or progressive disease.) This is assessed in each reporting period. When evaluating the best response, determine the disease status within the reporting period and compare it to all previous post-HCT reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status. See question 4 to indicate that this disease status was previously reported.
See the [Multiple Myeloma Response Criteria](#) section for multiple myeloma and solitary plasmacytoma disease status definitions. See [Plasma Cell Leukemia Response Criteria](#) for plasma cell leukemia disease status definitions.

At any response level, if some but not all criteria are met, the best response should be downgraded to next lower level of response.

**Example:** A myeloma patient is transplanted in PR. In the 100-day reporting period all the CR criteria (3% plasma cells in the bone marrow, SPEP/UPEP negative) are met with the exception of a positive immunofixation on serum and urine (two disease assessments were performed in the reporting period indicating a positive immunofixation); in this case nCR should be reported as the best response to transplant.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may **NOT** be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).

---

Only report the best response to HCT from all reporting periods. See Examples below.

**Example 1:** A recipient with myeloma goes to transplant having established a PR prior to transplant, achieves a VGPR during the first 100 days, and then progresses during the six-month reporting period. The best response to transplant should be reported as “VGPR” on all subsequent forms. See below:

<table>
<thead>
<tr>
<th>Reporting Period</th>
<th>Disease Status</th>
<th>Q1. Best Response</th>
<th>Q5. Date Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transplant</td>
<td>PR</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>100-Days Post-HCT</td>
<td>VGPR</td>
<td>VGPR</td>
<td>[date of 1st confirmatory labs]</td>
</tr>
<tr>
<td>6-Months Post-HCT</td>
<td>Progression</td>
<td>VGPR</td>
<td>Previously reported</td>
</tr>
<tr>
<td>1-Year Post-HCT</td>
<td>PR</td>
<td>VGPR</td>
<td>Previously reported</td>
</tr>
</tbody>
</table>

**Example 2:** A recipient with myeloma goes to transplant having established a CR prior to transplant, maintains the response after transplant, and then relapses within the six-month reporting period. The best response to transplant would be reported as “CR” for all subsequent reporting periods. See below:
### Example 3:
A recipient with myeloma goes to transplant having established a PR prior to transplant and maintains the response throughout the 100-day reporting period. During the six-month reporting period, the recipient progresses and begins unplanned therapy to treat the worsening disease. During the one-year reporting period, the recipient achieves VGPR. The best response to transplant occurred during the 100-day reporting period because response to unplanned therapy is not captured using this set of questions. See below:

<table>
<thead>
<tr>
<th>Reporting Period</th>
<th>Disease Status</th>
<th>Q1. Best Response</th>
<th>Q5. Date Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transplant</td>
<td>PR</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>100-Days Post-HCT</td>
<td>PR</td>
<td>PR</td>
<td>[date of labs that first confirmed a continued PR]</td>
</tr>
<tr>
<td>6-Months Post-HCT</td>
<td>Progression</td>
<td>PR</td>
<td>Previously reported</td>
</tr>
<tr>
<td>1-Year Post-HCT</td>
<td>VGPR</td>
<td>PR</td>
<td>Previously reported</td>
</tr>
</tbody>
</table>

### Example 4:
A recipient with myeloma goes into transplant having established VGPR prior to transplant and maintains the response throughout the 100-day reporting period. During the six-month reporting period, the recipient achieves a CR and is placed on maintenance therapy. During the one-year reporting period the recipient maintains the CR. The best response to transplant occurred in the six-month reporting period. See below:

<table>
<thead>
<tr>
<th>Reporting Period</th>
<th>Disease Status</th>
<th>Q1. Best Response</th>
<th>Q5. Date Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transplant</td>
<td>VGPR</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>100-Days Post-HCT</td>
<td>VGPR</td>
<td>VGPR</td>
<td>[date of labs that first confirmed a continued VGPR]</td>
</tr>
<tr>
<td>6-Months Post-HCT</td>
<td>CR</td>
<td>CR</td>
<td>[date of labs that first confirmed CR]</td>
</tr>
<tr>
<td>1-Year Post-HCT</td>
<td>CR</td>
<td>CR</td>
<td>Previously reported</td>
</tr>
</tbody>
</table>

Include response to any post-HCT treatment planned as of Day 0. If post-transplant therapy is given as prophylaxis or maintenance for recipients in CR, or as preemptive therapy for recipients with minimal
residual disease, consider this “planned therapy” even if this was not documented prior to the transplant. Bisphosphonate therapy (e.g., Zometa) should not be considered when making this determination. Do not include any treatment administered as a result of relapse or progression.

**Question 4: Was the date of best response previously reported?**

Indicate if the best response was reported on a previous post-HCT plasma cell disorder form (Form 2116). If “yes,” continue with question 35. If “no,” continue with question 5.

If the best response is the same as the pre-transplant disease status, select “no,” report the date of the first assessment that confirmed the ongoing disease status post-HCT in question 5.

**Question 5: Date assessed:**

Enter the date the best response first began. In other words, report the date of the first assessment, not the date of the second confirmatory assessment. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathologic examination.

* Questions are often raised about how to report the best response and the date it first began when there is not a second assessment within the same reporting period. One way to approach this is if you have a second assessment that confirms the best disease response from the next reporting period available at the time the form is being completed, you can report the best disease response and the date the response first began. If you don’t have a second assessment to confirm the new disease status response at the time a form is being completed, you must report the disease response that was previously confirmed.

**Example 1:** A recipient with myeloma goes into transplant having established a PR prior to transplant. During the 100-day reporting period, the recipient achieves a VGPR. However, the second disease assessment to confirm the VGPR was not performed until one month later (which is in the next reporting period). Those results are available at the time the Day 100 disease form is being completed. The best response to transplant would be reported as “VGPR” with the date it first began in the 100-day reporting period. The recipient maintains the VGPR in the six-month reporting period. The best response to transplant would be reported as “VGPR” with the date as “previously reported” in the six-month reporting period.

**Example 2:** A recipient with myeloma goes into transplant having established a PR prior to transplant. During the 100-day reporting period, the recipient achieves a VGPR. However a second disease assessment to confirm the VGPR response is not available when the form is being completed. The best response to transplant would be reported as “PR” with the date continuing disease response was
confirmed.

**Example 3:** A recipient with myeloma goes into transplant having established a PR prior to transplant. During the 100-day reporting period, the recipient achieves a VGPR. However a second disease assessment to confirm the VGPR response is not available when the form is being completed. The best response to transplant would be reported as “PR” with the date continuing disease response was confirmed in the 100-day reporting period. When completing the six-month form, a second disease assessment to confirm a VGPR response is available. The best response to transplant would be reported as “VGPR.” However, since the VGPR first began during the Day 100 reporting period, an error correction needs to be completed to update the disease status and date first achieved on the Day 100 report.

• Under normal circumstances, a marrow aspirate is used to obtain the differential cell count, review morphology of the cells, and perform cytogenetic studies, flow cytometry, etc. A biopsy is obtained to evaluate the overall cellularity of the marrow. In the case of myeloma, the marrow plasma cells tend to be a patchy infiltrate rather than a diffuse infiltrate as in the case of acute leukemia. Therefore, it is possible that the plasma cell numbers may vary between the aspirate and the biopsy.  
• The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used as source documentation when reporting the data for questions 6-9.  
• If the bone marrow pathology report states a range for plasma cells, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).  
• If the report states > 90% plasma cells, enter 91% on the form.  
• If the report states a marrow packed with plasma cells or sheets of plasma cells, report 99% on the form.  
• If the report states < 5% plasma cells, enter 4% on the form.

**Questions 6-7: Plasma cells in bone marrow aspirate:**

Indicate whether the percentage of plasma cells in the bone marrow aspirate was “known” or “unknown” at the time of best response to transplant. If “known,” report the percentage of plasma cells in the bone marrow aspirate documented on the pathology report in question 7. If “unknown,” continue with question 8.

**Questions 8-9: Plasma cells in bone marrow biopsy:**

Indicate whether the percentage of plasma cells in the bone marrow biopsy was “known” or “unknown” at the time of best response to transplant. If “known,” report the percentage of plasma cells in the bone marrow biopsy documented on the pathology report in question 9. If “unknown,” continue with question 10.

**Questions 10-11: Serum monoclonal protein (M-spike): (only from electrophoresis)**

Monoclonal gammopathy is defined as the increased production of one type of immunoglobulin by a single
clone of cells. The abnormal protein produced is called paraprotein or M-protein. Indicate whether the serum monoclonal immunoglobulin was “known” or “unknown” at the time of best response to transplant. If “known,” report the value and unit of measure documented on the laboratory report in question 11. If “unknown” or “not applicable,” continue with question 12.

“Not applicable” is appropriate for recipients with non-secretory myeloma.

**Questions 12: Serum immunofixation:**

Serum immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the blood. If “known” at the time of best response to transplant, continue with question 13. If “unknown” or “not applicable,” continue with question 16.

“Not applicable” is appropriate for recipients with non-secretory myeloma.

**Question 13: Specify monoclonal immunoglobulin result:**

If monoclonal immunoglobulin is “present,” continue with question 14. If “absent,” continue with question 16.

**Question 14: Original monoclonal bands:**

Indicate “yes” if the original monoclonal band was present or “no” if it was not present.

**Question 15: New monoclonal (or oligoclonal) bands:**

Indicate “yes” if a new monoclonal (or oligoclonal) band was present or “no” if it was not present.

**Questions 16-17: Total urinary protein excretion:**

Indicate whether the amount of urinary protein was “known” or “unknown” at the time of best response to transplant. The value reported here should be based on a 24-hour urine collection. If “known,” report the laboratory value in question 17. If “unknown,” continue with question 18.

**Questions 18-19: Urinary monoclonal protein (M-spike):**

**Urinary Monoclonal Protein**

Questions 18-19 are intended to capture the 24-hour urine monoclonal protein results, not the 24-hour protein excretion (questions 16-17 capture the total protein secretion/24 hours). The results will be reported as XX g or XX g/dL. If the value is reported in XX g/dL, it can be multiplied by the volume of the urine to determine the 24-hour urine monoclonal protein. Do not report immunofixation results here.
Example:
(totai in g/dL of monoclonal protein) \times (total urine volume) = \text{urinary M-protein/24 hours}
(0.145 g/dL of monoclonal protein) \times (1500 mL total urine) \times (1 \text{ dL}/100 \text{ mL}) = 2.175 \text{ g/24 hours}

Indicate whether the amount of urinary monoclonal protein was “known” or “unknown” at the time of best response to transplant. The value reported here should be based on a 24-hour urine collection. If “known,” report the laboratory value in question 19. If “unknown” or “not applicable,” continue with question 20.

“Not applicable” is appropriate for recipients with non-secretory myeloma.

**Question 20: Urinary immunofixation:**

Urine immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the urine. Indicate if the results of urinary immunofixation were “known” or “unknown” at the time of best response to transplant. If “known,” continue with question 21. If “unknown” or “not applicable,” continue with question 24.

“Not applicable” is appropriate for recipients with non-secretory myeloma.

**Question 21: Specify monoclonal immunoglobulin result:**

If monoclonal immunoglobulin was “present,” continue with question 22. If “absent,” continue with question 24.

**Question 22: Original monoclonal bands:**

Indicate “yes” if the original monoclonal band was present or “no” if it was not present.

**Question 23: New monoclonal (or oligoclonal) bands:**

Indicate “yes” if a new monoclonal (or oligoclonal) band was present or “no” if it was not present.

**Questions 24-25: Serum free light chains – κ (kappa):**

Indicate whether the serum κ (kappa) free light chain level was “known” or “unknown” at the time of best response to transplant. This value should reflect the quantity of serum free light chains, not a quantification of total light chains. If “known,” report the value and unit of measure documented on the laboratory report in question 25 and continue with question 26. If “unknown” or “not applicable,” continue with question 27.

**Question 26: Upper limit of normal for κ free light chain:**

Indicate the upper limit of normal for κ (kappa) free light chains value and the unit of measure used at your...
Questions 27-28: Serum free light chain – λ (lambda):

Indicate whether the serum λ (lambda) free light chain level was “known” or “unknown” at the time of best response to transplant. This value should reflect the quantity of serum free light chains, not a quantification of total light chains. If “known,” report the value and unit of measure documented on the laboratory report in question 28 and continue with question 29. If “unknown” or “not applicable,” continue with question 30.

Question 29: Upper limit of normal for λ free light chain:

Indicate the upper limit of normal for λ (lambda) free light chains value and the unit of measure used at your institution.

Question 30: Was the disease status assessed by cytogenetic testing (conventional or FISH)?

Flow Cytometry

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in question 31.

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient’s disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

If a cytogenetic assessment was performed to assess disease status at the time of best response to transplant, select “yes” and continue with question 31.

If a cytogenetic assessment was not performed, check “no” and continue with question 35.

Question 31: Was the disease status assessed via FISH?

FISH, fluorescence in situ hybridization, is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in plasma cell disorders. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells.

Indicate if FISH studies were obtained at the time of best response to transplant. If FISH studies were
obtained, select “yes” and continue with question 32.

If no FISH studies were obtained or it is unknown if FISH studies were performed, select “no” and continue with question 33.

**Question 32: Date assessed:**

Enter the date of FISH assessment at the time of best response. Report the date the sample was collected for the laboratory.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 33: Was the disease status assessed via conventional cytogenetics?**

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Cytogenetics may also be referred to as karyotyping or g-banding.

Indicate if cytogenetic studies were obtained at the time of best response to transplant. If cytogenetic studies were obtained, select “yes” and continue with question 34.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select “no” and continue with question 35.

**Question 34: Date assessed:**

Enter the date of conventional cytogenetic assessment at the time of best response. Report the date the sample was collected for the laboratory.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.
Q35-60: Hematologic and Organ Parameters at the Time of Best Response (for Amyloid Patients only)

Complete questions 35-60 for amyloid patients only. If diagnosis was other than amyloidosis or there is no history of it, continue with question 61.

The response time for amyloidosis tends to occur well after transplant, so the “best response” to transplant may not occur within the first 100 days. The intent of this question is to determine the best overall response to HCT, which could include any response to planned therapy post-HCT, or to therapy given for maintenance or prophylaxis. DO NOT include any response to treatment given for relapsed or progressive disease. This is assessed in each reporting period. When evaluating the best response, determine the disease status within the reporting period and compare it to all previous post-HCT reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status.

**Question 35: Specify the recipient’s best hematologic response to the HCT:**

Indicate the recipient’s best hematologic response to HCT to date. See Amyloidosis Response Criteria for disease status definitions.

If best response is CR, PR, NR, SD, or progressive disease, continue with question 36.

If the recipient’s hematologic status was not assessed during the reporting period, select “not assessed” and continue with question 38. “Not applicable” should rarely, if ever, be chosen.

**Questions 36-37: Date assessed:**

Indicate if the date the best hematologic response to transplant was assessed is “known,” “unknown,” or “previously reported.” If the hematologic response is known, report the date in question 37. If the date is unknown, select “unknown” and continue with question 38. If the best response to transplant was already reported in a previous reporting period, select “previously reported” and continue with question 38.

**Question 38: Specify the recipient’s best cardiac response to the HCT:**

Indicate the recipient’s best cardiac response to HCT to date. See Amyloidosis Response Criteria for disease status definitions.
If the recipient’s cardiac status was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of cardiac involvement in their disease, select “not applicable.”

**Questions 39-40: Date assessed:**

Indicate if the date the best cardiac response to transplant was assessed is “known,” “unknown,” or “previously reported.” If the cardiac response is known, report the date in question 40. If the date is unknown, select “unknown” and continue with question 41. If the best response to transplant was already reported in a previous reporting period, select “previously reported” and continue with question 41.

**Question 41: Was there clinical improvement in GI involvement in response to the HCT (decrease in diarrhea)?**

Indicate if there was clinical improvement of GI involvement to date. Judgment is required by a clinician to determine if there is evidence of improvement. If “yes” or “no,” continue with question 42. If “unknown,” continue with question 44.

**Questions 42-43: Date assessed:**

Indicate if the date the GI involvement was assessed is “known,” “unknown,” or “previously reported.” If the date the GI response was assessed is known, report the date in question 43. If the date is unknown, select “unknown” and continue with question 44. If the best response to transplant was already reported in a previous reporting period, select “previously reported” and continue with question 44.

**Question 44: Specify the recipient’s best hepatic response to the HCT:**

Indicate the recipient’s best hepatic response to HCT to date. See [Amyloidosis Response Criteria](http://CIBMTR.org) for disease status definitions.

If the recipient’s hepatic status was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of hepatic involvement in their disease, select “not applicable.”

**Questions 45-46: Date assessed:**

Indicate if the date the best hepatic response to transplant was assessed is “known,” “unknown,” or “previously reported.” If the hepatic response is known, report the date in question 46. If the date is unknown, select “unknown” and continue with question 47. If the best response to transplant was already reported in a previous reporting period, select “previously reported” and continue with question 47.

**Question 47: Specify the best response of the autonomic neuropathy to the HCT:**

Indicate the recipient’s best autonomic neuropathy response to HCT to date. See [Amyloidosis Response](http://CIBMTR.org)
Criteria for disease status definitions.

If the recipient’s autonomic neuropathy was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of disease related autonomic neuropathy, select “not applicable.”

Questions 48-49: Date assessed:

Indicate if the date the best autonomic neuropathy response to transplant was assessed is “known,” “unknown,” or “previously reported.” If the autonomic neuropathy response is known, report the date in question 49. If the date is unknown, select “unknown” and continue with question 50. If the best response to transplant was already reported in a previous reporting period, select “previously reported” and continue with question 50.

Question 50: Specify the best response of peripheral neuropathy to the HCT:

Indicate the recipient’s best peripheral neuropathy response to HCT to date. See Amyloidosis Response Criteria for disease status definitions.

If the recipient’s peripheral neuropathy was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of disease-related peripheral neuropathy, select “not applicable.”

Questions 51-52: Date assessed:

Indicate if the date the best peripheral neuropathy response to transplant was assessed is “known,” “unknown,” or “previously reported.” If the peripheral neuropathy response is known, report the date in question 52. If the date is unknown, select “unknown” and continue with question 53. If the best response to transplant was already reported in a previous reporting period, select “previously reported” and continue with question 53.

Question 53: Specify the recipient’s best renal response to the HCT:

Indicate the recipient’s best renal response to HCT to date. See Amyloidosis Response Criteria for disease status definitions.

If the recipient’s renal status was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of renal involvement in their disease, select “not applicable.”

Questions 54-55: Date assessed:

Indicate if the date the best renal response to transplant was assessed is “known,” “unknown,” or “previously reported.” If the renal response is known, report the date in question 55. If the date is unknown, select “unknown” and continue with question 56. If the best response to transplant was already reported in a
previous reporting period, select “previously reported” and continue with question 56.

**Questions 56-57: Did any other system respond to the HCT?**

Indicate if any other system was assessed for response to HCT. If the recipient had other site involvement reported in questions 179-185 of the Pre-HCT Plasma Cell Disorder form (Form 2016) and that site was assessed, the response to HCT must be reported here, even if there was no response.

Indicate the involved system/site in question 57.

**Question 58: Specify best response to HCT for this system:**

Indicate if the site’s/system’s best response to transplant was “response,” “no response/stable disease,” “progressive disease,” or “not applicable.”

**Questions 59-60: Date assessed:**

Indicate if the date the other site’s/system’s best response to transplant was assessed is “known,” “unknown,” or “previously reported.” If the other site’s/system’s response is known, report the date in question 60. If the date is unknown, select “unknown” and continue with question 61. If the best response to transplant was already reported in a previous reporting period, select “previously reported” and continue with question 61.
Q61-101: Post-HCT Therapy

**Question 61: Was therapy given since the date of last report for reasons other than relapse or progressive disease? (Include any maintenance and consolidation therapy):**

Indicate if the recipient received therapy post-transplant for any reason other than relapse or progressive disease since the date of last report. If “yes,” continue with question 62. If “no” or “unknown,” continue with question 100.

Recipients are generally transplanted under a specific protocol that defines the systemic therapy the recipient is intended to receive as a preparative regimen prior to the HCT; the infection and GVHD prophylaxis to be administered pre- and/or post-HCT; and any systemic therapy, radiation, and/or other treatments to be administered post-HCT as planned (or maintenance) therapy. Planned (maintenance or consolidation) therapy is given to help prolong a remission. This protocol may be either a research protocol or standard-of-care protocol and should be referred to when completing this section.

Additionally, if post-transplant therapy is given as prophylaxis or maintenance for recipients in CR, or as preemptive therapy for recipients with minimal residual disease, consider this “planned therapy” even if this was not documented prior to the transplant. However, bisphosphonate therapy (e.g., Zometa) should not be reported as a planned therapy since it is universally administered to myeloma patients. Additionally, supportive care such as Denosumab (e.g. Prolia) should not be reported as planned therapy.

Do not include any treatment administered as a result of relapse or progression.

For the purposes of this question, a line of therapy is one or more cycles of a defined treatment program given to a patient with no progression of disease in between. A new line of therapy may be started for reasons including drug toxicities, planned changes to medications, etc. If a drug dose was changed due to toxicity, do not report this as a new line of therapy; however, if a drug is stopped and a new one started due to toxicity, report this as a new line of therapy.

**Example 1:** A recipient with myeloma goes into transplant having established nCR prior to transplant and maintains the response throughout the 100-day reporting period. During the six-month reporting period, the recipient achieves a CR and is placed on maintenance lenalidomide therapy at 15 mg/day.

**Example 2:** A recipient with myeloma goes into transplant having established PR prior to transplant and achieves a VGPR in the 100-day reporting period. During the six-month reporting period, the recipient maintains the VGPR and is placed on maintenance lenalidomide therapy at 10 mg/day. During the one-year reporting period, the recipient progresses and unplanned treatment is initiated. Only the maintenance
lenalidomide would be reported in questions 61-99.

**Question 62: Systemic therapy:**

Systemic therapy may be injected into a vein or given orally, and is delivered to the whole body via the blood stream. If “yes,” continue with question 63. If “no,” continue with question 91.

**Questions 63-64: Date therapy started:**

Indicate if the date the therapy started was “known” or “unknown.” If known, enter the date the recipient began this line of therapy in question 64. If the start date was reported on a previous report, report the same date again when the start/stop dates overlap reporting periods. If “unknown,” continue with question 65.

If the start date is partially known (i.e., the recipient started treatment in mid-July 2010), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Questions 65-66: Date therapy stopped:**

Indicate if the date the therapy stopped is “known” or “unknown.” If the stop date is known and the recipient is receiving therapy administered in cycles, report the date the recipient started the last cycle for this line of therapy in question 66. If “unknown,” continue with question 67.

If the recipient is receiving therapy administered on a daily basis (e.g., lenalidomide therapy at 10 mg/day) report the last date the recipient received the line of therapy.

If therapy won’t be stopped until the next reporting period or later, question 65 should be left blank. Override the error with “UA,” unable to answer.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Questions 67-68: Number of cycles:**

Systemic therapy is usually administered in cycles with rest periods between the cycles. This enables cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from the damage. A cycle can last one or more days and may repeat weekly, bi-weekly, or monthly. A systemic therapy course may consist of multiple cycles.

Indicate if the number of cycles is “known” or “unknown.” If known, report the number of cycles the recipient received during the reporting period for the line of therapy being reported in question 68. If the therapy is not given in cycles or the number of cycles is not known, select “unknown” and continue with question 69.
Questions 69-90: Specify systemic therapy:

Daratumumab
If the recipient received Daratumumab (Darzalex), please report this drug in “Other systemic therapy.”

Treatments vary based on protocol and in most cases are administered in the outpatient setting. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. Indicate “yes” or “no” for each chemotherapy treatment drug administered for the line of therapy being reported. Do not leave any yes/no responses blank. If the recipient received a chemotherapy treatment that is not listed, check “yes” for “other systemic therapy” and specify the treatment in question 90. Report the generic name of the agent, not the brand name.

Question 91: Radiation therapy:

Radiation therapy uses high-energy radiation to kill cancer cells. For multiple myeloma, external beam radiation is used most frequently. In this method, a beam of radiation is delivered to a specific part of the body, such as a lytic lesion or plasmacytoma. Indicate if the recipient received radiation during this reporting period post-HCT. If “yes,” continue with question 92. If “no,” continue with question 96.

Questions 92-93: Date therapy started:

Indicate if the date the therapy started is “known” or “unknown.” If known, enter the date the line of radiation therapy began in question 93.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Questions 94-95: Date therapy stopped:

Indicate if the date the therapy started is “known” or “unknown.” If known, enter the date the line of radiation therapy ended in question 95.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 96: Best response to line of therapy:

Amyloidosis
Indicate the best response to the line of therapy. See the Multiple Myeloma Response Criteria section for multiple myeloma and solitary plasmacytoma disease status definitions. See Plasma Cell Leukemia Response Criteria for plasma cell leukemia disease status definitions.

For more information on determining what baseline values to use to determine best response, see Appendix G.

At any response level, if some but not all criteria are met, the best response should be downgraded to next lower level of response.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).

If the disease response following this line of therapy is unknown, select “unknown.”

If the recipient had POEMS syndrome, but no evidence of myeloma, select “Not Applicable.”

**Question 97: Date response established:**

Any response requires two consecutive assessments (of the same labs, where applicable based on response criteria) made at any time before the start of a new therapy. Enter the date the best response to the line of therapy was established. In other words, report the date of the first assessment, not the date of the second confirmatory assessment. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation.

**Question 98: Did disease relapse/progress following this line of therapy?**

Indicate “yes” if a relapse or progression occurred following the line of therapy being reported and continue with question 99. Documentation of relapse or progression requires two consecutive assessments (of the same labs, where applicable based on response criteria) made at any time before classification as relapse or progression, and/or the start of a new therapy. Indicate “no” if the recipient did not relapse or progress.
following this line of therapy and continue with question 100.

See Multiple Myeloma Response Criteria for progressive disease and Relapse from CR disease status definitions.

**Question 99: Date of relapse/progression:**

Enter the date the relapse or progression was established following the line of therapy. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. However, if there was not a second assessment (where applicable by response criteria) obtained prior to the start of new therapy, report the date the new therapy started as the date of relapse/progression. Continue with question 100.

Copy questions 62-99 to report more than one line of therapy.

* It is possible that the relapse or progression would be reported twice if already reported in question 98. Question 98 is asking about relapse or progression following any planned/maintenance therapy. Question 100 is asking about relapse or progression at any time, regardless of whether therapy was given or not.

**Question 100: Has the disease relapsed or progressed since the date of last report?**

Indicate “yes” if a relapse or progression occurred during the reporting period and continue with question 101. Documentation of relapse or progression requires two consecutive assessments (of the same labs, where applicable based on response criteria) made at any time before classification as relapse or progression, and/or the start of a new therapy. Indicate “no” if the recipient did not relapse or progress during the reporting period and continue with question 102.

See Multiple Myeloma Response Criteria for progressive disease and Relapse from CR disease status definitions.

**Question 101: Specify the date of disease relapse or progression:**

Enter the date the relapse or progression was established following the line of therapy. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. However, if there was not a second assessment (where required) obtained prior to the start of new therapy, report the date the new therapy started as the date of relapse/progression. Continue with question 102.
Q102-136: Disease Status at the Time of Evaluation for this Reporting Period

* Under normal circumstances, the marrow aspirate is used to obtain the differential cell count, review morphology of the cells, and to perform cytogenetic studies, flow cytometry, etc. The biopsy is obtained to evaluate the overall cellularity of the marrow. In the case of myeloma, the marrow plasma cells tend to be a patchy infiltrate rather than a diffuse infiltrate as in the case of acute leukemia. Therefore, it’s possible that the plasma cell numbers may vary between the aspirate and biopsy.
  • The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used as source documentation when reporting the data for questions 102-105.
  • If the bone marrow pathology report states a range for plasma cells, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
  • If the report states > 90% plasma cells, enter 91% on the form.
  • If the report states a marrow packed with plasma cells or sheets of plasma cells, report 99% on the form.
  • If the report states < 5% plasma cells, enter 4% on the form.

Questions 102-103: Plasma cells in bone marrow aspirate:

Indicate if the percentage of plasma cells in the bone marrow aspirate was “known” or “unknown” at the time of evaluation for this reporting period. If “known,” report the percentage of plasma cells in bone marrow aspirate documented on the pathology report in question 103. If “unknown,” continue with question 104.

Questions 104-105: Plasma cells in bone marrow biopsy:

Indicate whether the percentage of plasma cells in the bone marrow biopsy was “known” or “unknown” at the time of evaluation for this reporting period. If “known,” report the percentage of plasma cells in the bone marrow biopsy documented on the pathology report in question 105. If “unknown,” continue with question 106.

Questions 106-107: Serum monoclonal protein (M-spike): (only from electrophoresis)

Monoclonal gammopathy is defined as the increased production of one type of immunoglobulin by a single clone of cells. The abnormal protein produced is called paraprotein or M-protein. Indicate whether the serum monoclonal immunoglobulin was “known” or “unknown” at the time of evaluation for this reporting period. If “known,” report the value and unit of measure documented on the laboratory report in question 107. If “unknown” or “not applicable,” continue with question 108.
“Not applicable” is appropriate for recipients with non-secretory myeloma.

**Questions 108: Serum immunofixation:**

Serum immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the blood. If “known” at the time of evaluation for this reporting period, continue with question 109. If “unknown” or “not applicable” continue with question 112.

“Not applicable” is appropriate for recipients with non-secretory myeloma.

**Question 109: Specify monoclonal bands:**

If monoclonal immunoglobulin was “present,” continue with question 110. If “absent,” continue with question 112.

**Question 110: Original monoclonal bands:**

Indicate “yes” if the original monoclonal band was present or “no” if it was not present.

**Question 111: New monoclonal (or oligoclonal) bands:**

Indicate “yes” if a new monoclonal band (or oligoclonal) was present or “no” if not present.

**Questions 112-113: Total urinary protein excretion:**

Indicate whether the amount of urinary protein was “known” or “unknown” at the time of evaluation for this reporting period. The value reported here should be based on a 24-hour urine collection. If “known,” report the laboratory value in question 113. If “unknown” or “not applicable,” continue with question 114.

**Questions 114-115: Urinary monoclonal protein (M-spike):**

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**Urinary Monoclonal Protein**

Questions 114-115 are intended to capture the 24-hour urine monoclonal protein results, not the 24-hour protein excretion (questions 112-113 capture the total protein secretion/24 hours). The results will be reported as XX g or XX g/dL. If the value is reported in XX g/dL, it can be multiplied by the volume of the urine to determine the 24-hour urine monoclonal protein. Do not report immunofixation results here.

**Example:**

(total in g/dL of monoclonal protein) x (total urine volume) = urinary M-protein/24 hours

(0.145 g/dL of monoclonal protein) x (1500 mL total urine) x (1 dL/100 mL) = **2.175 g/24 hours**
Indicate whether the amount of urinary monoclonal protein was “known” or “unknown” at the time of evaluation for this reporting period. The value reported here should be based on a 24-hour urine collection. If “known,” report the laboratory value in question 115 and continue with question 116. If “unknown” or “not applicable,” continue with question 116.

“Not applicable” is appropriate for recipients with non-secretory myeloma.

**Question 116: Urinary immunofixation:**

Urine immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the urine. Indicate if the results of urinary immunofixation were “known” or “unknown” at the time of evaluation for the reporting period. If “known,” continue with question 117. If “unknown” or “not applicable,” continue with question 120.

“Not applicable” is appropriate for recipients with non-secretory myeloma.

**Question 117: Specify monoclonal immunoglobulin result:**

If monoclonal immunoglobulin was “present,” continue with question 118. If “absent,” continue with question 120.

**Question 118: Original monoclonal bands:**

Indicate “yes” if the original monoclonal band was present or “no” if it was not present.

**Question 119: New monoclonal (or oligoclonal) bands:**

Indicate “yes” if a new monoclonal (or oligoclonal) band was present or “no” if it was not present.

**Questions 120-121: Serum free light chains – κ (kappa):**

Indicate whether the serum κ (kappa) free light chain level was “known” or “unknown” at the time of evaluation for the reporting period. This value should reflect the quantity of serum free light chains, not a quantification of total light chains. If “known,” report the value and unit of measure documented on the laboratory report in question 121. If “unknown” or “not applicable,” continue with question 123.

**Question 122: Upper limit of normal for κ free light chain:**

Indicate the upper limit of normal for κ (kappa) free light chains value and unit of measure used at your institution.
**Questions 123-124: Serum free light chain – λ (lambda):**

Indicate whether the serum λ (lambda) free light chain level was “known” or “unknown” at the time of evaluation for the reporting period. This value should reflect the quantity of serum free light chains, not a quantification of total light chains. If “known,” report the value and unit of measure documented on the laboratory report in question 124. If “unknown” or “not applicable,” continue with question 126.

**Question 125: Upper limit of normal for λ free light chain:**

Indicate the upper limit of normal for λ (lambda) free light chains value and the unit of measure used at your institution.

**METHOD**

This section should reflect the recipient’s most recent disease assessment. Not all recipients have cytogenetic or FISH abnormalities identified to monitor disease status. If no disease assessments exist for the applicable method, check “no.”

Cytogenetic assessments may be performed for many reasons post-transplant, including monitoring for secondary malignancy. If the recipient did not have any identified cytogenetic or FISH abnormalities at diagnosis or during their pre-transplant course, and post-HCT follow-up assessments continue to show that no abnormalities are detected, report “no” for these assessment data fields. However, if routine post-HCT cytogenetic or FISH assessments identify a new abnormality associated with the recipient’s disease process, begin reporting those assessments; report the assessment identifying the new abnormality, as well as all subsequent assessments for the abnormality by that method.

If the recipient had cytogenetic or FISH abnormalities prior to transplant, ensure that post-HCT assessments of the applicable method are reported.

**Example:** The recipient has IGH abnormalities identified by FISH testing prior to transplant; however, they had a normal karyotype on all pre-transplant assessments. Post-transplant, FISH studies incorporating an IGH probe should be reported; conventional cytogenetic studies would not be reported (answer question 131 as “no”) unless the recipient develops abnormalities associated with their disease detectable by conventional cytogenetics; the study identifying the new abnormalities and all subsequent conventional cytogenetic studies would be reported.

**DATE**
If more than one test in the same assessment category is done on different days, report the date of the most definitive diagnostic assessment within a reasonable time frame of the date of contact (approximately 30 days). If there was only a single assessment performed within the reporting period, it should be reported, even if it was more than 30 days prior to the date of contact.

**Example:** The recipient continues to have a positive serum immunofixation; however, two days after their latest immunofixation, they have a bone marrow biopsy performed. The bone marrow biopsy does not show evidence of disease. Report the date of the serum immunofixation, since it is the most disease specific given that it continues to reveal evidence of disease in a patient who is clearly not disease free.

**Question 126: Was the disease status assessed by cytogenetic testing (conventional or FISH)?**

**Flow Cytometry**
Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in question 127.

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient’s disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

If a cytogenetic assessment was performed at the time of evaluation for this reporting period, select “yes” and continue with question 127.

If no cytogenetic assessments were performed, check “no” and continue with question 135.

**Question 127: Was the disease status assessed via FISH?**

FISH, fluorescence in situ hybridization, is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in plasma cell disorders. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells.

Indicate if FISH studies were obtained at the time of evaluation for this reporting period. If FISH studies were obtained, select “yes” and continue with question 128.

If no FISH studies were obtained, select “no” and continue with question 131.
Question 128: Date assessed:

Enter the date of FISH assessment at the time of evaluation for the reporting period. Report the date the sample was collected for the laboratory.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 129: Was disease detected?

Indicate if evidence of disease was detected on the sample sent for FISH assessment. If FISH results were consistent with evidence of disease, check “yes” and continue with question 130.

If FISH results were not consistent with evidence of disease, check “no” and continue with question 131.

Question 130: Was the status considered a disease relapse or progression?

Indicate if the FISH abnormalities were considered to be relapsed or progressive disease. Criteria for cytogenetic relapse or progression are established by clinical judgment, and should reflect the clinical decision of the transplant physician. A recipient may be reported to have cytogenetic relapse or progression even in the setting of hematologic CR. Criteria for complete remission are based on hematologic (biochemical markers) and pathologic (marrow) characteristics and are independent of cytogenetic markers of disease.

If the recipient has FISH abnormalities that the physician considers to be consistent with cytogenetic relapse, check “yes” and continue with question 131.

If the recipient has FISH abnormalities that the physician does not consider to be consistent with molecular relapse, check “no” and continue with question 131.

Question 131: Was the disease status assessed via conventional cytogenetics?

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Cytogenetics may also be referred to as karyotyping or g-banding.

Indicate if cytogenetic studies were obtained at the time of evaluation for this reporting period. If cytogenetic studies were obtained, select “yes” and continue with question 132.

If no cytogenetic studies were obtained, select “no” and continue with question 135.
**Question 132: Date assessed:**

Enter the date of conventional cytogenetic assessment at the time of evaluation for this reporting period. Report the date the sample was collected for the laboratory.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 133: Was disease detected?**

Indicate if evidence of disease was detected on the sample sent for conventional cytogenetic assessment. If conventional cytogenetic results were consistent with evidence of disease, check “yes” and continue with question 134.

If conventional cytogenetic results were not consistent with evidence of disease, check “no” and continue with question 135.

**Question 134: Was the status considered a disease relapse or progression?**

Indicate if the conventional cytogenetic abnormalities were considered to be relapsed or progressive disease. Criteria for cytogenetic relapse or progression are established by clinical judgment, and should reflect the clinical decision of the transplant physician. A recipient may be reported to have cytogenetic relapse or progression even in the setting of hematologic CR. Criteria for complete remission are based on hematologic (biochemical markers) and pathologic (marrow) characteristics, and are independent of cytogenetic markers of disease.

If the recipient has conventional cytogenetic abnormalities that the physician considers to be consistent with cytogenetic relapse, select “yes” and continue with question 135.

If the recipient has conventional cytogenetic abnormalities that the physician does not consider to be consistent with molecular relapse, check “no” and continue with question 135.

**Question 135: What was the disease status?**

*Not Applicable for Amyloidosis*

Report “Not Applicable (Amyloidosis with no evidence of myeloma)” for question 135 if the recipient’s primary disease is Amyloidosis. Current status of amyloidosis data are captured in questions 137-161.

Report the disease status at the time of evaluation for this reporting period. See the Multiple Myeloma...
Response Criteria section for multiple myeloma and solitary plasmacytoma disease status definitions. See Plasma Cell Leukemia Response Criteria for plasma cell leukemia disease status definitions.

At any response level, if some but not all criteria are met, the disease status should be downgraded to next lower level of response.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).

If the disease response prior to transplant is unknown, select “unknown” and continue with the signature lines.

If the recipient had amyloidosis or POEMS syndrome, but no evidence of myeloma, select “Not Applicable (POEMS or Amyloidosis with no evidence of myeloma)”

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

**Question 136: Date assessed:**

Enter the date of the most recent disease evaluation. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. A PET scan may be used if a PET scan was previously obtained and only in limited circumstances (e.g., plasmacytomas, lytic lesions).

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.
Q137-162: Current Status of Amyloidosis for this Reporting Period (for Amyloid Patients Only)

Complete questions 137-162 for Amyloid patients only. If diagnosis was other than amyloidosis or there is no history of it, continue with signature line.

Current Disease Status
The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

Specify the recipient’s current disease status for each of the following hematologic and organ systems:

Question 137: Specify the recipient’s current hematologic status:

Indicate the recipient’s current hematologic status at the time of evaluation for this reporting period. See Amyloidosis Response Criteria for disease status definitions.

If the recipient's hematologic status was CR, PR, NR, or progressive disease, continue with question 138.

If the recipient’s hematologic status was not assessed during the reporting period, select “not assessed” and continue with question 140. “Not applicable” should rarely, if ever, be chosen.

Questions 138-139: Date assessed:

Indicate if the date of hematologic assessment is “known” or “unknown.” If the date of assessment for hematologic status is known, report the date in question 139. If the date is unknown, select “unknown” and continue with question 140.

Question 140: Specify the recipient's current cardiac status:

Indicate the recipient’s current cardiac status at the time of evaluation for this reporting period. See Amyloidosis Response Criteria for disease status definitions.

If the recipient’s cardiac status was not assessed during the reporting period, select “not assessed.” If the
recipient never had evidence of cardiac involvement in their disease, select “not applicable.”

Questions 141-142: Date assessed:
Indicate if the date of cardiac assessment is “known” or “unknown.” If the date of assessment for cardiac status is known, report the date in question 142. If the date is unknown, select “unknown” and continue with question 143.

Question 143: Was there clinical improvement in GI involvement since the date of last report?
Indicate if there was clinical improvement of GI involvement at the time of evaluation for this reporting period. Judgment is required by a clinician to determine if there is evidence of improvement. If “yes” or “no,” continue with question 144. If “unknown,” continue with question 146.

Questions 144-145: Date assessed:
Indicate if the date the GI involvement was assessed is “known” or “unknown.” If the date the GI response was assessed is known, report the date in question 145. If the date is unknown, select “unknown” and continue with question 146.

Question 146: Specify the recipient’s current hepatic status:
Indicate the recipient’s current hepatic status at the time of evaluation for this reporting period. See Amyloidosis Response Criteria for disease status definitions.
If the recipient’s hepatic status was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of hepatic involvement in their disease, select “not applicable.”

Questions 147-148: Date assessed:
Indicate if the date of hepatic assessment is “known” or “unknown.” If the date of assessment for hepatic status is known, report the date in question 148. If the date is unknown, select “unknown” and continue with question 149.

Question 149: Specify the current status of autonomic neuropathy:
Indicate the recipient’s current autonomic neuropathy status at the time of evaluation for this reporting period. See Amyloidosis Response Criteria for disease status definitions.
If the recipient’s autonomic neuropathy was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of disease related autonomic neuropathy, select “not applicable.”
Questions 150-151: Date assessed:
Indicate if the date of autonomic neuropathy assessment is “known” or “unknown.” If the date of assessment for autonomic neuropathy status is known, report the date in question 151. If the date is unknown, select “unknown” and continue with question 152.

Question 152: Specify the current status of peripheral neuropathy:
Indicate the recipient’s current peripheral neuropathy status at the time of evaluation for this reporting period. See Amyloidosis Response Criteria for disease status definitions.
If the recipient’s peripheral neuropathy was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of disease related peripheral neuropathy, select “not applicable.”

Questions 153-154: Date assessed:
Indicate if the date of autonomic neuropathy assessment is “known” or “unknown.” If the date of assessment for autonomic neuropathy status is known, report the date in question 154. If the date is unknown, select “unknown” and continue with question 155.

Question 155: Specify the recipient’s current renal status:
Indicate the recipient’s current renal status at the time of evaluation for this reporting period. See Amyloidosis Response Criteria for disease status definitions.
If the recipient’s renal status was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of renal involvement in their disease, select “not applicable.”

Questions 156-157: Date assessed:
Indicate if the date of hepatic assessment is “known” or “unknown.” If the date of assessment for hepatic status is known, report the date in question 157. If the date is unknown, select “unknown” and continue with question 158.

Questions 158-159: Was any other system assessed for current status?
Indicate if any other system was assessed at the time of evaluation for the reporting period. If the recipient had other site involvement reported in questions 179-185 of the Pre-HCT Plasma Cell Disorder form (Form 2016) and that site was assessed, the status should be reported here.
Indicate the involved system/site in question 159.
Question 160: Specify the current status of this system:
Indicate if the recipient’s current response is “response,” “no response/stable disease,” “progressive disease,” or “not applicable.”

Questions 161-162: Date assessed:
Indicate if the date the other site/system was assessed at the time of evaluation for the reporting period is “known” or “unknown.” If the other site/system response is known, report the date in question 162. If the date is unknown, select “unknown” and continue with the signature lines.
2018/2118: Hodgkin and Non-Hodgkin Lymphoma

Hodgkin lymphoma (HL or Hodgkin disease) is a cancer of the immune system that is marked by the presence of a type of cell called the Reed-Sternberg cell. The two major types of Hodgkin lymphoma are classical Hodgkin lymphoma (90-95% of cases) and nodular lymphocyte-predominant Hodgkin lymphoma (5-10% of cases).

Classical Hodgkin lymphoma can be further subdivided into four histologic subtypes: nodular sclerosis (NS), mixed cellularity (MC), lymphocyte deplete (LD), and lymphocyte rich (LR). Symptoms include the painless enlargement of lymph nodes, spleen, or other immune tissue. Generalized pruritus is also common and may precede the diagnosis by months. The most common sites of involvement include cervical, supraclavicular, and mediastinal lymph nodes. Central nervous system involvement may occur in rare cases. Other symptoms include fever, weight loss, fatigue, and/or night sweats.

Non-Hodgkin lymphoma (NHL) is a large group of cancers derived from lymphocytes (white blood cells). Non-Hodgkin lymphomas can occur at any age and are often marked by enlarged lymph nodes, fever, night sweats, and weight loss. There are many different types of non-Hodgkin lymphoma. These types can be divided into aggressive (fast-growing), intermediate, or indolent (slow-growing), and can develop from either B-cells or T-cells.

Lymphomas that occur after allogeneic bone marrow or stem cell transplantation are usually B-cell non-Hodgkin lymphomas and are collectively known as post-transplant lymphoproliferative disorders (PTLD).

Table 1. How does HL differ from NHL?

<table>
<thead>
<tr>
<th></th>
<th>HL</th>
<th>NHL</th>
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</thead>
<tbody>
<tr>
<td>Subtypes</td>
<td>2</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Peak Age</td>
<td>20s</td>
<td>Over age 60</td>
</tr>
</tbody>
</table>

Acute Lymphoblastic Leukemia / Lymphoma

Due to the aggressive nature of precursor T-cell and precursor B-cell lymphoblastic lymphoma (or lymphoma / leukemia), the primary disease reported for recipients with these malignancies should be acute lymphoblastic leukemia (Precursor T-cell ALL or Precursor B-cell ALL).
Cases/year  |  8,000 |  60,000  
Common Sites  |  Neck, mediastinum | Various  
Severity of Symptoms  |  Usually mild | Often severe  
5-Year Survival Rate  |  > 80% | Varies

Graphic 1 shows the development of B-cells from stem cells in the bone marrow to memory B-cells and plasma cells in the lymphoid tissue. Neoplasms may develop at different points during B-cell development, including diffuse large B-cell lymphoma from germinal center B-cells or mantle cell lymphoma from memory B-cells.

**Graphic 1. B-cell Development.**

Lymphoma Response Criteria
2018: LYM Pre-HCT
2118: LYM Post-HCT
Lymphoma Response Criteria

Metabolic Criteria

Complete Remission (CR)

Complete metabolic remission requires all of the following:

- A score of 1, 2, or 3 with or without a residual mass on a PET 5 point scale; and
- Disappearance of any previously non-measured lesions; and
- No new lesions; and
- No evidence of FDG-avid disease in the marrow.

Partial Remission

Partial metabolic remission requires all of the following:

- Score 4 or 5 on a PET 5 point scale with reduced uptake compared with baseline; and
- No new lesions.

Stable Disease

Does not meet metabolic criteria for complete remission, partial remission, or progressive disease.

Progressive Disease (after Partial Remission, Stable Disease), Relapsed Disease (after Complete Remission)

Metabolic progression or relapse requires at least one of the following:

- Score 4 or 5 on a PET 5 point scale with increased uptake compared with baseline; or
- Any new FDG-avid foci consistent with lymphoma; or
- New or recurrent FDG avid foci in the bone marrow.

Radiographic Response Criteria

The following acronyms are used in the radiographic response criteria provided below:
**LDi**: longest transverse diameter of a lesion  
**SDi**: shortest axis perpendicular to the LDi  
**SPD**: sum of the product of the perpendicular diameters for multiple lesions  
**PPD**: cross product of the LDi and perpendicular diameter

**Complete Remission (CR)**

Complete radiographic remission requires all of the following:

- All target nodes / nodal masses must have regressed as measured by CT to ≤ 1.5 cm in longest diameter; and  
- Disappearance of any previously non-measured lesions; and  
- No extralymphatic sites of disease; and  
- No organomegally.

Normal morphology of **bone marrow** is also required for a complete radiological remission if the marrow was an involved site. Immunohistochemical stains must be negative if morphology is indeterminate.

**Partial Remission**

Partial radiographic remission requires all of the following:

- ≥ 50% decrease in the SPD of up to 6 target measurable nodes and extranodal sites; and  
- No increase in the size of previously non-measurable lesions; and  
- No new lesions.

If **splenomegaly** is present, a > 50% decrease in spleen length is also required to report a partial radiological remission.

**Stable Disease**

Does not meet radiographic criteria for complete remission, partial remission, or progressive disease.

**Progressive Disease (after Partial Remission, Stable Disease), Relapsed Disease (after Complete Remission)**

Radiographic progression or relapse requires at least one of the following:

- An individual node must be abnormal with:  
  - LDi >1.5 cm; and
- ≥ 50% increase from nadir in the PPD; or
- An increase in LDi or SDi from nadir
  - ≥ 0.5 cm increase in LDi or SDi from nadir for any lesion ≤ 2 cm; or
  - ≥ 1.0 cm increase in LDi or SDi from nadir for any lesion > 2 cm; or
- A 50% increase in spleen length compared to its prior increase beyond baseline; or
- New or recurrent splenomegally; or
- Clear progression of pre-existing non-measured lesions; or
- Regrowth of any previously resolved lesions; or
- A new node > 1.5 cm in any axis; or
- A new extranodal site > 1.0 cm in any axis or if < 1.0 cm in any axis, its presence must be unequivocally attributable to lymphoma; or
- Assessable disease of any size unequivocally attributable to lymphoma; or
- New or recurrent involvement of the bone marrow.

1 For lesions too small to measure on CT, assign 5mm x 5mm as the default value and then 0 mm x 0 mm when the lesion is no longer visible. For a node >5 mm x 5 mm, but smaller than normal, use the actual measurement of the node for calculations.


Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/20/2018</td>
<td>LYM Response Criteria</td>
<td>Modify</td>
<td>Modified the response criteria to show the metabolic response criteria first and then the radiographic response criteria for ease of use.</td>
</tr>
<tr>
<td>05/10/2018</td>
<td>LYM Response Criteria</td>
<td>Add</td>
<td>Added “Relapsed Disease” to “Progressive Disease” criteria and included clarification on when to report these disease status.</td>
</tr>
<tr>
<td>Date</td>
<td>LYM Response Criteria</td>
<td>Action</td>
<td>Notes</td>
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</tbody>
</table>
Complete this form for recipients whose primary disease, reported on the Disease Classification Form (Form 2402), is Hodgkin Lymphoma (HL) or non-Hodgkin Lymphoma (NHL). One exception is Waldenstrom’s macroglobulinemia / lymphoplasmacytic lymphoma, for which, a Waldenstrom’s Macroglobulinemia Form (Form 2019) will be completed instead.

**Acute Lymphoblastic Leukemia / Lymphoma**
Due to the aggressive nature of precursor B- and precursor T-cell lymphoblastic lymphoma (or lymphoma/leukemia), the primary disease to report for recipients with these malignancies should be acute lymphoblastic leukemia (B- lymphoblastic leukemia/lymphoma or early T-cell precursor lymphoblastic leukemia). If the recipient’s primary disease is acute lymphoblastic lymphoma, complete an ALL Pre-Infusion Data Form (Form 2011). Do not complete a LYM Pre-Infusion Data Form (Form 2018).

Is this the report of a second or subsequent transplant or cellular therapy for the same disease?
Report “No” and go to question 1 in any of the following scenarios:
- this is the first infusion reported to the CIBMTR;
- this is the first infusion given to treat the recipient’s current disease subtype; or
- this is a second or subsequent infusion for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior infusion, prior infusion was autologous with no consent, etc.).

If this is a report of a second or subsequent infusion for the same disease subtype and this baseline lymphoma disease insert was completed previously, report “Yes” and go to question 166.

Links to sections of form:
- Q1-55: Disease Assessment at Diagnosis
- Q56-68: Laboratory Studies at Diagnosis
- Q69-81: Assessment of Nodal and Organ Involvement at Diagnosis
- Q82-139: Disease Assessment at Transformation
- Q140-152: Laboratory Studies at Transformation
- Q153-165: Assessment of Nodal and Organ Involvement at Transformation
- Q166-223: Pre-HCT or Pre-Infusion Therapy
- Q224-232: Disease Assessment at the Failure of the 1st Line of Therapy
- Q233-287: Disease Assessment at the Last Evaluation Prior to the Start of the Preparative Regimen / Infusion
Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
</table>
Q1-55: Disease Assessment at Diagnosis

Question 1-2: Specify the lymphoma histology (at diagnosis)

If the recipient had **CLL** which transformed into **DLBCL** (Richter’s transformation) or **Hodgkin lymphoma (HL)**, report the DLBCL or HL histology in question 1 and the transformation from CLL in question 82. If a transformation did occur, also complete a CLL Pre-Infusion Data Form (Form 2013).

If the recipient has **multiple types of lymphoma at diagnosis or has a transformation**, report the least aggressive lymphoma histology at diagnosis (question 1) and of the most aggressive lymphoma as a transformation (questions 83-85). The occurrence of transformation and the resultant histology must be determined by a physician.

Indicate the lymphoma histology at diagnosis. Report the specific histology in question 2 if any of the options reported for question 1 are:

- Other B-cell lymphoma
- Other T-cell / NK-cell lymphoma

**Question 3: Assignment of DLBCL (germinal center B-cell type vs. Activated B-cell type) subtype was based on:**

Only complete question 3 if one of the following was reported as the histology at diagnosis (question 1):

- Diffuse, large B-cell lymphoma- Germinal center B-cell type
- Diffuse, large B-cell lymphoma- Activated B-cell type (non-GCB)

Otherwise, skip question 3 and go to question 4.

Report the method(s) used to confirm the histology at diagnosis. Check all that apply. If the method of diagnosis is not clear from the available documentation, report “Unknown method.”

**Question 4: Was documentation submitted to the CIBMTR? (e.g., path report from diagnosis)**

Indicate whether documents were attached to support / clarify the center’s responses to questions 1-3. Attaching pathology reports at diagnosis in FormsNet3SM may prevent future data queries. For further instructions on how to attach documents in FormsNet3SM, refer to the [Training Guide](#).
Question 5: Were immunohistochemical stains obtained? (at diagnosis, prior to any transformation)

Immunohistochemical staining (IHC) is a process where tissue samples are treated with antibodies and dye. The antibodies bind to specific antigens on the surfaces of the cells, allowing for the identification of those cell surface markers under microscopy. Testing is often documented in the pathology report from the tissue sample, on which, IHC was used.

Report “Yes” and go to question 6 if IHC was done at diagnosis.

If testing was not done or it is not known whether testing was performed, report “No” or “Unknown” respectively and go to question 25.

Questions 6-24: Immunohistochemical stain results

Testing may be performed on multiple sample types at diagnosis. Report testing performed on samples taken from the node / mass, if available. If IHC was not done on the node / mass or the results are not known, report testing performed on the bone marrow instead. Additionally, IHC results are documented differently across hospitals / laboratories. Consult a physician if the results are not clear.

Report “Positive,” “Negative,” or “Unknown” for each marker based on the IHC results at diagnosis. If the report documents “dim” for a specific marker, report this as “Positive.” Report “Unknown” for markers which were not tested or were tested, but the results are not known.

If “Positive” is reported for any of the markers listed below, indicate whether the percent of cells positive for this marker (as determined by IHC) is known. If so, report the percent of cells positive for the specified marker.

- BCL-2
- BCL-6
- C-MYC
- Ki-67

If the percent is documented as a range, report the average. If the percent is documented as less than a specified percent, report the percent specified minus one (e.g., report < 10% as 9%). If the percent is documented as more than a specified percent, report the percent specified plus one. (e.g., report > 90% as 91%).

Question 25: Were cytogenetics tested (karyotyping or FISH)?

Cytogenetics is the study of chromosomes. This assessment involves testing blood or bone marrow for
known chromosomal abnormalities that reflect the recipient’s disease. For more information about cytogenetic testing and terminology, see Appendix C, Cytogenetic Assessments. Indicate whether cytogenetic studies were performed at diagnosis. Do not report any testing performed after treatment was started for the disease histology specified in question 1.

If cytogenetic studies were obtained at diagnosis, report “Yes” and go to question 26.

If cytogenetic studies were not obtained at diagnosis or it is not known whether chromosome studies were performed, report “No” or “Unknown” respectively and go to question 56.

**Question 26-27: Were cytogenetics tested via FISH?**

If FISH studies were performed at diagnosis, report “Yes” for question 26 and indicate whether clonal abnormalities were detected in question 27.

If FISH studies were not performed at this time point, report “No” for question 26 and go to question 51. Examples include: no FISH study performed or FISH sample was inadequate. See Appendix C, Cytogenetic Assessments, for assistance interpreting FISH results.

**Question 28-49: Specify cytogenetic abnormalities (FISH)**

For each abnormality:

- Report “Yes” if FISH testing detected the abnormality at diagnosis.
- Report “No” if FISH testing for the abnormality was done at diagnosis and was negative.
- Report “Not done” if FISH testing for the abnormality was not included or could not be successfully performed (e.g., inadequate sample) at diagnosis.

If a clonal abnormality is detected, but cannot be reported in questions 28-47, report “Yes” for question 48 and specify the abnormality in question 49. If multiple “other abnormalities” were detected, report “see attachment” in question 49 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 50: Was documentation submitted to the CIBMTR? (e.g., FISH report)**

Indicate if a FISH testing report is attached to support the findings reported in questions 26-49. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 51-52: Were cytogenetics tested via karyotyping?**

If karyotyping was performed at diagnosis, report “Yes” for question 51 and indicate whether clonal
abnormalities were detected in question 52.

If karyotyping was not performed at this time point, report “No” for question 51 and go to question 56. Examples include: no karyotyping performed or karyotyping sample was inadequate.

See Appendix C, Cytogenetic Assessments, for assistance interpreting karyotype results.

**Question 53-54: Specify cytogenetic abnormalities (karyotyping)**

Check any abnormalities detected by karyotyping at diagnosis. If karyotyping detected an abnormality that is not specified in question 53, check “Other abnormality” and report the abnormality in question 54. If multiple “other abnormalities” were detected at diagnosis, report “see attachment” for question 54 and attach the karyotyping report to the form. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 55: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping report is attached to support the findings reported in questions 51-54. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.
Q56-68: Laboratory Studies at Diagnosis

Questions 56-68 will be enabled / disabled in FormsNet3SM based on the histology reported in question 1. Reporting instructions for specific questions are provided at the bottom of this page for reference.

All values reported in questions 56-68 must reflect testing performed prior to any treatment for the histology specified in question 1. If testing was not performed near the time of diagnosis (within approximately 30 days) and prior to the initiation of treatment, the center should report “Unknown” for that value.

For each laboratory study, indicate whether the test result was “Known” or “Unknown” at the time of diagnosis. If “Known,” report the result and the unit of measure. If “Known” is reported for LDH (question 66), also specify the upper limit of normal and corresponding unit of measure in question 68.

**Laboratory Studies Enabling / Disabling Rules**

- **Question 56-57 (WBC):** Only answer for mantle cell lymphoma and Hodgkin lymphoma (all histologies).
- **Question 58-59 (hemoglobin):** Only answer for follicular lymphoma (all histologies) and Hodgkin lymphoma (all histologies).
- **Question 60-61 (absolute lymphocyte count):** Only answer for Hodgkin lymphoma (all histologies).
- **Question 62-63 (lymphocytes):** Answer for all histologies.
- **Question 64-65 (serum albumin):** Only answered for Hodgkin lymphoma (all histologies).
- **Question 66-68 (LDH):** Answered for all histologies.
Q69-81: Assessment of Nodal and Organ Involvement at Diagnosis

All values reported in questions 69-81 must reflect testing / evaluations performed prior to any treatment for the histology specified in question 1. If testing / evaluation was not done near the time of diagnosis (within approximately 30 days) and prior to the initiation of treatment, the center should report “Unknown” for that value.

**Question 69-70: Was a PET (or PET/CT) scan performed?**

Positron Emission Tomography (PET) is a type of nuclear medicine imaging in which a patient receives a small amount of radioactively labeled sugar. Because cancer cells absorb sugar more avidly than other cells of the body, the radioactively labeled sugar accumulates in these areas and reveals tumors as bright spots. A PET/CT combines the results of the PET scan along with the results of a CT (computed tomography) scan.

If a PET (or PET/CT) scan was performed at diagnosis, report “Yes” for question 69 and specify whether the scan was positive for lymphoma in question 70. Consult a physician to confirm how complete question 70 if the scan report is unclear.

If a PET or (PET/CT) scan was not performed at diagnosis, report “No” for question 69 and go to question 71.

**Question 71: Did the recipient have known nodal involvement?**

Nodal involvement may be assessed by a physician palpating lymph nodes, pathology from a lymph node biopsy, or radiological assessment (e.g., PET or CT imaging). Report “Yes” and go to question 72 if nodal involvement was detected by any of these methods. Otherwise, report “No” and go to question 75.

**Question 72-73: Specify total number of nodal regions involved**

Lymph node regions or groups occur above and below the diaphragm. Nodal regions include cervical (neck), axillary (underarm), mediastinal (thoracic), mesenteric (abdominal), para-aortic (pelvic),inguinal (groin), epitrochlear (inside of arm just above elbow), and popliteal (back of knee). Indicate the total number of nodal regions with evidence of lymphoma involvement. Refer to Graphic 1 below for identification of nodal areas and specific nodes within each area.

Complete question 72 if the histology at diagnosis (question 1) was not follicular lymphoma. Otherwise,
complete question 73.

**Graphic 1. Nodal Areas**

**Question 74: Specify the size of the largest nodal mass**

Report the size of the largest known nodal mass as measured in centimeters. If the mass is given in three dimensions (for example: 3 cm x 5 cm x 4 cm), report the longest two dimensions.
**Question 75: Was there any known extranodal or splenic involvement? (at diagnosis, prior to any transformation)**

Extranodal refers to the presentation of lymphoma outside of the lymph nodes. Common areas of extranodal involvement may include bone, gastrointestinal tract, and skin. Splenic involvement in lymphoma is also common. It is usually evidenced by enlargement of the spleen (splenomegaly). Splenic or other extranodal involvement is most often detected by imaging techniques or pathological findings.

If extranodal or splenic involvement was identified, indicate “Yes” and go to question 76.

If there was no evidence of extranodal or splenic involvement or it is not known, report “No” or “Unknown” respectively and go to question 78.

**Questions 76-77: Specify site(s) of involvement:**

Check each site with known lymphomatous involvement. If an involved site was documented, but is not listed as an option for question 76, check “Other site” and report all other sites of lymphomatous involvement in question 77.

**Question 78: Stage of organ involvement: (at diagnosis)**

Use the staging criteria below to indicate the organ involvement at diagnosis. If staging at diagnosis is not available or unknown, select “Unknown.”

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Involvement of a single lymph node region or of a single extralymphatic organ or site</td>
</tr>
<tr>
<td>Stage II</td>
<td>Involvement of two or more lymph node regions on same side of diaphragm, or localized involvement of an extralymphatic organ or site, and one or more lymph node regions on same side of diaphragm</td>
</tr>
<tr>
<td>Stage III</td>
<td>Involvement of lymph node regions on both sides of diaphragm, which may also be accompanied by localized involvement of extralymphatic organ or site, the spleen, or both</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Diffuse or disseminated involvement of one or more extralymphatic organs in tissues with or without associated lymph node enlargement/involvement</td>
</tr>
</tbody>
</table>

**Graphic 2. Lymphoma Staging**

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Question 79: Were systemic symptoms (B symptoms) present?

Systemic symptoms, also known as “B” symptoms, are defined as follows:

- unexplained fever > 38°C (100.4°F)
- night sweats
- unexplained weight loss of > 10% of body weight over 6 months
Evidence of systemic symptoms is significant because it may indicate the presence of disease in parts of the body not identified using standard testing methods. The presence or absence of systemic symptoms may be indicated in the staging (e.g., II-B or II-A).

If there was evidence of systemic symptoms at diagnosis, select “Yes”. Otherwise, select “No.”

If documentation is not clear or is not available to determine if systemic symptoms were present at diagnosis or prior to first therapy, select “Unknown.”

**Question 80-81: ECOG score (at diagnosis)**

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. If a performance score is not documented in the source documentation (e.g., inpatient progress note, physician’s clinic note), data management professionals should not assign a performance score based on analysis of available documents. Rather, a physician should provide documentation of the performance score.

If the performance score has been documented using Karnofsky or Lansky scales, refer to Appendix L: Karnofsky / Lansky Performance Status for assistance converting the score to the ECOG scale.

Report whether the recipient’s ECOG score at diagnosis is known in question 80. If “Known,” report the score in question 81. Otherwise, go to question 82.

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Q82-139: Disease Assessment at Transformation

Question 82: Is the lymphoma histology reported at diagnosis a transformation from CLL?

CLL may evolve to a more aggressive diffuse large B-cell lymphoma (DLBCL). This is commonly referred to as Richter’s syndrome or Richter’s transformation. Note, CLL may also transform to Hodgkin lymphoma.

If recipient’s lymphoma histology at diagnosis (question 1) is transformation from CLL, report “Yes” and go to question 166. Also, complete a CLL Pre-Infusion Data Form (Form 2013). Otherwise, report “No” and go to question 83.

Question 83-85: Did the recipient transform to a different lymphoma histology between diagnosis and the start of the preparative regimen / infusion? (not CLL)

Transformation may occur when a slow-growing lymphoma with an indolent clinical history changes to a more aggressive lymphoma. An example of a common transformation would include follicular lymphoma evolving to a diffuse large B-cell lymphoma (DLBCL).

If the recipient has multiple types of lymphoma at diagnosis or has a transformation, report the least aggressive lymphoma histology at diagnosis (question 1) and the most aggressive lymphoma as a transformation (questions 83-85). The occurrence of transformation and the resultant histology must be determined by a physician.

If the recipient’s lymphoma histology transformed between diagnosis and the start of the preparative regimen (or date of infusion if no preparative regimen), report “Yes” for question 83 and specify the histology at transformation in question 84. Report the specific histology in question 85 if any of the following options were reported for question 84:

- Other B-cell lymphoma
- Other T-cell / NK-cell lymphoma

If a transformation did not occur after or concurrently with diagnosis, indicate “No” for question 83 and go to question 166.

Question 87: Was the date of transformation the same as the date of diagnosis?

If a concurrent diagnosis (multiple histologies) has occurred, it is not necessary to repeat the diagnosis
information in the transformation section of the report.

Report “Yes” and go to question 166 if the transformation was identified at the time of the original lymphoma diagnosis.

Report “No” and go to question 88 if the transformation was identified after the date of the original lymphoma diagnosis.

**Question 88: Date of transformation:**

Report the date the transformation was diagnosed. Enter the date the sample was collected for examination. If the date of transformation was determined at an outside center, and no documentation of a pathological or laboratory assessment is available, a dictated date within a physician note may be reported.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, [General Guidelines for Completing Forms](#).

**Question 89: Were immunohistochemical stains obtained? (at transformation)**

See [question 5](#) for a description of immunohistochemical stains (IHC).

Report “Yes” and go to question 90 if IHC was done at transformation.

If testing was not done or it is not known whether testing was performed, report “No” or “Unknown” respectively and go to question 109.

**Questions 90-108: Immunohistochemical stain results**

Testing may be performed on multiple sample types at transformation. Report testing performed on samples taken from the node / mass, if available. If IHC was not done on the node / mass or the results are not known, report testing performed on the bone marrow instead. Additionally, IHC results are documented differently across hospitals / laboratories. Consult a physician if the results are not clear.

Report “Positive,” “Negative,” or “Unknown” for each marker based on the IHC results at transformation. If the report documents “dim” for a specific marker, report this as “Positive.” Report “Unknown” for markers which were not tested or were tested, but the results are not known.

If “Positive” is reported for any of the markers listed below, also indicate if the percent of cells positive for this marker (as determined by IHC) is known. If so, report the percent of cells positive for the specified marker.
• BCL-2
• BCL-6
• C-MYC
• Ki-67

If the percent is documented as a range, report the average. If the percent is documented as less than a specified percent, report the percent specified minus one (e.g., report <10% as 9%). If the percent is documented as more than a specified percent, report the percent specified plus one. (e.g., report >90% as 91%).

**Question 109: Were cytogenetics tested (karyotyping or FISH)?**

Cytogenetics is the study of chromosomes. This assessment involves testing blood or bone marrow for known chromosomal abnormalities that reflect the recipient’s disease. For more information about cytogenetic testing and terminology, see Appendix C, Cytogenetic Assessments. Indicate whether cytogenetic studies were performed at transformation.

If cytogenetic studies were obtained at transformation, report “Yes” and go to question 110.

If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, report “No” or “Unknown” respectively and go to question 140.

**Question 110-111: Were cytogenetics tested via FISH?**

If FISH studies were performed at transformation, report “Yes” for question 110 and indicate whether clonal abnormalities were detected in question 111.

If FISH studies were not performed at this time point, report “No” for question 110 and go to question 135. Examples include: no FISH study performed or FISH sample was inadequate.

**Question 112-133: Specify cytogenetic abnormalities (FISH)**

For each abnormality:

- Report “Yes” if FISH testing detected the abnormality at transformation.
- Report “No” if FISH testing for the abnormality was done at transformation and was negative.
- Report “Not done” if FISH testing for the abnormality was not attempted or could not be successfully performed (e.g., inadequate sample) at transformation.

If a clonal abnormality is detected, but cannot be reported in questions 112-131, report “Yes” for question
132 and specify the abnormality in question 133. If multiple “other abnormalities” were detected, report “see
attachment” in question 133 and attach the final report(s) for any other abnormalities detected. For further
instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 134: Was documentation submitted to the CIBMTR? (e.g., FISH report)
Indicate if a FISH testing report is attached to support the findings reported in questions 110-133. For
further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 135-136: Were cytogenetics tested via karyotyping?
If karyotyping was performed at transformation, report “Yes” for question 135 and indicate whether clonal
abnormalities were detected in question 136.
If karyotyping was not performed at this time point, report “No” for question 135 and go to question 140.
Examples include: no karyotyping performed or karyotyping sample was inadequate.

Question 137-138: Specify cytogenetic abnormalities (karyotyping)
Check any abnormalities detected by karyotyping at transformation. If karyotyping detected an abnormality
that is not specified in question 137, check “Other abnormality” and report the abnormality in question 138. If
multiple “other abnormalities” were detected at transformation, report “see attachment” for question 138 and
attach the karyotyping report to the form. For further instructions on how to attach documents
inFormsNet3SM, refer to the Training Guide.

Refer to Appendix C, Cytogenetic Assessments for assistance interpreting karyotyping results.

Question 139: Was documentation submitted to the CIBMTR?
Indicate if a karyotyping report is attached to support the findings reported in questions 135-139. For further
instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.
Q140-152: Laboratory Studies at Transformation

Questions 140-152 will be enabled / disabled in FormsNet3SM based on the histology reported in question 84. Reporting instructions for specific questions are provided at the bottom of this page for reference.

All values reported in questions 140-152 must reflect testing performed prior to any treatment for the histology specified in question 84. If testing was not performed near the time of transformation (within approximately 30 days) and prior to the initiation of treatment, the center should report “Unknown” for that value.

For each laboratory study, indicate whether the test result was “Known” or “Unknown” at the time of transformation. If “Known,” report the result and the unit of measure. If “Known” is reported for LDH (question 150), also specify the upper limit of normal and corresponding unit of measure in question 152.

Laboratory Studies Enabling / Disabling Rules

- **Question 140-141 (WBC)**: Only answer for mantle cell lymphoma and Hodgkin lymphoma (all histologies).
- **Question 142-143 (hemoglobin)**: Only answer for follicular lymphoma (all histologies) and Hodgkin lymphoma (all histologies).
- **Question 144-145 (absolute lymphocyte count)**: Only answer for Hodgkin lymphoma (all histologies).
- **Question 146-147 (lymphocytes)**: Answer for all histologies.
- **Question 148-149 (serum albumin)**: Only answered for Hodgkin lymphoma (all histologies).
- **Question 150-152 (LDH)**: Answered for all histologies.
Q153-165: Assessment of Nodal and Organ Involvement at Transformation

All values reported in questions 153-165 must reflect testing / evaluations performed prior to any treatment for the histology specified in question 84. If testing / evaluation was not done near the time of transformation (within approximately 30 days) and prior to the initiation of treatment, the center should report “Unknown” for that value.

**Question 153-154: Was a PET (or PET/CT) scan performed?**

See the instructions for questions 69-70 for a description of PET scans.

If a PET (or PET/CT) scan was performed at transformation, report “Yes” for question 153 and specify whether the scan was positive for lymphoma in question 154. Consult a physician to confirm how complete question 154 if the scan report is unclear.

If a PET or (PET/CT) scan was not performed at transformation, report “No” for question 153 and go to question 155.

**Question 155: Did the recipient have known nodal involvement?**

Nodal involvement may be assessed by a physician palpating lymph nodes, pathology from a lymph node biopsy, or radiological assessment (e.g., PET or CT imaging). Report “Yes” and go to question 156 if nodal involvement was detected by any of these methods. Otherwise, report “No” and go to question 159.

**Questions 156-157: Specify total number of nodal regions involved**

See the instructions for questions 72-73 for general information regarding nodal involvement.

Complete question 156 if the histology at transformation (question 84) was not follicular lymphoma. Otherwise, complete question 157.

**Question 158: Specify the size of the largest nodal mass**

Report the size of the largest known nodal mass as measured in centimeters. If the mass is given in three dimensions (for example: 3 cm x 5 cm x 4 cm), report the longest two dimensions.
Question 159: Was there any known extranodal or splenic involvement? (at transformation)

Refer to the instructions for question 75 for a description of extranodal and splenic involvement.

If extranodal or splenic involvement was identified, indicate “Yes” and continue with question 160.

If there was no evidence of extranodal or splenic involvement or it is not known, report “No” or “Unknown” respectively and go to question 162.

Questions 160-161: Specify site(s) of involvement:

Check each site with known lymphomatous involvement. If an involved site was documented, but is not listed as an option for question 160, check “Other site” and report all other sites of lymphomatous involvement in question 161.

Question 162: Stage of organ involvement: (at transformation)

Refer to Table 1 as well as Graphics 2 and 3 for information regarding organ involvement / staging. Indicate the stage of organ involvement at transformation. If this information is not available or not known, select “Unknown.”

Question 163: Were systemic symptoms (B symptoms) present?

See the instructions for question 79 for a description of systemic symptoms. Indicate whether systemic symptoms were present at transformation. If documentation is not clear or is not available, select “Unknown.”

Question 164-165: ECOG score (at transformation)

See the instructions for questions 80-81 for more information about reporting ECOG scores. Indicate whether the recipient’s ECOG score at transformation is known in question 164. If “Known,” report the score in question 165. Otherwise, go to question 166.
Q166-223: Pre-HCT Therapy

The FormsNet3SM application allows questions 167-233 to be reported multiple times. Complete these questions for each line of therapy administered on or after the date of diagnosis of lymphoma and prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given). When submitting the paper version of the form for more than one line of therapy, copy the “Pre-HCT or Pre-Infusion Therapy” section and complete a copy of the section for each line of therapy administered.

If this is a subsequent infusion and the 2018 was completed for the previous infusion, lines of therapy do not need to be reported in duplication on the subsequent 2018. Please report from post previous infusion to time of preparative regimen (or infusion) for the current HCT or cellular therapy. If no 2018 was completed previously, all lines of therapy from original diagnosis to current preparative regimen (or infusion) will have to be completed.

A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.). If a recipient’s disease status changes resulting in a change to treatment, a new line of therapy should be reported. Additionally, if therapy is changed because a favorable disease response was not achieved, a new line of therapy should be reported.

Question 166: Was therapy given?

Indicate if the recipient received treatment for their primary disease between diagnosis and the start of the preparative regimen (or infusion if no preparative regimen was given). This includes systemic chemotherapy, immunotherapy, intrathecal therapy, radiation therapy, surgery, and cellular therapies. Do not report a prior HCT in questions 166-223. If therapy was given to treat lymphoma during the time frame indicated above, report “Yes” and go to question 167. If reporting “No” or “Unknown,” go to question 233.

Question 167: Systemic therapy

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein / central line or given orally. Do not report intrathecal therapy as systemic therapy. If systemic therapy was administered as part of the line of therapy being reported, report “Yes” and go to question 168. If not, report “No” and go to question 180.

Question 168-169: Date therapy started

Indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 169. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in
the General Instructions, General Guidelines for Completing Forms.

If the date therapy started is “Unknown,” go to question 170.

**Question 170-171: Date therapy stopped**

Indicate if therapy stop date is “Known” or “Unknown.” If the therapy is being given in cycles, report the date the recipient **started the last cycle** for this line of therapy in question 171. Otherwise, report the final administration date for the therapy being reported. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy stopped is “Unknown,” go to question 172.

**Question 172-173: Number of cycles**

Systemic therapy is usually administered in cycles with rest periods in-between. This enables cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from the damage sustained during therapy. A cycle can last one or more days and can repeat weekly, bi-weekly, or monthly. A single systemic therapy course may consist of multiple cycles.

Indicate whether the number of cycles is “Known” or “Unknown.” If “Known,” enter the number of cycles the recipient received in question 173. If “Unknown,” go to question 174.

If therapy is not being administered in cycles (e.g., daily chemotherapy), report “Unknown” for question 172 and go to question 174.

**Question 174-175: Was a standard drug regimen given?**

Systemic chemotherapy / immunotherapy may involve administration of multiple drugs / agents during the line of therapy. Rather than reporting each drug separately, standard combination regimens should be reported using the options in question 175 when available. Review the regimen options provided in question 175. If the recipient’s line of therapy included one of the regimens listed, report “Yes” for question 174 and indicate the regimen that was given in question 175. If the recipient did not receive one of the standard regimens provided in question 175 as part of the line of therapy being reported, indicate “No” for question 174 and go to question 176.

Only one regimen may be reported for question 175. Generally, each regimen should be reported as a separate line of therapy. If the recipient received a regimen specified in question 175 as well as additional systemic therapy drugs as part of the line of therapy being reported, indicate the standard regimen in question 175 and report the additional drugs in questions 176-178.
The BEACOPP regimen may be reported as standard or escalated dosing. The center should choose the option most consistent with their treatment guidelines. If it is not clear which option to report, consult the transplant physician.

If none of the standard regimens specified in question 175 were given as part of the line of therapy being reported, indicate “No” for question 174 and go to question 176.

**Question 176-178: Were systemic drugs given?**

Questions 176-178 are intended to capture systemic therapy drugs / agents not already reported in questions 174-175. If part or all of the recipient’s regimen can be reported in questions 174-175, report them in those questions and do not report them again in questions 176-178. If all systemic therapy drugs given as part of the line of therapy being reported were included in the regimen indicated in question 175, report “No” for question 176 and go to 179.

If the recipient received systemic chemotherapy drugs not already reported in questions 174-175 as part of the line of therapy being reported, report “Yes” for question 176 and specify the chemotherapy drug(s) in questions 177-178. Otherwise, report “No” for question 176 and go to question 179.

If the center needs to report a systemic chemotherapy drug (or drugs) in question 177, but it is not listed as an option, report “Other systemic therapy” and use question 178 to specify any drugs not already reported. Only report systemic chemotherapy drugs in questions 176-178.

**Question 179: Was this line of therapy given for stem cell mobilization (priming)?**

Report “Yes” if this line of therapy was given for stem cell priming. For example, R-ICE (rituximab, ifosfamide, carboplatin, and etoposide) may be used in a lymphoma patient to collect their peripheral blood stem cells (PBSCs) as they recover their white blood count. Report “No” if this line of therapy was not given for stem cell priming.

**Question 180: Intrathecal therapy**

Intrathecal therapy refers to chemotherapy administered via lumbar puncture to treat or prevent leukemic blasts in the central nervous system. Report “Yes” and go to question 181 if intrathecal therapy was given as part of the line of therapy being reported. Report “No” and go to question 188 if intrathecal therapy was not given as part of the line of therapy being reported.

**Question 181: Reason for intrathecal therapy**

Intrathecal therapy may be given to prevent disease in the central nervous system. It may also be given as treatment once disease has been detected. Indicate the reason intrathecal therapy was given. Report
“Unknown” if the reason cannot be determined.

**Question 182-183: Date therapy started**

Indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 183. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy started is “Unknown,” go to question 184.

**Question 184-185: Date therapy stopped**

Indicate if therapy stop date is “Known” or “Unknown.” If “Known,” report the final administration date in question 185. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy stopped is “Unknown,” go to question 186.

**Question 186-187: Specify intrathecal therapy**

Indicate the drug given as intrathecal therapy during the line of therapy being reported. If the drug is not listed as an option in question 186, report “Other intrathecal therapy” and specify the drug in question 187.

**Question 188: Intraocular therapy**

Intraocular therapy refers to chemotherapy administered via injection to the eye. Report “Yes” and go to question 189 if intraocular therapy was given as part of the line of therapy being reported. Report “No” and go to question 196 if intraocular therapy was not given as part of the line of therapy being reported.

**Question 189: Reason for intraocular therapy**

Intraocular therapy may be given to prevent disease in the eye. It may also be given as treatment once disease has been detected. Indicate the reason intraocular therapy was given. Report “Unknown” if the reason cannot be determined.

**Question 190-191: Date therapy started**

Indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 191. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.
If the date therapy started is “Unknown,” go to question 192.

**Question 192-193: Date therapy stopped**

Indicate if therapy stop date is “Known” or “Unknown.” If “Known,” report the final administration date in question 193. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy stopped is “Unknown,” go to question 194.

**Question 194-195 Specify intraocular therapy**

Indicate the drug given as intraocular therapy during the line of therapy being reported. If the drug is not listed as an option in question 194, report “Other intraocular therapy” and specify the drug in question 195.

**Question 196: Radiation therapy**

Radiation therapy utilizes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. Radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes. Radiation therapy may be given in conjunction with systemic chemotherapy or as a separate line of therapy.

If radiation therapy was given during or adjacent to administration of systemic therapy, report them together as single line of therapy on the form (i.e., one copy of questions 167-223). Otherwise, capture the radiation treatment as a separate line of therapy.

If the recipient received radiation therapy as part of the line of therapy being reported, report “Yes” and go to question 197. If not, report “No” and go to question 209.

**Question 197-198: Date therapy started**

Indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 198. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy started is “Unknown,” go to question 199.

**Question 199-200: Date therapy stopped**

Indicate if therapy stop date is “Known” or “Unknown.” If “Known,” report the final administration date in question 200. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.
If the date therapy stopped is “Unknown,” go to question 201.

**Question 201: What was the extent of the radiation field?**
Indicate if the recipient received radiation to each site listed.

**Question 202-203: Specify site(s) of radiation therapy**
Report all sites of radiation therapy administered between the start and stop dates reported in questions 197-200. If “Other site” is reported, specify all other sites in question 203.

**Question 204: Dose per fraction:**
Enter the dose per fraction in either grays (Gy) or centigrays (cGy).

**Question 205: Total number of fractions:**
Enter the total number of fractions (treatments) of radiation that were administered. The recipient may receive more than one fraction per day (hyperfractionation).

**Question 206: Total dose: (dose per fraction X total number of fractions)**
Enter the total dose of radiation given. If radiation was given as a single dose, the amount of radiation delivered in the single dose constitutes the total dose. If the radiation was given in fractionated doses, multiply the total number of fractions by the dose per fraction to determine the total dose. Enter the total dose of radiation in either grays (Gy) or centigrays (cGy).

**Example:**
Radiation Order: TBI, 200 cGy/day for three days (3 doses)
Total dose: 200 cGy x 3 doses = 600 cGy
Report “Total Dose” as: 600 cGy

The dose per fraction (question 204) multiplied by the total number of fractions (question 205) must be equal to the total dose reported in question 206.

**Question 207-208: Specify technique**
Indicate the technique used to deliver radiation therapy. If the technique was not “Electron beam” or “Proton,” report “Other” and specify the technique in question 208.

**Question 209: Surgery**
If the recipient underwent surgical treatment for lymphoma as part of the line of therapy being reported,
indicate “Yes” and go to question 210. If the recipient did not undergo surgical treatment, report “No” and go to question 215.

Do not report the initial diagnostic biopsy, even if surgery was required, as pre-HCT therapy.

**Question 210-211: Date of surgery**

Indicate whether the surgery date is “Known” or “Unknown.” If the date is known, report it in question 211. If the date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).

If the date is “Unknown,” go to question 212.

**Question 212-214: Specify site(s) of surgery:**

Indicate the site(s) of the surgery. Report “Yes” or “No” for “Splenectomy” and for “Other site.” If “Other site” is selected, specify all other sites in question 214

**Question 215: Photopheresis**

Photopheresis involves removing blood from the body, exposing it to psoralen and ultraviolet light, and then reinfusing it. Indicate whether photopheresis was administered as part of the line of therapy being reported.

Report “Yes” if the recipient received photopheresis as part of the line of therapy being reported. If not, report “no”.

**Question 216: Cellular Therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “Yes” if the recipient received cellular therapy as part of the line of therapy being reported. If not, report “No.”

**Question 217: Best response to line of therapy by CT (radiographic) criteria:**

Indicate the best response to the line of therapy using the international working group radiographic criteria provided in [LYM Response Criteria](#) section of the Forms Instruction Manual. If the recipient had palpable disease on a physical exam, those results can be reported in the CT (radiographic) criteria. Report “Not assessed” if no applicable assessments were performed after the line of therapy being reported and prior to the initiation of any new therapy.
**Question 218: Date assessed**

Report the date of the CT scan used to determine the response reported in question 217. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, *General Guidelines for Completing Forms*.

**Question 219: Best response to line of therapy by PET (metabolic) criteria:**

Indicate the best response to the line of therapy using the international working group metabolic criteria provided in *LYM Response Criteria* section of the Forms Instruction Manual. Report “Not assessed” if a PET scan was not performed after the line of therapy being reported and prior to the initiation of any new therapy.

**Question 220: Date assessed**

Report the date of the PET scan used to determine the response reported in question 220. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, *General Guidelines for Completing Forms*.

**Question 221: Was this line of therapy maintenance / consolidation?**

Report “Yes” if this line of therapy was being given for maintenance or consolidation. Report “No” if this line of therapy was not given for maintenance or consolidation. See below for general definitions.

**Consolidation:** Once a recipient has achieved a hematologic CR (1st, 2nd, 3rd or greater), they may receive several additional lines of therapy as part of a protocol or to eliminate known minimal residual disease.

**Maintenance:** Following induction and consolidation, a recipient may receive low dose chemotherapy over an extended period of time to maintain a CR. Maintenance therapy is usually given as a single drug taken in the outpatient setting when the recipient has no known evidence of disease.

**Question 222-223: Did disease relapse / progression occur following this line of therapy?**

Refer to the international working group criteria provided in LYM Response Criteria section of the Forms Instructions Manual for more information on how to determine recurrence / progression of disease. Report “Yes” if the recipient met the criteria (radiographic or metabolic) for relapse after starting this line of therapy and prior to starting a subsequent line of therapy. If “Yes” is reported, indicate the date of relapse / progression in question 223. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, *General Guidelines for Completing Forms*.

Report “No” if the recipient’s disease did not relapse or progress following this line of therapy. Also, report
“No” if the relapse / progression occurred after beginning a subsequent line of therapy. This episode of relapse / progression will be captured in the instance (i.e., copy) of questions 166-223 completed for the subsequent line of therapy. If “No” is reported, go to question 224.

If this is the last line of therapy administered prior to infusion, only report “Yes” if relapse occurred prior to infusion. Relapse occurring after the infusion date will be reported on the HL/NHL Post-Infusion Data Form (Form 2118).
Questions 224-232 will only be answered if the primary disease was reported as diffuse large B-cell lymphoma (DLBCL) either at transformation (question 84) or at diagnosis (question 1) if no transformation occurred. This includes the following DLBCL subtypes: cell of origin unknown, germinal center B-cell type, and activated B-cell type (non-GCB). If the recipient’s primary disease was not DLBCL, skip questions 224-232 and go to question 233.

**Question 224: Did recipient achieve a CR after 1st line of therapy?**

Refer to the international working group criteria provided in LYM Response Criteria section of the Forms Instruction Manual. Report “Yes” and go to question 233 if the recipient achieved a CR (radiographic or metabolic) in response to their first line of therapy. CR must be achieved prior to the initiation a second line of therapy (or transplant) in order to report “Yes.” If the recipient did not achieve a CR in response to their first line of therapy, report “No” and go to question 225.

**Question 225-227: LDH**

Indicate whether the recipient’s LDH value was “Known” or “Unknown” during the time frame specified above. If “Known,” report the test result and corresponding units in question 226. Also, report the upper limit of normal and corresponding units for the test.

**Question 228: Stage of organ involvement: (at 1st relapse / progression)**

Use the staging criteria in Table 1 to determine the stage of organ involvement during the time frame specified above. Also refer to Graphic 2 and Graphic 3 for examples. If staging at this time point is not available or unknown, select “Unknown.”
Question 229-230: ECOG score (at failure of 1st line of therapy)

See the instructions for questions 80-81 for more information about reporting ECOG scores. Indicate whether the recipient’s ECOG score during the time frame specified above is known. If “Known,” report the score in question 230. Otherwise, go to question 231.

Question 231: Did the recipient have known extranodal involvement?

Extranodal refers to the presentation of lymphoma outside of the lymph nodes. Common areas of extranodal involvement may include bone, gastrointestinal tract, and skin. Splenic involvement in lymphoma is also common. It is usually evidenced by enlargement of the spleen (splenomegaly). Splenic or other extranodal involvement is most often detected by imaging techniques or pathological findings.

If extranodal involvement was identified, report “Yes” and go to question 232.

If there was no evidence of extranodal involvement or it is not known, report “No” or “Unknown” respectively and go to question 233.

Questions 232: Specify site(s) of involvement: (check all that apply)

Check each site with known lymphomatous involvement. If an involved site was documented, but is not listed as an option for question 232, check “Other site” and report all other sites of lymphomatous involvement in question 233.
Q233-287: Disease Assessment at Last Evaluation Prior to the Start of the Preparative Regimen / Infusion

All values reported in questions 233-287 must reflect the most recent testing prior to the start of the preparative regimen (or infusion if not preparative regimen was given). Do not report testing performed during a line of therapy reported in questions 167-223. If testing was not performed near the start of the preparative regimen / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable), the center should report “Unknown” for that value.

Question 233: Were cytogenetics tested (karyotyping or FISH)?

If cytogenetic studies were obtained at the last evaluation prior to the start of the preparative regimen / infusion, report “Yes” and go to question 224.

If cytogenetic studies were not obtained at the last evaluation prior to the start of the preparative regimen / infusion or it is not known whether studies were obtained, report “No” or “Unknown” respectively and go to question 264.

For more information about cytogenetic testing and terminology, see Appendix C, Cytogenetic Assessments.

Question 234-235: Were cytogenetics tested via FISH?

If FISH studies were performed at the last evaluation prior to the start of the preparative regimen / infusion, report “Yes” for question 234 and indicate whether clonal abnormalities were detected in question 235.

If FISH studies were not performed at the last evaluation prior to the start of the preparative regimen / infusion, report “No” for question 234 and go to question 259. Examples include: no FISH study performed or FISH sample was inadequate.

Question 236-257: Specify cytogenetic abnormalities (FISH)

Results reported in questions 236-257 must reflect testing performed at the last evaluation prior to the start of the preparative regimen / infusion.

For each abnormality:
Report “Yes” if FISH testing detected the abnormality.
Report “No” if FISH testing for the abnormality was done and was negative.
Report “Not done” if FISH testing for the abnormality was not attempted or could not be successfully performed (e.g., inadequate sample).

If a clonal abnormality is detected, but cannot be reported in questions 236-255, report “Yes” for question 256 and specify the abnormality in question 257. If multiple “other abnormalities” were detected, report “see attachment” in question 257 and attach the final report(s) for any other abnormalities detected. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 258: Was documentation submitted to the CIBMTR? (e.g., FISH report)**

Indicate if a FISH testing report is attached to support the findings reported in questions 234-257. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 259-260: Were cytogenetics tested via karyotyping?**

If karyotyping was performed at the last evaluation prior to the start of the preparative regimen / infusion, report “Yes” for question 259 and indicate whether clonal abnormalities were detected in question 260.

If karyotyping was not performed at the last evaluation prior to the start of the preparative regimen / infusion, report “No” for question 259 and go to question 264. Examples include: no karyotyping performed or karyotyping sample was inadequate.

**Question 261-262: Specify cytogenetic abnormalities (karyotyping)**

Results reported in questions 261-262 must reflect testing performed at the last evaluation prior to the start of the preparative regimen / infusion.

Check any abnormalities detected by karyotyping. If karyotyping detected an abnormality that is not specified in question 261, check “Other abnormality” and report the abnormality in question 262. If multiple “other abnormalities” were detected, report “see attachment” for question 262 and attach the karyotyping report to the form. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Refer to Appendix C, Cytogenetic Assessments for assistance interpreting karyotyping results.

**Question 263: Was documentation submitted to the CIBMTR?**

Indicate if a karyotyping report is attached to support the findings reported in questions 259-262. For further
instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 264-265: Hemoglobin**

Questions 264-265 will only be answered if the primary disease was follicular lymphoma (all histologies) and Hodgkin lymphoma (all histologies) either at transformation (question 84) or at diagnosis (question 1) if no transformation occurred.

Indicate whether the hemoglobin in the peripheral blood is “Known” or “Unknown” at the last evaluation prior to the start of the preparative regimen / infusion. If “Known,” report the laboratory value and unit of measure in question 265. If the hemoglobin at the last evaluation prior to the start of the preparative regimen / infusion is not known, report “Unknown” and go to question 266.

**Question 266-267: Absolute lymphocyte count**

Questions 266-267 will only be answered if the primary disease was reported as Hodgkin lymphoma (all histologies) either at transformation (question 84) or at diagnosis (question 1) if no transformation occurred.

Indicate whether the absolute lymphocyte count in the peripheral blood is “Known” or “Unknown” at the last evaluation prior to the start of the preparative regimen / infusion. If “Known,” report the laboratory value and unit of measure in question 267. If the absolute lymphocyte count at the last evaluation prior to the start of the preparative regimen / infusion is not known, report “Unknown” and go to question 268.

**Question 268: Was minimal residual disease (MRD) assessed during the pre-HCT or pre-infusion evaluation?**

Minimal residual disease assessments include flow cytometry, PCR, and next generation sequencing. If testing was performed by any of these three methods on blood or bone marrow specimens at the last evaluation prior to the preparative regimen / infusion, report “Yes” and go to question 269. If testing by these methods was not done or it is not known whether testing was performed, report “No” or “Unknown” respectively and go to question 282.

**Question 269-272: Flow cytometry**

Indicate the result of flow cytometry testing performed at the last evaluation prior to the start of the preparative regimen / infusion. If testing was “Positive,” report the sample source in questions 270-271. Also, report the date the sample was collected in question 272. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If all flow cytometry testing was negative or testing was not done at the last evaluation prior to the start of
the preparative regimen, report “Negative” or “Not done” respectively for question 269 and go to question 273.

**Question 273-276: PCR**

Indicate the result of PCR testing performed at the last evaluation prior to the start of the preparative regimen / infusion. If testing was performed for multiple disease markers and any of the test results were positive, report “Positive” for question 273. If testing was “Positive,” report the sample source in questions 274-275. Also, report the date the sample was collected in question 276. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If all PCR testing was negative or testing not done at the last evaluation prior to the start of the preparative regimen, report “Negative” or “Not done” respectively for question 273 and go to question 277.

**Question 277-280: Next generation sequencing (NGS, 3rd gen)**

Indicate the result of next generation sequencing (NGS, 3rd gen) testing performed at the last evaluation prior to the start of the preparative regimen / infusion. If testing was performed for multiple disease markers and any of the test results were positive, report “Positive” for question 277. If testing was “Positive,” report the sample source in questions 278-279. Also, report the date the sample was collected in question 280. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If all next generation sequencing testing was negative or testing was not done at the last evaluation prior to the start of the preparative regimen, report “Negative” or “Not done” respectively for question 277 and go to question 281.

**Question 281: Was documentation submitted to the CIBMTR?**

Indicate if documentation is attached to support the findings reported in questions 269-280. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

**Question 282: Did the recipient have known nodal involvement?**

Nodal involvement may be assessed by a physician palpating lymph nodes, pathology from a lymph node biopsy, or radiological assessment (e.g., PET or CT imaging). Report “Yes” if nodal involvement was detected by any of these methods. Otherwise, report “No” and go to question 285.
Questions 283: Specify total number of nodal regions involved (follicular only)

Question 283 will only be answered if the primary disease was follicular lymphoma (all histologies) either at transformation (question 84) or at diagnosis (question 1) if no transformation occurred.

Refer to questions 72-73 for instructions on how to assess and report nodal involvement. Report the total number of nodal regions identified at the last evaluation prior to the start of the preparative regimen / infusion.

Questions 284: Specify the size of the largest nodal mass

Report the size of the largest known nodal mass as measured in centimeters. If the mass is given in three dimensions (for example: 3 cm x 5 cm x 4 cm), report the longest two dimensions.

Question 285: Was there any known extranodal or splenic involvement? (at last evaluation)

Refer to question 75 for a description of extranodal and splenic involvement. If extranodal or splenic involvement was identified at the last evaluation prior to the start of the preparative regimen / infusion, indicate “Yes” and continue with question 286.

If there was no evidence of extranodal or splenic involvement at the last evaluation prior to the start of the preparative regimen / infusion or it is not known, report “No” or “Unknown” respectively and submit the form.

Questions 286-287: Specify site(s) of involvement:

Check each site with known lymphomatous involvement at the last evaluation prior to the start of the preparative regimen. If an involved site was documented, but is not listed as an option for question 286, check “Other site” and report all other sites of lymphomatous involvement in question 287.
2118: LYM Post-Infusion

Complete this form for recipients whose primary disease, reported on the Disease Classification Form (Form 2402), is Hodgkin Lymphoma (HL) or non-Hodgkin Lymphoma (NHL). One exception is Waldenstrom’s macroglobulinemia / lymphoplasmacytic lymphoma, for which, a Waldenstrom’s Macroglobulinemia Form (Form 2019) will be completed instead.

**Acute Lymphoblastic Leukemia / Lymphoma**
Due to the aggressive nature of precursor B- and precursor T-cell lymphoblastic lymphoma (or lymphoma/leukemia), the primary disease to report for recipients with these malignancies should be acute lymphoblastic leukemia (B- lymphoblastic leukemia/lymphoma or early T-cell precursor lymphoblastic leukemia. If the recipient’s primary disease is acute lymphoblastic lymphoma, complete an ALL Post-Infusion Data Form (Form 2111). Do not complete a LYM Post-Infusion Data Form (Form 2118).

Links to Sections of Form
- Q1-20: Disease Assessment at the Time of Best Response to HCT or Cellular Therapy
- Q21-35: Post-HCT or Post-Infusion Therapy
- Q36-86: Disease Relapse or Progression Since the Date of Last Report
- Q87-90: Disease Status at the Time of Evaluation for This Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please [click here](#) or reference the retired manual section on the [Retired Forms Manuals](#) webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/20/2018</td>
<td>2118: LYM Post-Infusion Data</td>
<td>Modify</td>
<td>Changed the instruction for for reporting questions 88 and 89 by removing (strike through) and adding (red) text as indicated below. The center does not need to repeat all disease-specific assessments (biopsies, i.e., CT (radiographic) or PET scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression. If a disease-specific assessment did not occur during</td>
</tr>
</tbody>
</table>
this time period, please report the date of any disease related assessment (e.g. clinical assessments, labs, etc.) as the date assessed (Q88 or Q90) regardless of what the parent question states about the specific CT (radiographic) or PET criteria.

<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Action</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/19/18</td>
<td>2118: LYM Post-Infusion Data</td>
<td>Modify</td>
<td>Change the instruction for question 89 by removing (strike through) and adding (red) text as indicated below. The current disease status should reflect the most recent disease evaluations performed during the reporting period. Report “Not assessed” and submit the form if the recipient’s primary disease is a non-PET avid lymphoma or a PET scan was not performed during the reporting period since the infusion.</td>
</tr>
<tr>
<td>3/19/18</td>
<td>Comprehensive Disease Specific Manuals</td>
<td>Add</td>
<td>Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119). The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.</td>
</tr>
<tr>
<td>1/30/18</td>
<td>2118: LYM Post-Infusion Data</td>
<td>Modify</td>
<td>Version 3 of the 2118: LYM Post-Infusion Data section of the Forms Instructions Manual released. Version 3 corresponds to revision 4 of the Form 2118.</td>
</tr>
</tbody>
</table>
**Q1-20: Disease Assessment at the Time of Best Response to HCT or Cellular Therapy**

**Post-Infusion Therapy**

Prior versions of the lymphoma post-infusion manuals have instructed centers to stop tracking the best response to HCT or cellular therapy if the recipient began treatment for **persistent disease**. The current version of the manual instructs centers to continue tracking/reporting the best response even if the recipient started treatment as prophylaxis (to prevent a relapse), maintenance (to prevent a progression) or consolidation for minimal residual or persistent disease at the time of infusion. Centers should not report a disease response achieved after the initiation of treatment for relapse or progression in questions 1 and 4.

**Question 1: What was the best response by CT (radiographic) criteria to HCT or cellular therapy since the date of the last report?**

The intent of questions 1 is to determine the best overall response to HCT or cellular therapy based on **radiographic** response criteria. If the recipient was already in a radiographic complete remission (CR) at the start of the preparative regimen / infusion report “Continued Complete Remission” for question 1 and go to question 4.

When evaluating the best response, determine the disease status within the reporting period using the radiographic international working group criteria provided in the in **LYM Response Criteria** section of the Forms Instructions Manual. Compare this response to all previous post-infusion reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status. See question 2 to indicate that this disease status was previously reported.

Include response to any post-infusion treatment planned as of Day 0. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR, consider this “planned therapy,” even if this was not documented prior to the transplant. Also, include response to a treatment for persistent (i.e., minimal residual disease) disease.

**Do not include response any treatment for relapse or progression.** If a recipient started treatment for relapse or progression report the best response prior to the initiation of treatment (even if this was confirmed in a prior reporting period).
See best response to infusion reporting scenarios below for reporting examples.

**Question 2: Was the date of best response previously reported?**

If the best response to HCT / cellular therapy was first documented during the current reporting period, report “No” and go to question 3. If the best response was achieved during a previous reporting period (and therefore reported on a previous LYM Post-Infusion Data Form), report “Yes” and go to question 4.

Do not report “Yes” if completing this form for the 100 day reporting period.

**Question 3: Date assessed**

Report the date the best response to HCT / cellular therapy was established. This should be the earliest date when all radiographic international working group criteria for the response reported in question 1 were met. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 4: What was the best response by PET (metabolic) criteria to HCT or cellular therapy since the date of the last report?**

The intent of questions 4 is to determine the best overall response to HCT or cellular therapy based on metabolic response criteria. If the recipient was already in a metabolic CR at the start of the preparative regimen / infusion report “Continued Complete Remission” for question 4. If the recipient’s primary disease is a non-PET avid lymphoma, report “Not assessed” for question 4.

When evaluating the best response, determine the disease status within the reporting period using the metabolic international working group criteria provided in the in LYM Response Criteria section of the Forms Instructions Manual. Compare this response to all previous post-infusion reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status. See question 5 to indicate that this disease status was previously reported.

Include response to any post-infusion treatment planned as of Day 0. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR, consider this “planned therapy,” even if this was not documented prior to the transplant. Also, include response to a treatment for persistent disease.

**Do not include response any treatment for relapse or progression.** If a recipient started treatment for relapse or progression report the best response prior to the initiation of treatment (even if this was confirmed in a prior reporting period).

See best response to infusion reporting scenarios below for reporting examples.
**Question 5: Was the date of best response previously reported?**

If the best response to HCT / cellular therapy was first documented during the current reporting period, report “No” and go to question 6. If the best response was achieved during a previous reporting period (and therefore reported on a previous LYM Post-Infusion Data Form), report “Yes.”

Do not report “Yes” if completing this form for the 100 day reporting period.

**Question 6: Date assessed**

Report the date the best response to HCT / cellular therapy was established. This should be the earliest date when all metabolic international working group criteria for the response reported in question 1 were met. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Best Response to Infusion Reporting Scenarios:**

**A.** A recipient in complete metabolic and radiographic remission at the time of infusion has a disease relapse detected on their first PET/CT scan post-HCT.

100 Day Follow-Up Form:

**Question 1:** Report “Continued complete remission.” This option should be used for all recipients in radiographic CR at the time of infusion regardless of post-infusion disease assessments.

**Question 4:** Report “Continued complete remission.” This option should be used for all recipients in metabolic CR at the time of infusion regardless of post-infusion disease assessments.

**B.** A recipient in complete radiographic remission and partial metabolic remission at the time of infusion achieves a complete metabolic remission during the 100 day reporting period (on 6/1/2016). PET/CT studies during the 6 month reporting period continue to show no evidence of disease.

100 Day Follow-Up Form:

**Question 1:** Report “Continued complete remission.” This option should be used for all recipients in radiographic CR at the time of infusion regardless of post-infusion disease assessments.

**Question 4:** Report “Complete Remission.” Use this option to indicate a metabolic CR was achieved post-infusion for recipients not in metabolic CR at the time of infusion.

**Question 5:** Report “No.” The date of best response has not been previously reported. Never report “Yes” for question 5 on the day 100 follow-up form.

**Question 6:** Report 6/1/2016 as indicated in the scenario.

Six Month Follow-Up Form:

**Question 1:** Report “Continued complete remission.” This option should be used for all recipients in
radiographic CR at the time of infusion regardless of post-infusion disease assessments.

Question 4: Report “Complete Remission.” Use this option to indicate a metabolic CR was achieved post-infusion for recipients not in metabolic CR at the time of infusion.

Question 5: Report “Yes.” The date of best response was reported on the day 100 follow-up form.

C. A recipient in partial metabolic and radiographic remission at the time of infusion achieves a complete metabolic and radiographic remission during the 100 day reporting period (on 5/1/2014). A PET scan performed during the 6 month reporting period detects relapse and the recipient’s disease status remains “Relapse” on the 6 month date of contact despite multiple treatments.

100 Day Follow-Up Form:

Question 1: Report “Complete Remission.” Use this option to indicate a radiographic CR was achieved post-infusion for recipients not in radiographic CR at the time of infusion.

Question 2: Report “No.” The date of best response has not been previously reported. Never report “Yes” for question 2 on the day 100 follow-up form.

Question 3: Report 5/1/2014 as indicated in the scenario.

Question 4: Report “Complete Remission.” Use this option to indicate a metabolic CR was achieved post-infusion for recipients not in metabolic CR at the time of infusion.

Question 5: Report “No.” The date of best response has not been previously reported. Never report “Yes” for question 2 on the day 100 follow-up form.

Question 6: Report 5/1/2014 as indicated in the report scenario.

Six Month Follow-Up Form:

Question 1: Report “Complete Remission.” Use this option to indicate a radiographic CR was achieved post-infusion for recipients not in metabolic CR at the time of infusion.

Question 2: Report “Yes.” The date of best response was reported on the day 100 follow-up form.

Question 4: Report “Complete Remission.” Use this option to indicate a metabolic CR was achieved post-infusion for recipients not in metabolic CR at the time of infusion.

Question 5: Report “Yes.” The date of best response was reported on the day 100 follow-up form.

Disease Assessments at Time of Best Response

Only complete questions 7-20 if the date of best response has been reported for questions 3 or 6. Otherwise, skip questions 7-20 and go to question 21.

For reporting purposes, the definition of “at the time of best response” depends on the reporting period. See Disease Assessment Time Windows below. Only consider assessments with samples collected within the time window which corresponds to the follow-up form being completed. If assessments were performed during the reporting period, but the samples were not collected within the indicated time window, consider
them “Not done” when completing questions 7-20.

Table 1. Disease Assessment Time Windows

<table>
<thead>
<tr>
<th>Follow-Up Form</th>
<th>Approximate Time Window</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 Day</td>
<td>+/- 15 days of date of best response (Question 3 / 6)</td>
</tr>
<tr>
<td>6 Month</td>
<td>+/- 15 days of date of best response (Question 3 / 6)</td>
</tr>
<tr>
<td>Annual</td>
<td>+/- 30 days of date of best response (Question 3 / 6)</td>
</tr>
</tbody>
</table>

If the date of best radiographic response (question 3) and the date of best metabolic response (question 6) are both reported and are not the same, use the earlier of the two dates when determining the approximate time window.

**Question 7: Was minimal residual disease (MRD) assessed at the time of best response?**

Minimal residual disease assessments include flow cytometry, PCR, and next generation sequencing. If testing was performed by any of these three methods on blood or bone marrow specimens at time of best response, report “Yes” and go to question 8. If testing by these methods was not done on blood or bone marrow at the time of best response or it is not known whether testing was performed, report “No” or “Unknown” respectively and go to question 21.

**Question 8-11: Flow cytometry**

Indicate the result of flow cytometry testing performed on blood or bone marrow at the time of best response. If testing was “Positive” or “Negative,” report the sample source in questions 9-10. Also, report the date the sample was collected in question 11. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If flow cytometry testing was not done at the last evaluation prior to the start of the preparative regimen, report “Not done” for question 8 and go to question 12.

**Question 12-15: PCR**

Indicate the result of PCR testing performed at the time of best response. If testing was performed for multiple disease markers and any of the test results were positive, report “Positive” for question 12. If testing was “Positive” or “Negative,” report the sample source in questions 13-14. Also, report the date the sample was collected in question 15. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.
If PCR testing was not done at the last evaluation prior to the start of the preparative regimen, report "Not done" for question 12 and go to question 16.

**Question 16-19: Next generation sequencing**

Indicate the result of next generation sequencing (NGS, 3rd gen) testing performed at the time of best response. If testing was performed for multiple disease markers and any of the test results were positive, report "Positive" for question 16. If testing was "Positive" or "Negative," report the sample source in questions 17-18. Also, report the date the sample was collected in question 19. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If next generation sequencing testing was not done at the last evaluation prior to the start of the preparative regimen, report "Not done" for question 16 and go to question 20.

**Question 20: Was documentation submitted to the CIBMTR?**

Indicate if documentation is attached to support the findings reported in questions 7-19. For further instructions on how to attach documents in FormsNet3<sup>SM</sup>, refer to the Training Guide.
Q21-35: Post-HCT or Post-Infusion Therapy

The FormsNet3 application allows questions 22-35 to be reported multiple times. Complete these questions for each line of therapy administered during the reporting period for reasons other than relapse, progression, or new MRD identified post-HCT. When submitting the paper version of the form for more than one line of therapy, copy the “Pre-HCT or Pre-Infusion Therapy” section and complete a copy of the section for each line of therapy administered.

A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.). If a recipient’s disease status changes resulting in a change to treatment, a new line of therapy should be reported. Additionally, if therapy is changed because a favorable disease response was not achieved, a new line of therapy should be reported.

Question 21: Was therapy given since the date of last report for reasons other than relapse or progressive disease?

Indicate if the recipient received treatment post-infusion for reasons other than relapse or progressive disease during the current reporting period. Recipients generally receive a HCT / cellular therapy under a specific protocol which defines radiation and / or systemic therapy to be given prior to infusion; prophylactic medications to be administered pre- and / or post-infusion; as well as any systemic therapy, radiation, and / or other treatments to be administered post-infusion as planned (or maintenance) therapy. Planned (maintenance) therapy is given to prolong a remission. Planned therapy may be described in a research protocol or standard of care protocol. Refer to these documents (if available) when completing this section. If post-infusion therapy is given as prophylaxis or maintenance for recipients in CR or to treat persistent disease or minimal residual disease which has not progressed since the infusion, report the therapy in questions 21-35. **Do not include any treatment administered as a result of relapse or progression.**

If therapy was given for reasons other than relapse or progression during the reporting period, report “Yes” and go to question 22. If “No,” go to question 36.
Question 22: Systemic therapy

Systemic therapy is delivered via the bloodstream and distributed throughout the body. Therapy may be injected into a vein / central line or given orally. Do not report intrathecal therapy as systemic therapy. If systemic therapy was administered as part of the line of therapy being reported, report “Yes” and go to question 23. If not, report “No” and go to question 32.

Question 23-24: Date therapy started

If this line of therapy continued from a prior reporting period, report “Not applicable” for question 23 and go to question 25. Otherwise, indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 24. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy started is “Unknown,” go to question 25.

Question 25-26: Date therapy stopped

If this line of therapy continued beyond the date of contact for this reporting period, report “Not applicable.” Otherwise, indicate if therapy stop date is “Known” or “Unknown.” If the therapy is being given in cycles, report the date the recipient started the last cycle for this line of therapy in question 26. Otherwise, report the final administration date for the therapy being reported. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy stopped is “Unknown,” go to question 27.

Question 27-28: Specify therapy given

Report the drug given as part of this line of therapy. If multiple lines of therapy were given during the reporting period, they must be reported separately. If the drug given is not listed as an option for question 27, report “Other systemic therapy” and specify the drug in question 28.

Question 29: Reason systemic therapy stopped

Only complete question 29 if the stop date was reported in question 26. Otherwise, skip question 29 and go to question 30.

If systemic therapy was stopped during the reporting period, indicate the reason it was stopped and go to question 30.
**Question 30-31: Was therapy given as part of clinical trial?**

Indicate whether treatment was administered as part of a clinical trial. Consult the physician overseeing treatment if it is not clear whether the therapy is being given as part of a clinical trial. If “Yes,” report the clinicaltrials.gov number in question 31. Otherwise, go to question 32.

If the clinical trial number (NCT number) is not clearly documented, it can be looked up using the Find a Study feature on [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

If the recipient is participating in a clinical trial that is not registered with clinicaltrials.gov, but is registered elsewhere, leave question 31 blank and override the validation error using the code “Unable to answer.” Also, attach documentation which displays the clinical trial number and corresponding registry to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the [Training Guide](#).

**Question 32: Radiation therapy**

Radiation therapy utilizes high-energy x-rays, gamma rays, electron beams, or proton beams to kill cancer cells. Radiation therapy may be used to kill cells that have invaded other tissues and lymph nodes. Radiation therapy may be given in conjunction with systemic chemotherapy or as a separate line of therapy.

If radiation therapy was given during or adjacent to administration of systemic therapy, report them together as single line of therapy on the form (i.e., one copy of questions 22-35). Otherwise, capture the radiation treatment as a separate line of therapy.

If the recipient received radiation therapy as part of the line of therapy being reported, report “Yes.” Otherwise, report “No.”

**Question 33: Cellular Therapy**

Cellular therapy treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g., cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g., CAR T-cells).

Report “Yes” if the recipient received cellular therapy as part of the line of therapy being reported. If not, report “No.”

**Question 34-35: Other therapy**

Indicate if the recipient received any other therapy (not already reported in questions 22-33) given for reasons other than relapse or progression. as part of this line of therapy. Do not report supportive therapies
(e.g., transfusions, growth factors) or a subsequent HCT in questions 34-35. If “Yes,” specify all other therapies given in question 35. If “No,” go to question 36.
Q36-86: Disease Relapse or Progression Since the Date of Last Report

Question 36: Did the recipient experience a relapse or progression since the date of the last report? (by any method)

Relapse / progression may be detected by imaging assessments (CT, PET, MRI) as well as molecular, cytogenetic, and clinical / hematologic methods. Radiographic and metabolic relapse and progression criteria are provided in the LYM Response Criteria section of the Forms Instruction Manual for reference. If relapse or progression was detected during the reporting period by any of the methods listed above, report “Yes” for question 36 and go to question 37. If no assessments detected relapse / progression or testing was not done during the reporting period, report “No” or “Unknown” respectively and go to question 54.

Question 37-38: Was disease detected by molecular testing (e.g., PCR)

Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient’s disease. Molecular assessment is the most sensitive method of detection, and can indicate known genetic abnormalities (e.g., immunoglobulin (Ig) or T-cell receptor gene rearrangements, or other specific lymphoma gene rearrangements). PCR and next generation sequencing are examples of molecular tests.

If molecular testing detected disease during the reporting period, report “Yes” and specify the date the sample was collected in question 38. If multiple tests were performed during the reporting period, report the earliest date disease was detected.

If a molecular assessment was performed and found no evidence of disease or if molecular assessments were not performed, report “No” or “Not done” respectively and go to question 39.

Question 39: Was disease detected by cytogenetic testing (karyotyping or FISH)?

For more information about cytogenetic testing and terminology, see Appendix C, Cytogenetic Assessments. Indicate whether cytogenetic studies detected disease during the reporting period.

Report “Yes” and go to question 40 if cytogenetic studies detected disease during the reporting period.

Report “No” and go to question 44 if cytogenetic studies were performed during the reporting period, but did not detect disease.

Report “Unknown” and go to question 44 if cytogenetic studies were not performed during the reporting
period. Examples include: no studies performed or samples were inadequate.

**Question 40-41: Was disease detected via FISH?**

See [Appendix C, Cytogenetic Assessments](#), for assistance interpreting FISH results.

If FISH testing found evidence of disease, report “Yes” and specify the date the sample was collected in question 41. If multiple tests were performed during the reporting period, report the earliest date disease was detected.

If FISH testing was performed and found no evidence of disease or if FISH assessments were not performed, report “No” and go to question 42. Examples include: no studies performed or samples were inadequate.

**Question 42-43: Was disease detected via karyotyping?**

See [Appendix C, Cytogenetic Assessments](#), for assistance interpreting karyotype results.

If karyotyping found evidence of disease, report “Yes” and specify the date the sample was collected in question 43. If multiple tests were performed during the reporting period, report the earliest date disease was detected.

If karyotyping was performed and found no evidence of disease or if karyotyping was not done, report “No” and go to question 42. Examples include: no studies performed or samples were inadequate.

**Question 44-45: Was disease relapse or progression detected by radiological assessment?**

Indicate whether relapse or progression was detected by any imaging assessments, including CT, PET, and MRI, during the reporting period. Radiographic and metabolic response criteria are provided in the [LYM Response Criteria](#) section of the Forms Instruction Manual for reference.

If relapse or progression was detected by imaging assessments during the reporting period, report “Yes” and indicate the date of assessment in question 45. If multiple imaging assessments detected relapse / progression, report the date of the earliest assessment.

If imaging assessments did not detect relapse / progression or imaging assessments were not performed, report “No” or “Not done” respectively and go to question 46.

**Question 46-47: Was disease relapse or progression detected clinical / hematologic assessment?**

Clinical / hematologic methods include pathology and laboratory evaluations as well as physical examination. Report “Yes” if any of these methods detected relapse / progression during the reporting
period. Also, report the date relapse / progression was detected in question 47. If multiple clinical / hematologic assessments detected relapse / progression during the reporting period, report the date of the earliest assessment.

If testing by clinical / hematologic methods did not detect relapse / progression or testing was not performed, report “No” or “Not done” respectively and go to question 52.

**Question 48: Did the recipient have known nodal involvement?**

Nodal involvement may be assessed by a physician palpating lymph nodes, pathology from a lymph node biopsy, or radiological assessment (e.g., PET or CT imaging). Report “Yes” if nodal involvement was detected by any of these methods at the time of relapse or progression. Otherwise, report “No.”

**Question 49: Was there any known extranodal or splenic involvement?**

Extranodal refers to the presentation of lymphoma outside of the lymph nodes. Common areas of extranodal involvement may include bone, gastrointestinal tract, and skin. Splenic involvement in lymphoma is also common. It is usually evidenced by enlargement of the spleen (splenomegaly). Splenic or other extranodal involvement is most often detected by imaging techniques or pathological findings.

If extranodal or splenic involvement was identified at the time of relapse or progression, indicate “Yes” and go to question 50.

If there was no evidence of extranodal or splenic involvement or it is not known, report “No” or “Unknown” respectively and go to question 52.

**Question 50-51: Specify site(s) of involvement:**

Check each site with known lymphomatous involvement at the time of relapse or progression. If an involved site was documented, but is not listed as an option for question 50, check “Other site” and report all other sites of lymphomatous involvement in question 51.

**Question 52: Was a biopsy performed to confirm relapse / progression?**

Report “Yes” and go to question 53 if a biopsy was performed to evaluate relapse or progression. If a biopsy was not performed or it is not known if a biopsy was performed, report “No” or “Unknown” respectively and go to question 54.

**Question 53: Was documentation submitted? (e.g., path report)**

Attach the pathology report, if available, for the biopsy performed to evaluate relapse or progression. For
further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide. Indicate “Yes” if the report is attached. Otherwise, report “No.”

**Question 54: Was intervention given for relapsed disease, progressive disease, or minimal residual disease? (since the date of last report)**

Indicate if the recipient received treatment post-infusion for relapse, progression, or new MRD identified post-HCT. Do not report treatment given for MRD which has persisted since the time of HCT in questions 54-86. This therapy will be captured in questions 21-35. If “Yes” is reported for question 54, go to question 55. Otherwise, go to question 87. See question 55 for definitions of each of these indications for treatment.

**Question 55: Specify reason for which therapy was given**

Select all indications for which treatment was administered during the reporting period. See below for definitions of each indication.

- **Relapsed Disease:** The recipient was in CR at the time of infusion or the recipient achieved a CR post-infusion. In either case, treatment is administered for a relapse which occurred post-infusion.

- **Progressive Disease:** The recipient’s disease progressed following a period of stable disease or after achieving a partial remission.

- **Minimal Residual Disease:** Recipient is in hematologic CR, but has evidence of disease relapse by more sensitive assessments including molecular, flow cytometry or cytogenetic methods. *Do not report MRD which has persisted from the time of HCT in questions 54-86.*

**Question 56: Systemic therapy**

Systemic therapy is delivered via the blood stream and distributed throughout the body. Therapy may be injected into a vein / central line or given orally. Do not report intrathecal therapy as systemic therapy. If systemic therapy was administered as part of the line of therapy being reported, report “Yes” and go to question 57. If not, report “No” and go to question 65.

**Question 57-58: Date therapy started**

If the systemic therapy being reported began during a prior reporting period, report “Not applicable” for question 57 and go to question 59. Otherwise, indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began this line of therapy in question 58. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.
If the date therapy started is “Unknown,” go to question 59.

**Question 59-60: Date therapy stopped**

If the systemic therapy being reported continued beyond the date of contact for the current reporting period, report “Not applicable” for question 59 and go to question 61. Otherwise, indicate if therapy stop date is “Known” or “Unknown.” If the systemic therapy is being given in cycles, report the date the recipient **started the last cycle** for this therapy in question 60. Otherwise, report the final administration date for the therapy being reported. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).

If the date therapy stopped is “Unknown,” go to question 61.

**Question 61-62: Specify therapy given**

Treatments vary based on protocol. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. Select all chemotherapy drugs administered as part of the line of therapy being reported. If the recipient received a systemic therapy which is not listed, select “Other systemic therapy” and specify the treatment in question 62. Report the generic name of the agent, not the name brand.

**Question 63-64: Was therapy given as part of clinical trial?**

Indicate whether treatment was administered as part of a clinical trial. Consult the physician overseeing treatment if it is not clear whether the therapy is being given as part of a clinical trial. If “Yes,” report the clinical trial number in question 64. Otherwise, go to question 65.

If the clinical trial number (NCT number) is not clearly documented, it can be looked up using the Find a Study feature on [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

If the recipient is participating in a clinical trial that is not registered with clinicaltrials.gov, but is registered elsewhere, leave question 64 blank and override the validation error using the code “Unable to answer.” Also, attach documentation which displays the clinical trial number and corresponding registry to the form in FormsNet3SM. For further instructions on how to attach documents in FormsNet3SM, refer to the [Training Guide](#).

**Question 65: Intrathecal therapy**

Report “Yes” if intrathecal therapy was given to treat relapsed or progressive disease and go to question 66. Report “No” if intrathecal therapy was not given and go to question 72.
**Question 66-67: Date therapy started**

Indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began intrathecal therapy in question 67. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).

If the date therapy started is “Unknown,” go to question 68. If the intrathecal therapy being reported began during a prior reporting period, report “Not applicable” for question 66 and go to question 68.

**Question 68-69: Date therapy stopped**

Indicate if therapy stop date is “Known” or “Unknown.” If “Known,” report the final administration date in question 69. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).

If the date therapy stopped is “Unknown,” go to question 70. If the recipient is still receiving intrathecal therapy, report “Not applicable” for question 68 and go to question 70.

**Question 70-71: Specify intrathecal therapy**

Indicate the drug given as intrathecal therapy during the line of therapy being reported. If the drug is not listed as an option in question 70, report “Other intrathecal therapy” and specify the drug in question 71.

**Question 72: Intraocular therapy**

Intraocular therapy refers to chemotherapy administered via injection to the eye. Report “Yes” and go to question 73 if intraocular therapy was given as part of the line of therapy being reported. Report “No” and go to question 79 if intraocular therapy was not given as part of the line of therapy being reported.

**Question 73-74: Date therapy started**

If the intraocular therapy being reported began during a prior reporting period, report “Not applicable” for question 73 and go to question 75. Otherwise, indicate whether the therapy start date is “Known” or “Unknown.” If the therapy start date is known, report the date the recipient began therapy in question 74. If the start date is partially known (e.g., the recipient started in mid-July 2010), use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).

If the date therapy started is “Unknown,” go to question 75.
**Question 75-76: Date therapy stopped**

If the systemic therapy being reported continued beyond the date of contact for the current reporting period, report “Not applicable” for question 75 and go to question 77. Otherwise, indicate if intraocular therapy stop date is “Known” or “Unknown.” If “Known,” report the final administration date in question 76. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If the date therapy stopped is “Unknown,” go to question 77.

**Question 77-78 Specify intraocular therapy**

Indicate the drug given as intraocular therapy during the line of therapy being reported. If the drug is not listed as an option in question 77, report “Other intraocular therapy” and specify the drug in question 78.

**Question 79: Radiation therapy**

See question 32 for a description of radiation therapy.

If radiation therapy was given during or adjacent to administration of systemic therapy, report them together as single line of therapy on the form (i.e., one copy of questions 55-86). Otherwise, capture the radiation treatment as a separate line of therapy.

If the recipient received radiation therapy as part of the line of therapy being reported, report “Yes.” Otherwise, report “No.”

**Question 80: Cellular Therapy**

See question 33 for a description of cellular therapy.

Report “Yes” if the recipient received cellular therapy as part of the line of therapy being reported. Otherwise, report “No.”

**Question 81-82: Other therapy**

Indicate if the recipient received any other therapy (not already reported in questions 55-80) given to treat relapse, progression, or MRD as part of this line of therapy. Do not report supportive therapies (e.g., transfusions, growth factors) or a subsequent HCT in questions 81-82. If “Yes,” specify all other therapies given in question 82. If “No,” go to question 83.
Question 83: Best response to line of therapy by CT (radiographic) criteria:

Indicate the best response to the line of therapy using the international working group radiographic criteria provided in LYM Response Criteria section of the Forms Instruction Manual. Report “Not assessed” if no applicable assessments were performed after the initiation of the line of therapy being reported and prior to the initiation of any new therapy. “Not assessed” should be rarely used for the best radiographic response as this includes bone marrow biopsies (when applicable) and clinical exams to assess lymphadenopathy and/or splenomegaly.

If the line of therapy being reported began during a prior reporting period, report the best response since the therapy was started.

Question 84: Date assessed

Report the date of the CT scan used to determine the response reported in question 83. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the best response was established during a prior reporting period, report the date of the scan from the prior reporting period.

Question 85: Best response to line of therapy by PET (metabolic) criteria:

Indicate the best response to the line of therapy using the international working group metabolic criteria provided in LYM Response Criteria section of the Forms Instruction Manual. Report “Not assessed” if the recipient’s primary disease is a non-PET avid lymphoma or a PET scan was not performed after the line of therapy being reported and prior to the initiation of any new therapy.

If the line of therapy being reported began during a prior reporting period, report the best response since the therapy was started.

Question 86: Date assessed

Report the date of the PET scan used to determine the response reported in question 85. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the best response was established during a prior reporting period, report the date of the scan from the prior reporting period.
Q87-90: Disease Status at the Time of Evaluation for this Reporting Period

**Question 87: What is the current disease status? (by CT (radiographic) criteria)**

Indicate the current disease status, based on radiographic criteria, using the international working group criteria provided in [LYM Response Criteria](#) section of the Forms Instruction Manual. The current disease status should reflect the most recent disease evaluations performed during the reporting period.

Report “Not assessed” and go to question 89 if no applicable assessments were performed during the reporting period. Otherwise, indicate the current disease status and go to question 88.

The center does not need to repeat all disease-specific assessments (i.e., CT (radiographic) or PET scans) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression. If a disease-specific assessment did not occur during this time period, please report the date of any disease related assessment (e.g. clinical assessments, labs, etc.) as the date assessed (Q88 or Q90) regardless of what the parent question states about the specific CT (radiographic) or PET criteria.

**Question 88: Date assessed**

Report the date of the CT scan used to determine the response reported in question 87. Where applicable, the date of the bone marrow biopsy and / or physical exam may be used.

If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).

**Question 89: What is the current disease status? (by PET (metabolic) criteria)**

Indicate the current disease status, based on metabolic criteria, using the international working group criteria provided in [LYM Response Criteria](#) section of the Forms Instruction Manual. The current disease status should reflect the most recent disease evaluations performed during the reporting period. Report “Not assessed” and submit the form if the recipient’s primary disease is a non-PET avid lymphoma or a PET scan was not performed since the infusion. Otherwise, indicate the current disease status and go to question 90.

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved,
the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

**Question 90: Date assessed**

Report the date of the PET scan used to determine the response reported in question 90. If the date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, [General Guidelines for Completing Forms](#).
Lymphoplasmacytic lymphoma (LPL) and subtype Waldenström’s macroglobulinemia (WM) are specific presentations of Non-Hodgkin lymphoma that are characterized by abnormal cellular populations containing small B-cells, plasma cells, and plasmacytoid lymphocytes. Additional hallmarks of Waldenström’s macroglobulinemia are bone marrow involvement (which may be present in lymphoplasmacytic lymphoma) and IgM paraprotein. Patients typically present with symptoms associated with anemia, such as weakness and fatigue. Workup often reveals normocytic, normochromic anemia. Additional findings may include IgM paraprotein, clinical hyperviscosity syndrome, and neuropathy. LPL will generally involve the bone marrow and, in some cases, the lymph nodes and other extranodal sites. A significant number of patients with WM will also have organomegaly and adenopathy. Advanced age, decreased performance status, anemia, and elevated ß2 microglobulin have been associated with poorer outcomes, though there is no validated staging system to establish prognosis.¹


WM Response Criteria
2019: WM Pre-HCT
2119: WM Post-HCT
Waldenstrom’s Macroglobulinemia Response Criteria

Complete response (CR)

- Disappearance of monoclonal protein on immunofixation (both serum and urine)
- No histologic evidence of bone marrow involvement
- Resolution of adenopathy and/or organomegaly on CT
- Resolution of clinical signs or symptoms attributed to WM/LPL

Complete response requires confirmatory immunofixation.

Partial response (PR)

- $\geq 50\%$ reduction of serum monoclonal IgM spike on serum electrophoresis
- $\geq 50\%$ reduction of adenopathy and organomegaly on physical exam or CT
- No new symptoms and no clinical signs of active disease

Minor response/stable disease (MR/SD)

- 25–49% reduction of serum monoclonal IgM spike on serum electrophoresis
- No new symptoms and no clinical signs of active disease
  Or
- $< 25\%$ reduction and $< 25\%$ increase of serum monoclonal IgM spike on serum electrophoresis
- No progression of adenopathy, organomegaly, cytopenias, or clinically significant symptoms attributed to WM/LPL

Progressive disease (PD)

- $\geq 25\%$ increase in serum monoclonal IgM spike from lowest nadir on serum electrophoresis
- Progression of clinically significant findings or symptoms (for example, anemia, adenopathy, constitutional symptoms, amyloidosis, etc.) attributed to WM/LPL

Progression identified by increasing monoclonal protein on serum electrophoresis requires confirmatory test.

Not assessed

Patient’s disease was not assessed by any method, including physical examination.
The Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures WM/LPL-specific pre-HCT data such as: the recipient's clinical and genetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HCT treatments administered, and disease manifestations prior to the preparative regimen.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Non-Hodgkin lymphoma and the subtype is reported as Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma.

**Subsequent Transplant**

If this is a report of a second or subsequent transplant for the same disease subtype and **this baseline disease insert was not completed for the previous transplant** (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1.

If this is a report of a second or subsequent transplant for a **different disease** (e.g., patient was previously transplanted for a disease other than WM/LPL), begin at question 1.

If this is a report of a second or subsequent transplant for the **same disease and this baseline disease insert has previously been completed**, check yes and continue with the next question.

For the next question, indicate if this form is being completed for a **relapse or a progression of the same disease**. If “yes”, continue with question 76; if “no”, continue with question 121.

**Q1-2: Disease Assessment at Diagnosis**
**Q3-23: Clinical Features Present at Diagnosis**
**Q24-75: Laboratory Studies at Diagnosis**
**Q76-120: Pre-HCT Therapy**
**Q121-150: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen**
**Q151-152: Disease Status at Last Evaluation Prior to the Preparative Regimen**

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.
<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
</tbody>
</table>
Q1-2: Disease Assessment at Diagnosis

Question 1: What is the diagnosis?

Waldenström’s macroglobulinemia (WM) and lymphoplasmacytic lymphoma (LPL) are two closely related neoplasms. They are both characterized by an abnormal population of small B-cells, lymphoplasmacytoid cells, and plasma cells. WM is characterized by an IgM paraprotein and bone marrow involvement, whereas these two features may be absent in LPL.¹

Indicate if the patient was diagnosed with WM or LPL.


Question 2: What was the date of diagnosis?

Report the date of the first pathological diagnosis (e.g., bone marrow biopsy) of WM or LPL. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared. The date of diagnosis is important because the interval between diagnosis and HCT is often a significant indicator for the recipient’s prognosis post-HCT.

If the exact pathological diagnosis date is not known, use the process for reporting partial or unknown dates as described in [General Instructions, Guidelines for Completing Forms](#).
Q3-23: Clinical Features Present at Diagnosis

Question 3: Was peripheral neuropathy present?

Peripheral neuropathy often starts as tingling or burning in the distal extremities, and may progress to extremity numbness and weakness. The etiology of peripheral neuropathy in WM/LPL is not well understood in the absence of associated autoimmunity (such as cold agglutinin disease). Indicate if the patient reported peripheral neuropathy at diagnosis.

Questions 4-5: Did the recipient have known nodal involvement?

The majority of patients with WM or LPL will have bone marrow and, in some cases, lymph nodes involved by disease. Indicate if the patient had known nodal involvement at diagnosis. If “yes,” continue with question 5 and specify the size of the largest nodal mass. If “no,” continue with question 6.

Question 6: Was there any known extranodal or splenic involvement?

Additional sites of extranodal disease (e.g., splenomegaly, hepatomegaly, etc.) have been noted in the literature, especially in more advanced disease stages. Indicate if the patient had any known extranodal or splenic involvement at diagnosis. If “yes,” continue with question 7. If “no” or “unknown,” continue with question 15.

Questions 7-14: Specify the site(s) of involvement

Indicate “yes” or “no” for each site specified in questions 7-13. Do not leave any response blank. If “yes” is indicated for “other site,” specify the site in question 14. If extranodal or splenic involvement was indicated in question 6, at least one of the questions 7-13 must be answered “yes.”

Question 15: Were systemic symptoms (B symptoms) present?

Systemic or constitutional symptoms, often referred to as B symptoms, include fevers, drenching night sweats, and unintentional weight loss. Indicate if the patient reported B symptoms at diagnosis.

Question 16: Was clinical hyperviscosity syndrome present?

The clinical signs and symptoms of hyperviscosity syndrome include skin and mucosal bleeding, dizziness, retinopathy with visual disturbance, fatigue, and neurological dysfunction. Ophthalmologic examination often reveals characteristic venous engorgement of the retina. Indicate if hyperviscosity syndrome was clinically present at the time of diagnosis. If “yes,” continue with question 17. If “no” or “unknown,” continue with question 23.
Questions 17-22: Specify clinical symptoms present at diagnosis

Indicate “yes,” “no,” or “unknown” for each clinical symptom specified in questions 17-21. If clinical hyperviscosity syndrome was present (question 16), at least one of the questions 17-21 must be answered “yes.” If “yes” is indicated for “other,” specify clinical symptom in question 22.

Question 23: Was plasmapheresis or plasma exchange required?

Elevation of IgM paraprotein is associated with hyperviscosity. In an acute setting, plasmapheresis or plasma exchange may be used to rapidly reduce IgM paraprotein levels. Indicate if the patient required plasmapheresis or plasma exchange at diagnosis.
Q24-75: Laboratory Studies at Diagnosis

Report findings at the time of diagnosis. If multiple studies were performed prior to beginning therapy, report the latest values prior to the start of treatment.

Questions 24-25: Absolute lymphocyte count

Indicate whether the lymphocyte count was “known” or “unknown” at the time of WM or LPL diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 25. If “unknown,” continue with question 26.

Questions 26-27: Hemoglobin

Indicate whether the hemoglobin was “known” or “unknown” at the time of WM or LPL diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 27. If “unknown,” continue with question 28.

Questions 28-29: Platelets

Indicate whether the platelet count was “known” or “unknown” at the time of WM or LPL diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 29. If “unknown,” continue with question 30.

Questions 30-31: Bone marrow aspirate (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow aspirate was “known” or “unknown” at the time of diagnosis. If bone marrow aspirate was not examined, report “not applicable.” If “known,” report the extent of aspirate histologic involvement in question 31. If “unknown” or “not applicable,” continue with question 32.

Questions 32-33: Bone marrow biopsy (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow biopsy was “known” or “unknown” at the time of diagnosis. If bone marrow biopsy was not examined, report “not applicable.” If “known,” report the extent of biopsy histologic involvement in question 33. If “unknown” or “not applicable,” continue with question 34.

Question 34: Specify the type of histological involvement in marrow

WM and LPL are often characterized by histologic involvement of the bone marrow. However, there are
variations in the type of involvement: ²

- **Lymphoplasmacytoid**: This variant is primarily defined by small lymphocytes with some plasmacytoid lymphocytes and rare mature plasma cells. Lymphoplasmacytoid cells (plasmacytoid lymphocytes) are mononuclear cells with dark, irregular nuclei. They are slightly larger than a small lymphocyte. Additionally, mitotic and large cells are rare.

- **Lymphoplasmacytic**: In this variant, the involved cells are a mix of small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells. Mitotic and large cells are rare.

- **Polymorphous**: This variant can resemble either lymphoplasmacytoid or lymphoplasmacytic variants, but mitotic and large cells are more common. Large cells are still less common than in large cell lymphomas.

Specify the type of histologic involvement as indicated by the pathology report or transplant physician. Report “unknown” if the bone marrow was not examined, there was no bone marrow involvement, or if the type of histologic involvement cannot be specified.


**Question 35: Was flow cytometry (immunophenotyping) performed?**

Flow cytometry assessment is a method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics. Its primary clinical purpose in the setting of WM or LPL is to identify unique cell populations through immunophenotyping.

Indicate if flow cytometry was performed at diagnosis. If flow cytometry was performed, check “yes” and continue with question 36.

If flow cytometry was not performed or it is unknown if flow cytometry was performed, indicate “no” or “unknown” and continue with question 43.

**Questions 36-41: Specify cell population phenotype**

Flow cytometry utilizes fluorescent-tagged monoclonal antibodies to identify cell marker expression by binding to cell surface antigens. Certain cell or disease panels use different combinations of monoclonal antibodies to identify cell markers that typically characterize that population, either by their presence or absence. Flow cytometry report formatting is highly variable among labs. However, most laboratories will summarize significant findings, including characteristics of the neoplastic cell population. Indicate if the cell population was “positive” or “negative” for each marker. If certain monoclonal antibodies were not part of the panel used, indicate “not done.”
Question 42: Was documentation submitted to the CIBMTR? (e.g., flow cytometry report)

Indicate if a copy of the flow cytometry report at diagnosis is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the report. Attaching a copy of the report may prevent additional queries.

Questions 43-44: Serum ß2 macroglobulin

Elevation in ß2 microglobulin at diagnosis is considered a negative prognostic indicator. Indicate whether ß2 microglobulin was “known” or “unknown” at the time of WM or LPL diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 44. If “unknown,” continue with question 45.

Question 45: Serum heavy chain – IgM

Immunofixation is used to detect abnormal immunoglobulins in serum or urine, and to identify the heavy and/or light chain characterizing the clonal population. WM is generally characterized by an IgM monoclonal protein. Indicate whether an IgM paraprotein was identified on serum immunofixation.

Question 46: Urine heavy chain – IgM

Immunofixation is used to detect abnormal immunoglobulins in serum or urine, and to identify the heavy and/or light chain characterizing the clonal population. WM is generally characterized by an IgM monoclonal protein. Indicate whether an IgM paraprotein was identified on urine immunofixation.

Question 47: Serum light chain

Immunofixation is used to detect abnormal immunoglobulins in serum or urine, and to identify the heavy and/or light chain characterizing the clonal population. Report the light chain that was identified on serum immunofixation.

Question 48: Urine light chain

Immunofixation is used to detect abnormal immunoglobulins in serum or urine, and to identify the heavy and/or light chain characterizing the clonal population. Report the light chain that was identified on urine immunofixation.

Questions 49-51: Relative serum viscosity

Hyperviscosity syndrome is a common manifestation of WM and LPL. Indicate if relative serum viscosity was “known” or “unknown” at diagnosis. If “known,” report the laboratory value in question 50 and laboratory upper limit of normal in question 51. If “unknown,” continue with question 52.
Questions 52-53: Serum monoclonal protein (M-spike) (only from electrophoresis)

Indicate whether serum monoclonal protein quantification from electrophoresis was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 53. If serum electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 54.

Questions 54-55: Urinary monoclonal protein (M-spike)

Indicate whether 24-hour urine monoclonal protein quantification from electrophoresis was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 55. If urine electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 56.

Questions 56-58: LDH

LDH elevation at diagnosis is considered a negative prognostic indicator. Indicate whether LDH was “known” or “unknown” at diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 57; report the laboratory upper limit of normal and unit of measure in question 58. If “unknown,” continue with question 59.

Question 59: Cold agglutinins

Cold agglutinin disease is a common manifestation of WM and LPL. Cold agglutinins are autoantibodies that bind to the red blood cells, manifesting as autoimmune hemolytic anemia. Indicate if cold agglutinins were “positive” or “negative” at diagnosis. If cold agglutinins were not tested or it is unknown if cold agglutinins were tested, report “unknown.”

Question 60: Cryoglobulin

Cryoglobulins are immunoglobulins that aggregate as a gel at temperatures below 37°C. Cryoglobulins may be mixed immunoglobulins or a single component; the majority of cryoglobulin in WM or LPL patients will be mixed IgM-IgG. Indicate if cryoglobulin was “present” or “absent” at diagnosis. If cryoglobulin was not tested or it is unknown if cryoglobulin was tested, report “unknown.”

Questions 61-63: IgG

Indicate whether IgG level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 62; report the laboratory upper limit of normal value and unit of measure in question 63. If “unknown,” continue with question 64.
Questions 64-66: IgA

Indicate whether IgA level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 65; report the laboratory upper limit of normal value and unit of measure in question 66. If “unknown,” continue with question 67.

Questions 67-69: IgM

Indicate whether IgM level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 68; report the laboratory upper limit of normal value and unit of measure in question 69. If “unknown,” continue with question 70.

Question 70: Were cytogenetics tested (conventional or FISH)?

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing methods include conventional chromosome analysis (karyotyping) and fluorescence in situ hybridization (FISH) testing. For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at the time the recipient was diagnosed with WM or LPL, or prior to the start of treatment.

If cytogenetic studies were obtained, check “yes” and continue with question 71.

If cytogenetic studies were not obtained or it is unknown if cytogenetic studies were performed, indicate “no” or “unknown” and continue with question 76.

Question 71: Results of tests

If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), indicate “abnormalities identified” and continue with question 72.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 76.

Questions 72-74: Specify abnormalities.

Deletion of the long arm of chromosome 6 is the most common structural abnormality in WM and LPL. However, other structural and numeric abnormalities have been noted.

If question 71 indicates that abnormalities were identified at the time of WM or LPL diagnosis, questions 72-73 must be answered as “yes” or “no.” Do not leave either response blank. If the patient had any
abnormality other than del(6q), select “yes” for “other abnormality,” and specify in question 74.

**Question 75: Was documentation submitted to the CIBMTR? (e.g., cytogenetic or FISH report)**

Indicate if a copy of the cytogenetic or FISH report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the cytogenetic or FISH report. Attaching a copy of the report may prevent additional queries.
Q76-120: Pre-HCT Therapy

Complete a “Line of Therapy” section for each line of therapy administered prior to the start of the preparative regimen. If multiple lines of therapy are administered, copy and complete questions 77-120 for each line of therapy.

Question 76: Was therapy given (including chemotherapy used to mobilize stem cells)?

Indicate if the recipient received treatment for WM or LPL after diagnosis and before the start of the preparative regimen. If “yes,” continue with question 77. If “no,” continue with question 121.

Question 77: Systemic therapy

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body.

Indicate “yes” if the patient received systemic therapy and continue with question 78. If the patient did not receive systemic therapy, indicate “no” and continue with question 109.

Questions 78-79: Date therapy started

Indicate “known” if the therapy start date is documented and specify the start date in question 79. If the date is unknown, indicate this and continue with question 80.

Questions 80-81: Date therapy stopped

Indicate “known” if the therapy completion date is documented, and specify the date therapy stopped in question 81. If the patient received systemic therapy in cycles, specify the first day of the last cycle of systemic therapy. If the patient received a single line or single administration, indicate the last day systemic therapy was administered.

If the date is unknown, indicate this and continue with question 82.

Question 82: Number of cycles

Indicate if the number of cycles is “known” or “unknown.” If the number of cycles is known, continue with question 83 and specify the number of cycles of chemotherapy administered. If the patient received a single administration or one line of chemotherapy, indicate a single cycle. If the patient received a long-term maintenance therapy consisting of a single agent, indicate “known” for question 82; leave question 83 blank and override the error as “not applicable.”
If the number of cycles is unknown, continue with question 84.

**Questions 84-107: Specify systemic therapy agents**

Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Drugs may be administered in an inpatient or outpatient setting, and treatment may consist of one or multiple drugs. Additionally, drugs may be administered on a single day, over consecutive days, or continuously.

Indicate “yes” or “no” for each therapeutic agent listed. Do not leave any response blank. If the recipient received an agent that is not listed, check “yes” for “other systemic therapy” and specify the treatment in question 107.

**Question 108: Was this line of therapy given for stem cell mobilization (priming)?**

Systemic therapy may be given for stem cell priming. For example, mobilization occurs during the recovery phase after cyclophosphamide administration. As such, it may be administered with cytokines to overcome the suppressive effect of previous therapeutic agents. Indicate if this line of therapy was given for stem cell mobilization.

**Question 109: Radiation therapy**

Radiation therapy uses high-energy, ionizing radiation to kill malignant cells. Much like non-targeted systemic therapy, radiation therapy does not specifically target malignant cells and does have significant side effects. For that reason, high-dose radiation often targets a limited field.

Indicate if the recipient received radiation treatment for WM or LPL after the time of diagnosis and before the start of the preparative regimen. If “yes,” continue with question 110. If “no,” continue with question 117.

**Questions 110-111: Date therapy started**

Indicate “known” if the radiation therapy start date is documented, and specify the first date of radiation administration in question 111. If the date is unknown, indicate this and continue with question 112.

**Questions 112-113: Date therapy stopped**

Indicate “known” if the radiation therapy completion date is documented, and specify the last date of radiation administration in question 113. If the date is unknown, indicate this and continue with question 114.

**Questions 114-116: Specify site(s) of radiation therapy**

Specify radiation site(s). If question 109 is answered “yes,” at least one site of radiation therapy must be
specified in questions 114-116.

**Question 117: Best response to line of therapy**

Indicate the patient’s best response to this line of therapy.

*See [WM Response Criteria](#) for disease status definitions.*

**Question 118: Date assessed**

Enter the date the best response to the line of therapy was established. Report the date of the pathological (e.g., bone marrow biopsy) or radiological (e.g., CT scan) evaluation; if neither was reported, report the date of blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and/or laboratory evaluation. If the recipient was treated for extramedullary disease and a radiological assessment (e.g., X-ray, CT scan, MRI scan, PET scan) was performed to assess disease response, enter the date the imaging took place for radiologic assessment. If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically assessed the recipient’s response.

If the exact date is not known, use the process for reporting partial or unknown dates as described in *[General Instructions, Guidelines for Completing Forms](#)*.

**Question 119: Did disease relapse/progress following this line of therapy?**

Relapse is the recurrence of disease after CR. WM or LPL relapse is demonstrated by reappearance of disease characteristics including IgM paraprotein, lymphadenopathy and/or organomegaly, and bone marrow histologic involvement.

*See [WM Response Criteria](#) for disease status definitions.* Indicate if relapse or progression occurred following the line of therapy being reported. If question 117 is answered “progressive disease,” question 119 must be “yes.”

**Question 120: Date of relapse/progression**

Enter the date of the assessment that identified relapse or progression following the line of therapy. Enter the date the sample was collected for pathological and laboratory evaluation or enter the date the imaging took place. If the physician determined evidence of relapse in a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in *[General Instructions, Guidelines for Completing Forms](#)*.
Q121-150: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen

These questions are intended to determine the status of the recipient prior to the preparative regimen. Testing may be performed multiple times within the pre-transplant workup period (approximately 30 days) prior to the start of the preparative regimen; report the most recent laboratory value. Laboratory values obtained on the first day of the preparative regimen may be reported as long as the sample was drawn before any radiation or systemic therapy was administered.

Questions 121-122: Absolute lymphocyte count

Indicate whether the lymphocyte count was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 122. If “unknown,” continue with question 123.

Questions 123-124: Bone marrow aspirate (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow aspirate was “known” or “unknown” immediately prior to the start of the preparative regimen. If bone marrow aspirate was not examined, report “not applicable.” If “known,” report the extent of aspirate histologic involvement in question 124. If “unknown” or “not applicable,” continue with question 125.

Questions 125-126: Bone marrow biopsy (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow biopsy was “known” or “unknown” immediately prior to the start of the preparative regimen. If bone marrow biopsy was not examined, report “not applicable.” If “known,” report the extent of biopsy histologic involvement in question 126. If “unknown” or “not applicable,” continue with question 127.

Questions 127-128: Serum β2 macroglobulin

Indicate whether β2 microglobulin was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 128. If “unknown,” continue with question 129.
Questions 129-130: Relative serum viscosity

Hyperviscosity syndrome is a common manifestation of WM and LPL. Indicate if relative serum viscosity was "known" or "unknown" immediately prior to the start of the preparative regimen. If “known,” report the laboratory value in question 130. If “unknown,” continue with question 131.

Questions 131-132: Serum monoclonal protein (M-spike) (only from electrophoresis)

Indicate whether serum monoclonal protein quantification from electrophoresis was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the laboratory value and unit of measure in question 132. If serum electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 133.

Questions 133-134: Urinary monoclonal protein (M-spike)

Indicate whether 24-hour urine monoclonal protein quantification from electrophoresis was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the laboratory value in question 134. If urine electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 135.

Question 135: Cold agglutinins

Cold agglutinin disease is a common manifestation of WM and LPL. Cold agglutinins are autoantibodies that bind to the red blood cells, manifesting as autoimmune hemolytic anemia. Indicate if cold agglutinins were “positive” or “negative” immediately prior to the start of the preparative regimen. If cold agglutinins were not tested or it is unknown if cold agglutinins were tested, report “unknown.”

Question 136: Cryoglobulin

Cryoglobulins are immunoglobulins that aggregate as a gel at temperatures below 37°C. Cryoglobulins may be mixed immunoglobulins or a single component; the majority of cryoglobulin in WM or LPL patients will be mixed IgM-IgG. Indicate if cryoglobulin was “present” or “absent” immediately prior to the start of the preparative regimen. If cryoglobulin was not tested or it is unknown if cryoglobulin was tested, report “unknown.”

Questions 137-139: IgG

Indicate whether IgG level was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the laboratory value and unit of measure in question 138; report the laboratory upper limit of normal value and unit of measure in question 139. If “unknown,” continue with question 140.
Questions 140-142: IgA

Indicate whether IgA level was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the laboratory value and unit of measure in question 141; report the laboratory upper limit of normal value and unit of measure in question 142. If “unknown,” continue with question 143.

Questions 143-145: IgM

Indicate whether IgM level was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the laboratory value and unit of measure in question 144; report the laboratory upper limit of normal value and unit of measure in question 145. If “unknown,” continue with question 146.

Question 146: Were cytogenetics tested (conventional or FISH)?

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient’s disease. Testing methods include conventional chromosome analysis (karyotyping) and fluorescence in situ hybridization (FISH) testing. For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained immediately prior to the start of the preparative regimen.

If cytogenetic studies were obtained, check “yes” and continue with question 147.

If cytogenetic studies were not obtained or it is unknown if chromosome studies were performed, indicate “no” or “unknown” and continue with question 151.

Question 147: Results of tests

If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), indicate “abnormalities identified” and continue with question 148.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 151.

Question 148-150: Specify abnormalities

Deletion of the long arm of chromosome 6 is the most common structural abnormality in WM and LPL. However, other structural and numeric abnormalities have been noted.

If question 147 indicates that abnormalities were identified immediately prior to the start of the preparative regimen, questions 148-149 must be answered as “yes” or “no.” Do not leave either response blank. If the patient had any abnormality other than del(6q), select “yes” for “other abnormality,” and specify in question
150.
Q151-152: Disease Status at Last Evaluation Prior to the Preparative Regimen

**Question 151: What was the disease status at the last evaluation prior to the preparative regimen?**

Indicate the disease status of WM or LPL at last evaluation prior to the start of the preparative regimen.

See [WM Response Criteria](#) for disease status definitions.

**Question 152: Date assessed**

Enter the date of the most recent assessment of disease status within the pre-transplant work-up period (approximately 30 days) prior to the start of the preparative regimen. Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., SPEP), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluation; enter the date the imaging took place for radiographic assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in [General Instructions, Guidelines for Completing Forms](#).
2119: WM Post-HCT

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Non-Hodgkin lymphoma and the subtype is reported as Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma. The Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma Post-HCT Data (Form 2119) must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, 2300) completed. The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200, between the date of contact for the six-month follow-up and the date of contact for the one-year follow-up for Form 2200, etc.).

Q1-17: Disease Assessment at the Time of Best Response to HCT  
Q18-58: Post-HCT Therapy  
Q59-77: Laboratory Studies at the Time of Evaluation for this Reporting Period  
Q78-79: Disease Status at the Time of Evaluation for this Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
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| 3/19/18    | Comprehensive Disease Specific Manuals | Add               | Added the following instruction for applicable post-infusion disease-specific forms where current disease status is asked (2110, 2111, 2112, 2113, 2114, 2115, 2116, 2118, 2119).  
The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression. |
| 2/24/17    | Comprehensive Disease-Specific Manuals | Modify            | Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400) |
| 5/29/15    | 2119: WM Post-HCT                    | Modify            | Clarified explanatory text for questions 22-23:  
Indicate if the number of cycles is “known” or “unknown.” If the number of cycles is known, continue with question 23 and specify the number of cycles of chemotherapy administered. If the patient received a single |
administration or one line of chemotherapy, indicate a single cycle. If the patient received long-term maintenance therapy consisting of a single agent, indicate “known” for question 82; leave question 83 blank and override the error as “not applicable.” Indicate if the number of cycles is “known” or “unknown.” If known, report the number of cycles the recipient received during the reporting period for the line of therapy reported in question 23. If the therapy is not given in cycles or the number of cycles is not known, select “unknown” and continue with question 24. If the number of cycles is unknown, continue with question 24.
Q1-17: Disease Assessment at the Time of Best Response to HCT

Question 1: Compared to the disease status prior to the preparative regimen, what was the best response to HCT since the date of last report? (Include response to any therapy given for post-HCT maintenance or consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease)

Any specified therapy administered post-HCT to prolong remission or for minimal residual disease is considered part of the HCT and should be included when assessing the recipient’s response to transplant. Treatment given post-HCT for relapsed or persistent disease is not considered part of the HCT and should be excluded when assessing the response to HCT. If treatment was given post-HCT for relapsed or persistent disease, assess the patient’s best response prior to the start of therapy. If therapy was only given for reasons other than relapsed or persistent disease, assess the patient’s best response throughout the entire duration of the reporting period.

If the recipient was in remission at the start of the preparative regimen, indicate “continued complete remission” and continue with question 2.

If the recipient was not in remission at the start of the preparative regimen, indicate their best response to transplant and continue with question 2. If the recipient did not have their disease evaluated by any method of assessment, including physical examination, report “not assessed” and continue with question 18.

See WM Response Criteria for disease status definitions.

Question 2: Was the date of best response previously reported?

If the patient achieved their best response to transplant in the current reporting period, indicate “no” and continue with question 3.

If the recipient achieved their best response to transplant during a previous reporting period, indicate “yes” and continue with question 18.

Question 3: Date assessed

Report the date of the assessment that established the best disease response to transplant. Enter the date the sample was collected for pathological and laboratory evaluation.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
Questions 4-5: Absolute lymphocyte count

Indicate whether the lymphocyte count was “known” or “unknown” at the time of best response to transplant. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 5. If “unknown,” continue with question 6.

Questions 6-8: IgM

Indicate whether the IgM level was “known” or “unknown” at the time of best response to transplant. If “known,” report the laboratory value and unit of measure in question 7; report the laboratory upper limit of normal value and unit of measure in question 8. If “unknown,” continue with question 9.

Questions 9-10: Serum monoclonal protein (M-spike) (only from electrophoresis)

Indicate whether serum monoclonal protein quantification from electrophoresis was “known” or “unknown” at the time of best response to transplant. If “known,” report the laboratory value and unit of measure in question 10. If serum electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 11.

Questions 11-12: Urinary monoclonal protein (M-spike)

Indicate whether 24-hour urine monoclonal protein quantification from electrophoresis was “known” or “unknown” at the time of best response to transplant. If “known,” report the laboratory value and unit of measure in question 12. If urine electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 13.

Questions 13-14: Bone marrow aspirate (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow aspirate was “known” or “unknown” at the time of best response to transplant. If bone marrow aspirate was not examined, report “not applicable.” If “known,” report the extent of aspirate histologic involvement in question 14. If “unknown” or “not applicable,” continue with question 15.

Questions 15-16: Bone marrow biopsy (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow biopsy was “known” or “unknown” at the time of best response to transplant. If bone marrow biopsy was not examined, report “not applicable.” If “known,” report the extent of biopsy histologic involvement in question 16. If “unknown” or “not applicable,” continue with question 17.
Question 17: Specify the type of histological involvement in marrow

WM and LPL are often characterized by histologic involvement of the bone marrow. However, there are variations in the type of involvement.¹

- **Lymphoplasmacytoid:** This variant is primarily defined by small lymphocytes with some plasmacytoid lymphocytes and rare mature plasma cells. Lymphoplasmacytoid cells (plasmacytoid lymphocytes) are mononuclear cells with dark, irregular nuclei. They are slightly larger than a small lymphocyte. Additionally, mitotic and large cells are rare.
- **Lymphoplasmacytic:** In this variant, the involved cells are a mix of small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells. Mitotic and large cells are rare.
- **Polymorphous:** This variant can resemble either lymphoplasmacytoid or lymphoplasmacytic variants, but mitotic and large cells are more common. Large cells are still less common than in large cell lymphomas.

Specify the type of histologic involvement as indicated by the pathology report or transplant physician. Report “unknown” if the bone marrow was not examined, there was no bone marrow involvement, or if the type of histologic involvement cannot be specified.

Q18-58: Post-HCT Therapy

Complete a “Line of Therapy” section for each line of therapy administered during the current reporting period. If multiple lines of therapy were administered, copy and complete questions 19-56 for each line of therapy.

**Question 18: Was therapy given since the date of the last report for reasons other than relapse or progressive disease? (Include any maintenance and consolidation therapy)**

Indicate if the recipient received treatment for WM/LPL during the current reporting period for any reason other than relapsed or persistent disease, e.g., maintenance or consolidation therapy. If the patient received therapy for reasons other than relapsed or persistent disease, check “yes” and continue with question 19. If the patient did not receive therapy, or only received therapy for relapsed or persistent disease, check “no” and continue with question 57.

**Question 19: Systemic therapy**

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body.

Indicate “yes” if the patient received systemic therapy and continue with question 20. If the patient did not receive systemic therapy, indicate “no” and continue with question 48.

**Questions 20-21: Date therapy started**

Indicate “known” if the therapy start date is documented, and specify the start date in question 21. If the date is unknown, indicate this and continue with question 22.

**Questions 22-23: Number of cycles**

Indicate if the number of cycles is “known” or “unknown.” If known, report the number of cycles the recipient received during the reporting period for the line of therapy reported in question 23. If the therapy is not given in cycles or the number of cycles is not known, select “unknown” and continue with question 24.

**Questions 24-47: Specify systemic therapy agents**

Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Drugs may be administered in an inpatient or outpatient setting, and treatment may consist of one or multiple drugs. Additionally, drugs may be administered on a single day, over consecutive days, or continuously.
Indicate “yes” or “no” for each therapeutic agent listed. Do not leave any response blank. If the recipient received an agent that is not listed, check “yes” for “other systemic therapy” and specify the treatment in question 47.

**Question 48: Radiation therapy**

Radiation therapy uses high-energy, ionizing radiation to kill malignant cells. Much like non-targeted systemic therapy, radiation therapy does not specifically target malignant cells and does have significant side effects. For that reason, high-dose radiation often targets a limited field.

Indicate if the recipient received radiation treatment for WM or LPL during the current reporting period. If “yes,” continue with question 49. If “no,” continue with question 53.

**Question 49: Date therapy started**

Specify the first date of radiation administration. If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Questions 50-52: Specify radiation site(s)**

Specify radiation site(s). If question 48 is answered “yes,” at least one site of radiation therapy must be specified in questions 50-52.

**Question 53: Best response to line of therapy**

Indicate the patient’s best response to this line of therapy. See WM Response Criteria for disease status definitions.

**Question 54: Date assessed**

Enter the date the best response to the line of therapy was established. Report the date of the pathological (e.g., bone marrow biopsy), radiological (e.g., CT), or biochemical (e.g., SPEP) evaluation. Enter the date the sample was collected for examination for pathological and/or laboratory evaluation, or enter the date the imaging took place for radiologic assessment. If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically assessed the recipient’s response.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
**Question 55: Did disease relapse/progress following this line of therapy?**

Relapse is the recurrence of disease after CR. WM or LPL relapse is demonstrated by reappearance of disease characteristics, including IgM paraprotein, lymphadenopathy and/or organomegaly, and bone marrow histologic involvement.

WM or LPL progression criteria are specified in Table 2 above. Indicate if relapse or progression occurred following the line of therapy being reported. If question 53 is answered “progressive disease,” question 55 must be “yes.”

**Question 56: Date of relapse/progression**

Enter the date of the assessment that identified relapse or progression following the line of therapy and continue with question 59. Enter the date the sample was collected for pathological and laboratory evaluation or enter the date the imaging took place. If the physician determined evidence of relapse during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 57: Has disease relapsed or progressed since the date of last report?**

Relapse is the recurrence of disease after CR. WM or LPL relapse is demonstrated by reappearance of disease characteristics, including IgM paraprotein, lymphadenopathy and/or organomegaly, and bone marrow histologic involvement.

WM or LPL progression criteria are specified in Table 2 above. Indicate if relapse or progression occurred at any time during the reporting period.

**Question 58: Date of relapse/progression**

Enter the date of the assessment that identified relapse or progression during the reporting period. Enter the date the sample was collected for pathological and laboratory evaluation or enter the date the imaging took place. If the physician determined evidence of relapse during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
Q59-77: Laboratory Studies at the Time of Evaluation for this Reporting Period

These questions are intended to determine the status of the recipient at the last evaluation for this reporting period. Testing may have been performed multiple times during the reporting period; report the most recent laboratory values. Reported values should be within a reasonable time frame of the date of contact, or approximately one month prior to the date of contact. If the recipient received any treatment or therapy for relapse, progression, or persistent disease, leave this section of the form blank and continue with the signature section.

Questions 59-60: Absolute lymphocyte count

Indicate whether the lymphocyte count was “known” or “unknown” at the time of evaluation for the reporting period. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 60. If “unknown,” continue with question 61.

Questions 61-63: IgM

Indicate whether the IgM level was “known” or “unknown” at the time of evaluation for the reporting period. If “known,” report the laboratory value and unit of measure in question 62; report the laboratory upper limit of normal value and unit of measure in question 63. If “unknown,” continue with question 64.

Questions 64-65: Serum monoclonal protein (M-spike) (only from electrophoresis)

Indicate whether serum monoclonal protein quantification from electrophoresis was “known” or “unknown” at the time of evaluation for the reporting period. If “known,” report the laboratory value and unit of measure in question 65. If serum electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 66.

Questions 66-67: Urinary monoclonal protein (M-spike)

Indicate whether 24-hour urine monoclonal protein quantification from electrophoresis was “known” or “unknown” at the time of evaluation for the reporting period. If “known,” report the laboratory value and unit of measure in question 67. If urine electrophoresis was done and did not show monoclonal protein, report “0.” If “unknown,” continue with question 68.

Questions 68-69: Bone marrow aspirate (examined for histologic involvement)

Indicate whether the extent of histologic involvement in the bone marrow aspirate was “known” or “unknown”
at the time of evaluation for the reporting period. If bone marrow aspirate was not examined, report “not applicable.” If “known,” report the extent of aspirate histologic involvement in question 69. If “unknown" or “not applicable,” continue with question 70.

**Questions 70-71: Bone marrow biopsy (examined for histologic involvement)**

Indicate whether the extent of histologic involvement in the bone marrow biopsy was “known” or “unknown” at the time of evaluation for the reporting period. If bone marrow biopsy was not examined, report “not applicable.” If “known,” report the extent of biopsy histologic involvement in question 71. If “unknown” or “not applicable,” continue with question 72.

**Question 72: Specify the type of histological involvement in marrow**

WM and LPL are often characterized by histologic involvement of the bone marrow. However, there are variations in type of involvement.\(^1\)

- **Lymphoplasmacytoid:** This variant is primarily defined by small lymphocytes with some plasmacytoid lymphocytes and rare mature plasma cells. Lymphoplasmacytoid cells (plasmacytoid lymphocytes) are mononuclear cells with dark, irregular nuclei. They are slightly larger than a small lymphocyte. Additionally, mitotic and large cells are rare.

- **Lymphoplasmacytic:** In this variant, the involved cells are a mix of small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells. Mitotic and large cells are rare.

- **Polymorphous:** This variant can resemble either lymphoplasmacytoid or lymphoplasmacytic variants, but mitotic and large cells are more common. Large cells are still less common than in large cell lymphomas.

Specify the type of histologic involvement as indicated by the pathology report or transplant physician. Report “unknown” if the bone marrow was not examined, there was no bone marrow involvement, or if the type of histologic involvement cannot be specified.


**Question 73: Was there any clinical or radiological (e.g., CT, PET, PET/CT) evidence of organ involvement at the time of evaluation for this reporting period?**

Indicate whether the recipient had clinical or radiological evidence of organ involvement at the time of evaluation for the reporting period. This includes clinical manifestations of WM/LPL such as palpable lymphadenopathy or hyperviscosity syndrome, and radiological evidence such as organomegaly or lymphadenopathy. Do not include biochemical markers as clinical involvement, as they are captured in other
data fields in this form section.

**Questions 74-77: Specify site(s)**

Indicate “yes” or “no” for each site specified in questions 74-76. Do not leave any response blank. If “yes” is indicated for “other site,” specify the site in question 77. Include clinical manifestations (such as hyperviscosity syndrome or cold agglutinin disease) under “other site.” If the patient had clinical or radiological evidence of disease indicated in question 73, at least one of questions 74-76 must be answered “yes.”
Q78-79: Disease Status at the Time of Evaluation for this Reporting Period

Question 78: What is the current disease status?

Indicate the disease status of WM or LPL at last evaluation during the reporting period. See [WM Response Criteria](#) for disease status definitions.

The center does not need to repeat all disease-specific assessments (biopsies, scans, labs) each reporting period in order to complete current disease status data fields. Once a particular disease status is achieved, the center can continue reporting that disease status (based on labs / clinical assessments) until there is evidence of relapse / progression.

Question 79: Date assessed

Enter the date of the most recent assessment establishing disease status within the reporting period. The date reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., SPEP), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluation; enter the date the imaging took place for radiographic assessment, or the date of physical examination.

If the exact date is not known, use the process for reporting partial or unknown dates as described in [General Instructions, Guidelines for Completing Forms](#).
2028/2128: Aplastic Anemia

Aplastic Anemia is a disease in which the bone marrow does not produce enough red blood cells, white blood cells, or platelets for the body. The disease can be idiopathic, or can be caused by environmental exposure, pharmaceutical or drug exposure, or exposure to viral hepatitis. Symptoms of aplastic anemia include, but are not limited to pallor, weakness, frequent infection, and/or easy bruising.

2028: Aplastic Anemia Pre-HCT
2128: Aplastic Anemia Post-HCT
2028: Aplastic Anemia Pre-HCT

The Aplastic Anemia Pre-HSCT Data Form is one of the Comprehensive Report Forms. This form captures aplastic anemia-specific pre-HSCT data such as: disease assessment at diagnosis, laboratory studies at diagnosis, transfusion status prior to the start of the preparative regimen, and laboratory studies prior to the start of the preparative regimen.

This form must be completed for all recipients whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as severe aplastic anemia, paroxysmal nocturnal hemoglobinuria, or one of the following inherited abnormalities of erythrocyte differentiation or function: Shwachman-Diamond syndrome, Diamond-Blackfan anemia (pure red cell aplasia), or other constitutional anemia. Fanconi Anemia and Sickle Cell Anemia each have their own forms to complete (Forms 2029 and 2030, respectively).

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1.

If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than Aplastic Anemia), begin at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, check the indicator box and continue with question 31.

Q1-18: Disease Assessment at Diagnosis
Q19-49: Laboratory Studies at Diagnosis
Q50-52: Transfusion Status from Diagnosis to the Start of the Preparative Regimen
Q53-61: Laboratory Findings to the Start of the Preparative Regimen

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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<td>2028: Aplastic Anemia Pre-HCT</td>
<td>Add</td>
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<td>Comprehensive Disease-Specific Manuals</td>
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**Q1-18: Disease Assessment at Diagnosis**

**Question 1: What was the date of diagnosis of Aplastic Anemia?**

Report the date of first pathological evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear) that determined the diagnosis. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared. The date of diagnosis is important because the interval between diagnosis and HSCT is often a significant indicator for the recipient’s prognosis post-HSCT.

If the exact pathological diagnosis date is not known, use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](#).

**Question 2: Was the recipient’s bone marrow examined at diagnosis?**

Indicate whether a bone marrow examination was performed at diagnosis. If “yes,” continue with question 3. If “no,” continue with question 4.

**Question 3: Is a copy of the biopsy report attached?**

Indicate if a copy of the biopsy report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the biopsy report. Attaching a copy of the report may prevent additional queries.

**Question 4: Were the recipient’s cells tested for sensitivity to cross-linking agents (e.g., diepoxybutane [DEB], mitomycin C [MMC])?**

Studies that measure the sensitivity of a recipient’s cells to cross-linking agents (i.e., chromosome breakage studies) are often performed for patients with anemia. If the recipient’s cells were tested for sensitivity to these agents, select “yes” and continue with question 5.

If no tests for sensitivity to cross-linking agents were performed, continue with question 7.

If it is unknown if cross-linking sensitivity testing was performed, select “unknown” and continue with question 7.

**Question 5: Specify the test results:**

Indicate if the recipient’s sensitivity test results were normal, revealed increased chromosome breaks, or
were unknown.

**Question 6: Is a copy of the test report attached?**

Indicate if a copy of the report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the report. Attaching a copy of the report may prevent additional queries.

**Questions 7-10: What was the disease etiology?**

Indicate the disease etiology of aplastic anemia.

If the etiology of aplastic anemia is Diamond-Blackfan anemia, check the box for "Diamond-Blackfan anemia." Diamond-Blackfan anemia (DBA) is a hematologic disease in which the body does not create enough red blood cells. There are associated birth abnormalities and diagnosis is usually made early in life.

If the etiology of aplastic anemia is drug induced, check the box for "drug induced." If the specific drug causing the aplastic anemia is known, report it in question 8. If the specific drug is not known, select "drug unknown." Drugs that have been associated with aplastic anemia include, but are not limited to antibiotics (e.g., sulfonamides, chloramphenicol), diabetes medications (e.g., tolbutamide, carbutamide, chlorpropamide), anti-seizure medications, and phenothiazines (Thorazine, Compazine).  


If the etiology of aplastic anemia is from viral hepatitis, check the box for “viral hepatitis.” Use question 9 to report the specific type of hepatitis or select “type unknown” if the specific type causing aplastic anemia is not known.

Idiopathic aplastic anemia has no known cause. If the origin of aplastic anemia is unknown, check the box for “idiopathic.”

If the origin of aplastic anemia is from some other cause, check the box for “other.” Specify the other disease etiology using question 10, or select “etiology unknown” if the cause of aplastic anemia is not known.

**Question 11: Was testing for paroxysmal nocturnal hemoglobinuria (PNH) performed?**

Paroxysmal nocturnal hemoglobinuria (PNH) is a disease in which the red blood cells break down too quickly. The disease is characterized by anemia, red urine, and thrombosis. Indicate if the recipient had testing for paroxysmal nocturnal hemoglobinuria. If “yes,” continue with question 12. If “no,” continue with question 19.
If it is not known if the recipient received testing for paroxysmal nocturnal hemoglobinuria, select “unknown” and continue with question 19.

**Questions 12-18: Specify PNH test and results:**

Indicate which test(s) were performed for PNH. If a test was performed that is not listed, select “yes” for “other test” and specify the test using question 18. Do not leave any question blank.

Flow cytometry is a technique that counts and differentiates cell surface markers. CD55, CD16, and CD59 surface markers are associated with PNH.

Ham’s acid hemolysis test is performed to determine if red blood cells are more likely to break when placed in a mild acid.\(^2\)

Hemosiderinuria testing measures the amount of hemosiderin in the urine. Hemosiderin is found within cells and acts as an iron storage device. Hemosiderin in the urine often causes the urine to appear brown.

PIGA GPI anchor protein defects are associated with PNH. PIGA is an enzyme that is required to synthesize the GPI anchor. The GPI anchor allows proteins (such CD55, CD16, and CD59) to become attached to the surface of the cell. Defects in the PIGA enzyme, and subsequently the GPI anchor, prevent these surface marker proteins from becoming attached. Due to the lack of these proteins on the surface of red blood cells, the immune system may not recognize the cells causing them to be destroyed. Report assessments (such as molecular PCR testing) to detect defects in the PIGA gene or GPI anchor using this option.

Sugar water/sucrose lysis tests are performed to detect how fragile red blood cells become when placed in a high-sugar/low-salt environment.\(^2\) This environment causes the red blood cells to swell; fragile cells are more prone to break down.

\(^2\) Definitions of these tests were found at the A.D.A.M. Medical Encyclopedia at [http://www.nlm.nih.gov/medlineplus/encyclopedia.html](http://www.nlm.nih.gov/medlineplus/encyclopedia.html)
Q19-49: Laboratory Studies at Diagnosis

Report findings prior to any first treatment for aplastic anemia.

Questions 19-20: WBC:

Indicate whether the white blood count (WBC) is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “not known,” continue with question 21.

Question 21-22: Hemoglobin:

Indicate whether the hemoglobin is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “not known,” continue with question 24.

RBC and Platelet Transfusions
Currently, there is an error on the Form 2028 regarding transfusion history. The form should state: “Was RBC transfused less than or equal to \( \leq \) 30 days before the date of test?” and “Were platelets transfused less than or equal to \( \leq \) 7 days before the test.”

Question 23: Was RBC transfused < 30 days before date of test?

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

Indicate if red blood cells were transfused less than or equal to 30 days prior to the testing.

Questions 24-25: Platelets:

Indicate whether the platelet count is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “not known,” continue with question 27.

Question 26: Were platelets transfused < 7 days before date of test?

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support the counts.
Indicate if platelets were transfused less than or equal to 7 days prior to the testing.

**Questions 27-28: Neutrophils:**

Indicate whether the neutrophil count in the blood is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the value documented on the laboratory report. If “not known,” continue with question 29.

**Questions 29-30: Reticulocytes (uncorrected):**

Indicate whether the uncorrected reticulocyte count in the blood is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the value documented on the laboratory report. If “not known,” continue with question 31.

Report the absolute value of reticulocytes in ___ x 10^9/L. Do not report a percentage, the corrected reticulocyte count, or the reticulocyte production index.

**Question 31: Was therapy given for treatment of aplastic anemia prior to the start of the preparative regimen?**

Indicate if the recipient received treatment for aplastic anemia between the time of diagnosis and the start of the preparative regimen. If “yes,” continue with question 32. If “no” or “unknown,” continue with question 50.

If this is a report of a **second or subsequent transplant** for aplastic anemia and this baseline disease insert has previously been completed for a prior transplant, indicate if the recipient received treatment for aplastic anemia between Day 0 of the previous HCT and the start of the preparative regimen for the subsequent HCT.

**Questions 32-49: Specify what treatment(s) were given:**

Indicate the treatment(s) given to the recipient.

- **Androgens** (e.g., danazol, fluoxymesterone, oxymethalone, stanozole, testosterone) are male hormones that can cause the bone marrow to create more red blood cells.\(^1\)

- **ATG** (anti-thymocyte globulin), **ALS** (anti-lymphocyte serum), **ATS** (anti-thymocyte serum), and **ALG** (anti-lymphocyte globulin) are immunosuppressive therapies that attack lymphocytes (T cells).\(^2\)

- **Chelation therapy** (e.g., deferoxamine, deferasirox, deferiprone) for iron is the removal of iron from the body. Iron overload is a complication resulting from many red blood cell transfusions.\(^1\)
Corticosteroids (e.g., methylprednisolone) are used as an immunosuppressive therapy that causes the immune system to create fewer antibodies.\(^2\)

Cyclosporine (CsA, Neoral\(^\text{®}\), Sandimmune\(^\text{®}\)) is an immunosuppressive treatment that prevents T cells from becoming active.\(^1\)

Cytokines are groups of proteins that signal cell growth and differentiation. These growth factors stimulate the growth of red blood cells (erythropoietin) and white blood cells (G-CSF, GM-CSF, interleukin-3, pegfilgrastim). If the recipient received a cytokine or growth factor that was not listed in questions 33-38, select “yes” for question 39, and specify in question 40 which cytokine or growth factor was used.

Other immunosuppression includes those immunosuppressive therapies not already listed above. If the recipient received immunosuppressives not listed, such as mycophenolate mofetil or monoclonal antibodies (e.g., alemtuzumab, rituximab), select “yes” for question 41 and specify in question 42 which other immunosuppressant(s) were used.

Other treatment includes those treatments not already listed above. If the recipient received treatments not listed, such as chemotherapy (not given as the preparative regimen for transplant), select “yes” for question 43 and specify in question 44 which other treatment(s) were used.


Q50-52: Transfusion Status from Diagnosis to the Start of the Preparative Regimen

Question 50: Did the recipient receive red blood cell transfusions between diagnosis and the start of the preparative regimen?

If the recipient received red blood cell transfusions after diagnosis and before the start of the preparative regimen, select “yes” and continue with question 46. If the recipient did not receive red blood cell transfusions prior to the preparative regimen, indicate “no” and continue with question 52.

Question 51: Specify the total number of donor exposures (best estimate):

Indicate the total number of red blood cell transfusions the recipient received after diagnosis and before the start of the preparative regimen. Using your best judgment, estimate the total number of transfusions based on progress notes and transfusion summaries since diagnosis. For example, if you have progress notes from a referring physician that state the recipient received one red blood cell transfusion a month for one year and then two transfusions monthly for six months before arriving at your center for HCT (i.e., 24 RBC transfusions prior to the preparative regimen), indicate that the recipient had 21-30 donor exposures between diagnosis and the start of the preparative regimen.

Question 52: Did the recipient receive platelet transfusions between diagnosis and the start of the preparative regimen?

Indicate “yes” if the recipient received platelet transfusions after diagnosis and before the start of the preparative regimen. Indicate “no” if the recipient did not receive any platelet transfusions prior to the preparative regimen.
Q53-61: Laboratory Findings to the Start of the Preparative Regimen

Questions 53-54: Reticulocytes (uncorrected):

Indicate whether the uncorrected reticulocyte count in the blood is “known” or “not known” prior to the start of the preparative regimen. If “known,” report the value documented on the laboratory report. If “not known,” continue with question 55.

Report the absolute value of reticulocytes in __ x 10^9/L. Do not report a percentage, the corrected reticulocyte count, or the reticulocyte production index.

Question 55: Date of most recent bone marrow biopsy:

Report the date of the most recent bone marrow biopsy prior to the start of the preparative regimen. Enter the date the sample was collected for examination.

Question 56: Is a copy of the most recent bone marrow biopsy report attached?

Indicate if a copy of the biopsy report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the biopsy report. Attaching a copy of the report may prevent additional queries.

Question 57: Were any clinically important infections present or being treated within one week prior to the preparative regimen?

Indicate if there were any clinically important bacterial, viral, fungal, or parasitic infections present or being treated within one week prior to the start of the preparative regimen. If “yes,” continue with question 58. If “no,” continue with question 80.

If it is unknown if the recipient had a clinically important infection or was being treated for any clinically important infections within one week prior to the start of the preparative regimen, select “unknown” and continue with signature lines.

Questions 58-61: Report each infection organism, site and date of diagnosis:

For each infection, report the organism, site, and date of diagnosis.

Organism:

From the table “Codes for Commonly Reported Organisms,” select the code corresponding to the
identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. Report the code in the boxes provided. If the specific organism is not listed, use the “other, specify” code (198 – bacteria, 209 – Candida, 219 – Aspergillus, 259 – fungus, 329 – virus, 409 – parasite) and report the name of the organism in the space provided. If an organism is suspected, but not identified, report using codes 501-505 as applicable. If the source of the infection is not determined, use code 509.

**Bacterial infections:** Atypical bacteria (codes 101-119 and 501) are collected separately from other more common types of bacteria. Typical bacteria are codes 120-198 and 502. If more than one typical bacterial organism is found in a single site, include all the organisms in one listing; do not record each separately. Either write the code in the margin or use Report “Notes.”

**Fungal infections:** Note the inclusion of pneumocystis (formerly found under parasites). The most commonly found fungal infections are Candida (C. albicans, C. tropicalis, C. glabrata [also known as Torulopsis glabrata], C. parapsilosis, C. krusei), Aspergillus (A. fumigatus), Fusarium sp., and Zygomycetes.

**Viral infections:** These are caused by exposure to a new virus or reactivation of a dormant virus already present in the body. The most common viral infections are due to HSV (herpes simplex virus), VZV (varicella zoster virus, shingles), and CMV (cytomegalovirus).

**Parasitic infections:** Parasites are fairly rare. Toxoplasma gondii is often transmitted through the handling of a cat litter box. Giardia and Cryptosporidium can be found in contaminated water.

**Fever of undetermined origin:** Defined as “any fever (> 38°C) not associated with documented/suspected infection in a specific site,” data on fevers of undetermined origin are not collected by the CIBMTR, as the occurrence is too common for analysis.

**Site:**
From the table “Codes for Common Sites of Infection,” select the code corresponding to the site of the infection.

If three or more sites are infected with the same organism, enter code 2 (Disseminated – generalized, isolated at 3 or more distinct sites).

The CIBMTR acknowledges that a discrepancy exists between the CIBMTR definition (3 or more sites) and the BMT-CTN definition (2 or more sites) for disseminated infections. For the purposes of this form, please use “disseminated” when the same organism is isolated at three or more distinct sites.
**Date of Diagnosis:**
Report the collection date for the positive microbiology culture as the date of diagnosis for the infections. For suspected infections, enter the date of a radiology test or the date treatment was started as date of diagnosis.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).
2128: Aplastic Anemia Post-HCT

The Aplastic Anemia Post-HSCT Data Form is one of the Comprehensive Report Forms. This form captures aplastic anemia-specific post-HSCT disease assessment data for the reporting period.

This form must be completed for all recipients whose primary disease, as reported on the Pre-TED Disease Classification Form (Form 2402) as severe aplastic anemia, paroxysmal nocturnal hemoglobinuria, or one of the following inherited abnormalities of erythrocyte differentiation or function: Shwachman-Diamond syndrome, Diamond-Blackfan anemia (pure red cell aplasia), or other constitutional anemia. Fanconi Anemia and Sickle Cell Anemia each have their own forms to complete (Forms 2129 and 2130, respectively).

The Aplastic Anemia Post-HSCT Data (Form 2128) must be completed in conjunction with each Post-HSCT follow-up form completed (Forms 2100, 2200, and 2300). Form 2128 is designed to capture specific data occurring within the timeframe of each reporting period (e.g., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200 Six-Month follow-up, between the date of contact for the six-month follow-up Form 2200 and the date of contact for the one-year follow up Form 2200, etc).

Q1-6: Disease Assessment at the Time of Assessment for This Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
<tr>
<td>9/14/15</td>
<td>2028/2128: Aplastic Anemia</td>
<td>Modify</td>
<td>Updated questions number is 2028 and 2128 Aplastic Anemia Pre- and Post-HCT</td>
</tr>
</tbody>
</table>
Q1-6: Disease Assessment at the Time of Assessment for This Reporting Period

Question 1: Was the recipient red blood cell (RBC) transfusion independent since the date of the last report?

Indicate if the recipient was RBC transfusion independent since the date of the last report. A general guideline for RBC transfusion independence is that RBC transfusions have not been required for four or more weeks.

Some discretion may be required if the recipient received a transfusion for a surgical procedure or other reason. If a recipient received an RBC transfusion for a procedure and would otherwise be transfusion independent, the recipient may still be reported as being transfusion independent.

If the recipient was RBC transfusion independent since the date of the last report, select “yes” and continue with question 3.

If the recipient was not RBC transfusion independent since the date of the last report, select “no” and continue with question 2.

If it is not known if the recipient was RBC transfusion independent since the date of the last report, select “unknown” and continue with question 3.

Question 2: Date of the most recent RBC transfusion:

Indicate the date of the most recent RBC transfusion.

If the recipient was RBC transfusion independent for ≥ one month, but subsequently experienced a decline in RBCs and required transfusions, record the date of the last RBC transfusion before the date of decline.

If the date reported on question 2 is more than one month prior to the date of contact, evaluate if the recipient is RBC transfusion independent.

Question 3: Was the recipient platelet transfusion independent since the date of the last report?

Indicate if the recipient was platelet transfusion independent since the date of the last report. A general guideline for platelet transfusion independence is that platelet transfusions have not been required for seven or more days.
If the recipient was platelet transfusion independent since the date of the last report, select “yes” and continue with question 5.

If the recipient was not platelet transfusion independent since the date of the last report, select “no” and continue with question 4.

If it is unknown if the recipient was platelet transfusion independent since the date of the last report, select “unknown” and continue with question 5.

If the recipient was never dependent on platelet transfusions or if this question is not applicable, select “not applicable/never dependent” and continue with question 5.

**Question 4: Date of the most recent platelet transfusion:**

Indicate the date of the most recent platelet transfusion.

If the recipient was platelet transfusion independent for ≥ 14 days but subsequently experienced a decline in platelets and required transfusions, record the date of the last platelet transfusion before the date of decline.

If the date reported on question 4 is more than seven days prior to the date of contact, evaluate if the recipient is platelet transfusion independent.

**Questions 5-6: Specify reticulocyte level (uncorrected):**

Indicate whether the uncorrected reticulocyte count in the blood is “known” or “not known/transfused” since the date of last report. If the reticulocyte count was assessed multiple times during the reporting period, report the results of the latest reticulocyte count. If “known,” report the value documented on the laboratory report.

If the recipient had an RBC transfusion within 30 days prior to the latest reticulocyte count, select “not known/transfused” and do not report a value.

Report the absolute value of reticulocytes in ___ x 10^9/L. Do not report a percentage, the corrected reticulocyte count, or the reticulocyte production index.
Immune deficiencies (ID) are genetic disorders characterized by dysfunction of the immune system. Because immune deficiencies are caused by a broad range of genetic mutations, symptoms for each disorder vary. Immune deficiencies are often diagnosed at birth following newborn screening, or following severe and/or persistent infections. Symptoms of immune deficiencies include severe, protracted, difficult to treat infections, decreased weight and height for age, autoimmune disorders, and/or developmental delay. Hematopoietic cell transplant (HCT) is currently the major curative treatment for immune deficiencies.

- **2031: Immune Deficiencies Pre-HCT**
- **2131: Immune Deficiencies Post-HCT**
2031: ID Pre-HCT

The Immune Deficiency Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures ID-specific pre-HCT data such as: disease assessment at diagnosis, laboratory studies at diagnosis, clinical features assessed between diagnosis and the start of the preparative regimen, and pre-HCT therapy.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Disorders of the Immune System and specified as:

- Adenosine deaminase (ADA) deficiency / severe combined immunodeficiency (SCID)
- Absence of T and B cells SCID
- Absence of T, normal B cell SCID
- Omenn syndrome
- Reticular dysgenesis
- Bare lymphocyte syndrome
- Other SCID
- SCID, not otherwise specified
- Ataxia telangiectasia
- HIV infection
- DiGeorge anomaly
- Common variable immunodeficiency
- Leukocyte adhesion deficiencies, including GP180, CD-18, LFA, and WBC adhesion deficiencies
- Kostmann agranulocytosis (congenital neutropenia)
- Neutrophil actin deficiency
- Cartilage-hair hypoplasia
- CD40 ligand deficiency
- Other Immunodeficiencies
- Immune deficiency, not otherwise specific

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype, and this baseline disease insert has not been completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1. If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than ID), begin at question 1.
If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, check the indicator box and continue with question 116.

- Q1-8: Disease Assessment at Diagnosis
- Q9-50: Laboratory Studies at Diagnosis
- Q51-115: Clinical Features Assessed Between Diagnosis and the Start of the Preparative Regimen
- Q116-191: Pre-HCT Therapy for Immune Deficiency

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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</tr>
<tr>
<td>8/29/16</td>
<td>2031: ID Pre-HCT</td>
<td>Add</td>
<td>Added information box under question 33: If CD56+ cells were not tested, centers may report CD16+ results in these data fields.</td>
</tr>
<tr>
<td>8/26/16</td>
<td>2031: ID Pre-HCT</td>
<td>Add</td>
<td>Added information box under question 32: If CD20+ cells were not tested, centers may report CD19+ results in these data fields.</td>
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<tr>
<td>8/28/15</td>
<td>2031/2131: Immune Deficiencies</td>
<td>Add</td>
<td>Published new manual for 2031 &amp; 2131 Pre- and Post-HCT Immune Deficiencies Data</td>
</tr>
</tbody>
</table>
Q1-8: Disease Assessment at Diagnosis

Question 1: What was the date of diagnosis of Immune Deficiency (ID)?

Immune Deficiencies are characterized by multiple clinical, laboratory, and genetic features. Definitive diagnosis is often based on molecular testing such as detection of mutations in IL-2RG for common gamma chain deficiency (X-linked SCID) or ADA for adenosine deaminase (ADA) deficiency. Report the date the specimen was collected for molecular analysis.

If molecular analysis was not performed, but diagnosis of the recipient with ID was based on newborn screening, report the date of the newborn screening sample collection.

If the recipient had a strong family history of the disease and was tested in utero, the date of birth should be used as the date of diagnosis.

Questions 2-4: What is the immune deficiency molecular abnormality?

A variety of molecular abnormalities have been identified in those with immune deficiencies. Indicate the molecular abnormality used to diagnose the recipient’s immune deficiency.

If the recipient was diagnosed with Omenn Syndrome, indicate the identified molecular abnormality in question 3.

If the recipient has an identified molecular abnormality other than those listed, indicate the other molecular abnormality in question 4.

Table 1. Immunodeficiencies

<table>
<thead>
<tr>
<th>Disease</th>
<th>Circulating T cells</th>
<th>Circulating B cells</th>
<th>Molecular Abnormality</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common gamma chain (γc; CD132) deficiency</td>
<td>Markedly decreased</td>
<td>Normal or increased</td>
<td>Mutation in IL-2RG</td>
<td>X-Linked</td>
</tr>
<tr>
<td><em>May also be referred to as IL2RG deficiency or X-linked SCID</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenosine deaminase (ADA) deficiency</td>
<td>Absent from birth or progressive decrease</td>
<td>Absent from birth or progressive decrease</td>
<td>Mutation of ADA</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>Condition</td>
<td>Default Status</td>
<td>Alternative Status</td>
<td>Genetic Change</td>
<td>Recessiveness</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------</td>
<td>---------------------------------</td>
<td>--------------------</td>
<td>----------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Janus kinase 3 (JAK3) deficiency</td>
<td>Markedly decreased</td>
<td>Normal or increased</td>
<td>Mutation of JAK3</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>Recombination-activating gene 1 (RAG1) deficiency</td>
<td>Markedly decreased</td>
<td>Markedly decreased</td>
<td>Mutation of RAG1</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>Recombination-activating gene 2 (RAG2) deficiency</td>
<td>Markedly decreased</td>
<td>Markedly decreased</td>
<td>Mutation of RAG2</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>IL-7Rα deficiency</td>
<td>Markedly decreased</td>
<td>Normal or increased</td>
<td>Mutation of IL7RA</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>DNA cross-link repair 1C (DCLRE1C) / Artemis deficiency</td>
<td>Markedly decreased</td>
<td>Markedly decreased</td>
<td>Mutation of DCLRE1C/ARTEMIS</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>CD3γ (gamma) deficiency</td>
<td>Normal (reduced TCR expression)</td>
<td>Normal</td>
<td>Mutation of CD3G</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>CD3δ (delta) deficiency</td>
<td>Markedly decreased</td>
<td>Normal</td>
<td>Mutation of CD3D</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>CD3ε (epsilon) deficiency</td>
<td>Markedly decreased</td>
<td>Normal</td>
<td>Mutation of CD3E</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>CD3ζ (zeta)-chain deficiency</td>
<td>Markedly decreased</td>
<td>Normal</td>
<td>Mutation of CD3Z</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>Zeta-chain (TCR) associated protein kinase 70 dKa (ZAP-70) deficiency</td>
<td>Decreased CD8, normal CD4</td>
<td>Normal</td>
<td>Mutation in ZAP70</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>CD25 deficiency</td>
<td>Normal to decreased</td>
<td>Normal</td>
<td>Mutation in IL-2RA</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>CD45 deficiency</td>
<td>Markedly decreased</td>
<td>Normal</td>
<td>Mutation of PTPRC</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>Purine nucleoside phosphorylase (PNP) deficiency</td>
<td>Progressive Decrease</td>
<td>Normal</td>
<td>Mutation of PNP</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>Cernunnos-XLF / NHEJ1 deficiency</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Mutation in NHEJ1/Cernunnos</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>DNA ligase 4 deficiency</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Mutation in LIG4</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>DNA-protein kinase catalytic subunit (DNA-PKcs) deficiency</td>
<td>Markedly decreased</td>
<td>Markedly Decreased</td>
<td>Mutation of PRKDC</td>
<td>Autosomal Recessive</td>
</tr>
<tr>
<td>Adenylate kinase 2</td>
<td>Markedly Decreased</td>
<td>Decreased or</td>
<td>Mutation of AK2</td>
<td>Autosomal</td>
</tr>
<tr>
<td>Disorder</td>
<td>Abnormality</td>
<td>Mutation(s)</td>
<td>Inheritance Model</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>-------------------</td>
<td></td>
</tr>
<tr>
<td>(AK2) deficiency (reticular dysgenesis)</td>
<td>normal</td>
<td>Mutation(s) in RAG1, RAG2, ARTEMIS, IL7RA, RMRP, ADA, LIG4, IL2RG, AK2. Some cases have no defined gene mutation.</td>
<td>Recessive</td>
<td></td>
</tr>
<tr>
<td>Omenn syndrome</td>
<td>Present; restricted T-cell repertoire, and impaired function</td>
<td>Normal or decreased</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bare lymphocyte syndrome (MHC class II) deficiency</td>
<td>Normal number, decreased CD4 cells</td>
<td>Mutation in CIITA, RFX5, RFXAP, RFXANK transcription factors</td>
<td>Autosomal Recessive</td>
<td></td>
</tr>
<tr>
<td>Cartilage-hair hypoplasia (CHH) / metaphyseal dysplasia, McKusick type</td>
<td>Varies from severely decreased to normal; impaired lymphocyte proliferation</td>
<td>Normal</td>
<td>Autosomal Recessive</td>
<td></td>
</tr>
<tr>
<td>Orai1 deficiency</td>
<td>Normal number, but defective TCR-mediated activation</td>
<td>Mutation in ORAI1</td>
<td>Autosomal Recessive</td>
<td></td>
</tr>
</tbody>
</table>


**Question 5: Is the mutated protein or enzyme expressed?**

Immune Deficiency proteins or enzymes may be detected using tests such as Western blotting or an enzyme-linked immunosorbent assay (ELISA). Indicate whether the mutated protein or enzyme was expressed. If the protein or enzyme was expressed, select “yes.” If the protein or enzyme was not expressed, select “no.” If the test was not performed or the results of the test were inconclusive, select “unknown.”

**Question 6: What is the pattern of inheritance for the genetic disorder?**

Report the pattern of inheritance for the genetic disorder.

Sporadic inheritance indicates that there is no family history of the disease.
X-linked inheritance indicates that the genetic disease is located on the X chromosome and that the lack of a functioning copy of the gene causes the disease. Diseases inherited in an X-linked fashion are passed from parent to child via the X chromosome, a sex chromosome. X-linked disorders are much more common in males (XY) than females (XX) because only one copy of a mutation on the X chromosome is sufficient to cause the disorder in males, whereas females would require that the mutation is present on both X chromosomes to cause the disorder. X-linked SCID, or common gamma chain (γc; CD132) deficiency, is caused by a mutation in the IL2RG gene located on the chromosome X and is the most common type of primary immune deficiency. A second example of a disorder with X-linked inheritance is CD40 ligand deficiency. 

Autosomal recessive inheritance indicates that two non-functioning copies of the gene are required to cause the disease. In the majority of cases, the mutations for the genetic disease were passed from both parents to the child. Autosomes are non-sex chromosomes numbered 1-22. Because the disorder is recessive, mutations must be present on each chromosome in the pair (i.e., the mutation must be present on the maternal and paternal chromosome) for the disease to be expressed. For example, ADA deficiency (or ADA-SCID) is an autosomal recessive disease caused by mutations in the q13.12 location of the maternally- and paternally-inherited copies of chromosome 20.

If the inheritance pattern was autosomal dominant, leave the question blank and override the error.

Indicate the pattern of inheritance. If the pattern of inheritance is not known, select “unknown” and continue with question 7.


**Question 7: Are the parents of the patient consanguineous (related by blood ancestry)?**

Indicate if the recipient’s parents are related by blood ancestry. For example, if the parents of the recipient are first cousins (i.e., the parents are children of two siblings), the relationship is considered consanguineous. The limit for consanguinity is biological parents who are second cousins or less (Bittles A, Clin Genet 2001; 60; 89-98).

**Question 8: Are there other blood relatives in the patient’s family with immunodeficiency disease?**

Indicate if the recipient has blood relatives that have an immunodeficiency. Blood relatives include parents, siblings, grandparents, cousins, aunts, uncles, and other biological members of the recipient’s extended family, through great-grandparents.
Q9-50: Laboratory Studies at Diagnosis

Report findings prior to any first treatment of the immune deficiency for which the HCT is being performed.

**Question 9: Date CBC tested**

Report the date of CBC testing done within 6 weeks of diagnosis. Continue with question 10.

**Question 10: WBC**

Report the white blood cell (WBC) count and unit of measure as documented on the laboratory report. If the WBC was not tested, leave the count and unit fields blank and select “WBC not tested.” Continue with question 11.

**Question 11: Lymphocytes**

Report the percentage of lymphocytes as documented on the laboratory report. If lymphocytes were not tested, leave the count field blank and select “Lymphocytes not tested.” Continue with question 12.

**Question 12: Eosinophils**

Report the percentage of eosinophils as documented on the laboratory report. If eosinophils were not tested, leave the count field blank and select “Eosinophils not tested.” Continue with question 13.

**Question 13: Polymorphonuclear leukocytes (PMN)**

Polymorphonuclear leukocytes are white blood cells containing cytoplasmic granules. PMNs are also referred to as granulocytes and include neutrophils, basophils, and eosinophils; however, this question refers to neutrophils. Report the percentage of neutrophils. If neutrophils were not tested, leave the count field blank and select “Polymorphonuclear leukocytes (PMN) not tested.” Continue with question 14.

⚠️ **Transfusions**

Currently there is an error on the Form 2031 regarding transfusion history. The form should read: “transfused RBC less than or equal to 30 days from date of most current test” and “transfused platelets less than or equal to 7 days from date of most current test.”
Question 14: Hemoglobin

Report the hemoglobin count and the unit of measure as documented on the laboratory report. If the hemoglobin was not tested leave the count and unit fields blank and indicate “Hemoglobin not tested.” Indicate if red blood cells (RBC) were transfused ≤ 30 days from date of test. Continue with question 15.

Question 15: Platelets

Report the platelet count and unit of measure as documented on the laboratory report. If the platelet count was not tested leave the count and unit fields blank and indicate “Platelets not tested.” Indicate if platelets were transfused ≤ 7 days from date of test. Continue with question 16.

Immunoglobulin Analysis

Specify the following quantitative immunoglobulins measured at the time of diagnosis; if multiple studies were performed prior to the initiation of therapy, report the latest values prior to any first treatment of the immune deficiency.

Question 16: IgG

Report the IgG level and the unit of measure documented on the laboratory report. Continue with question 17. If IgG was not tested, leave the value and unit fields blank and indicate “IgG not tested,” and continue with question 18.

Question 17: Date Tested: IgG

Report the date of IgG testing and continue with question 18.

Question 18: IgM

Report the IgM level and the unit of measure documented on the laboratory report. Continue with question 19. If IgM was not tested, leave the value and unit fields blank and indicate “IgM not tested,” and continue with question 20.

Question 19: Date Tested: IgM

Report the date of IgM testing and continue with question 20.

Question 20: IgA

Report the IgA level and the unit of measure documented on the laboratory report. Continue with question 21. If IgA was not tested, leave the value and unit fields blank and indicate “IgA not tested,” and continue
with question 22.

**Question 21: Date Tested: IgA**

Report the date of IgA testing and continue with question 22.

**Question 22: IgE**

Report the IgE level in international units per milliliter (IU/ml). Continue with question 23. If IgE was not tested, leave the value field blank and indicate "IgE not tested," and continue with question 24.

**Question 23: Date Tested: IgE**

Report the date of IgE testing and continue with question 24.

**Question 24: Did the recipient receive supplemental intravenous immunoglobulins (IVIG) prior to any first treatment of ID?**

IVIG is a product made from pooled human plasma that primarily contains IgG. It is used to provide immune deficient recipients with antibodies to prevent infection.

Indicate whether the recipient received IVIG prior to any first treatment for ID. If “yes,” continue with question 25. If “no,” continue with question 26.

**Question 25: Was therapy ongoing within one month of immunoglobulin testing?**

Indicate whether the recipient received IVIG ≤30 days prior to the immunoglobulin testing reported in questions 16-23. If IVIG is given within 30 days of immunoglobulin testing, the IgG level would not represent the recipient’s native IgG. Continue with question 26.

**Lymphocyte Analysis**

Specify the lymphocyte analyses performed at the time of diagnosis; if multiple studies were performed prior to the initiation of therapy, report the latest values prior to any first treatment for ID.

**Question 26: Were lymphocyte analyses performed?**

Lymphocyte analyses include quantifying specific types of T cells, B Cells, and natural killer (NK) cells. Cells can be identified by cell-specific surface molecules using the clusters of differentiation (CD) nomenclature. For example, T cells can be classified as helper (CD4+) or cytotoxic (CD8+) cells depending on their cell surface markers designated with CD notation.
Indicate whether lymphocyte analyses were performed. If “yes,” continue with question 27. If “no,” continue with question 36.

**Question 27: Date of most recent testing performed**

Report the date of most recent lymphocyte testing performed prior to any treatment for Immune Deficiency. Continue with question 28.

**Question 28: Absolute lymphocyte count**

Report the absolute lymphocyte count in cells per microliter (cells/µL or cells/mm3). Continue with question 29.

**Question 29: CD3 (T cells)**

T cells are a type of lymphocyte that can be characterized by CD3. If the laboratory quantifies CD3 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD3 cells as an absolute value, then report the value in the count field and specify the count units. If CD3 cells were not tested, select the “CD3 (T cells) not tested” option. Continue with question 30.

**Question 30: CD4 (T helper cells)**

T helper cells are a subset of T cells characterized by CD4, sometimes reported as CD3+CD4+. If the laboratory quantifies CD4 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4 cells as an absolute value, then report the value in the count field and specify the count units. If CD4 cells were not tested, select the “CD4 (T cells) not tested” option. Continue with question 31.

**Question 31: CD8 (cytotoxic T cells)**

Cytotoxic T cells are a subset of T cells characterized by CD8, sometimes reported as CD3+CD8+. If the laboratory quantifies CD8 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD8 cells as an absolute value, then report the value in the count field and specify the count units. If CD8 cells were not tested, select the “CD8 (T cells) not tested” option. Continue with question 32.

**Question 32: CD20 (B lymphocyte cells)**

B cells are a type of lymphocyte that can be characterized by CD20. If the laboratory quantifies CD20 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD20 cells as an absolute value, then report the value in the count field and specify the count units. If CD20 cells were not tested, select the “CD20 (B lymphocyte cells) not tested” option. Continue with question 33.
Question 33: CD56 (natural killer (NK) cells)

NK cells are a type of lymphocyte that can be characterized by CD56. If the laboratory quantifies CD56 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD56 cells as an absolute value, then report the value in the count field and specify the count units. If CD56 cells were not tested, select the “CD56 (natural killer (NK) cells) not tested” option. Continue with question 34.

Question 34: CD4+ / CD45RA+ (naïve T cells)

Naïve T cells are a type of T cell that can be characterized by CD4+/CD45RA+. T cells are considered naïve prior to encountering an antigen. If the laboratory quantifies CD4+/CD45RA+ cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4+/CD45RA+ cells as an absolute value, then report the value in the count field and specify the count units. If CD4+/CD45RA+ cells were not tested, select the “CD4+/CD45RA+ (naïve T cells) not tested” option. Continue with question 35.

Question 35: CD4+ / CD45RO+ (memory T cells)

Memory T cells are a type of T cell that can be characterized by CD4+/CD45RO+. If the laboratory quantifies CD4+/CD45RO+ cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4+/CD45RO+ cells as an absolute value, then report the value in the count field and specify the count units. If CD4+/CD45RO+ cells were not tested, select the “CD4+/CD45RO+ (memory T cells) not tested” option. Continue with question 36.

Antibody Response

The immune system produces antibodies in response to antigens. Tests that measure the antibody response to different antigens help determine if the immune system is properly functioning.

Specify the antibody response assessment performed at the time of diagnosis; if multiple studies were performed prior to the initiation of therapy (including IVIG), report the latest values prior to any first treatment for ID.
Question 36: Date antibody responses were assessed

Report the date of most recent antibody response assessment performed prior to any treatment for ID. Continue with question 37.

Questions 37-43: Antibody response assessment

Specify the most recent antibody responses measured prior to any treatment for ID. For each of the antigens in questions 37-43, indicate if the antibody response was “Absent”, “Low”, “Normal”, or “Not Tested” based on normal values from the laboratory.

Unconjugated pneumococcal polysaccharide

The term unconjugated indicates that the pneumococcal capsule contains polysaccharides without the modification of proteins added to the surface to enhance the immune response.

Specify the number of serotypes producing a protective level out of the total serotypes tested from the vaccine. For example, if the Pneumococcal 23-valent vaccine was used for the test, then report the number of reactive serotypes out of the 23 serotype total.

Lymphocyte Function

Lymphocyte function tests assess immune function by measuring immune cell responses to antigens and mitogens relative to control responses.

Specify the lymphocyte function assessment performed at the time of diagnosis; if multiple studies were performed prior to the institution of therapy, report the latest values prior to any first treatment for ID.

Question 44: Date lymphocyte function was assessed

Report the date of most recent lymphocyte function assessment performed prior to any treatment for ID. Continue with question 45.

Questions 45-50: Lymphocyte analysis assessment

For each of the lymphocyte function tests listed in questions 45-50, indicate whether the lymphocyte response was “Absent (<10% of control)” “Low (10-30% of control)” “Normal (>30% of control)” or “Not tested.”
**Q51-115: Clinical Features Assessed Between Diagnosis and the Start of the Preparative Regimen**

**Infection Identified between Diagnosis and the Start of the Preparative Regimen**

Specify the presence of all clinically significant infections identified between diagnosis and the start of the preparative regimen. Only report an organism once, even if it was identified at the same site in subsequent infections.

**Questions 51: Hepatitis**

Hepatitis refers to inflammation (acute or chronic) of the liver with infectious or noninfectious etiologies. Hepatitis symptoms can include abdominal pain, jaundice, nausea, and vomiting. Laboratory tests such as aminotransferase (ALT/AST) and bilirubin measurements may be performed to monitor hepatic function. These lab values are frequently elevated in patients with hepatitis. Infectious causes of hepatitis in children with immune deficiencies include, but are not limited to hepatitis A virus, hepatitis B virus, hepatitis C virus, and adenovirus.¹

Indicate if the recipient developed infectious hepatitis. If “yes” continue with question 52. If “no” continue with question 55.


**Questions 52-53: Hepatitis: Organism(s)**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the hepatitis reported in question 51. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 52 and specify the organism in question 53. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 52-53 and specify the other organism(s). Continue with question 54.
Question 54: If hepatitis was present, was it a prominent feature of ID?

If infectious hepatitis was present, indicate if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 55.

Question 55: Meningitis / encephalitis

Meningitis is an inflammation of the meninges, membranes encasing the central nervous system. Encephalitis is inflammation of the brain tissue itself. Meningitis and encephalitis may co-occur as meningoencephalitis. Common symptoms include headache, lethargy, confusion, fever, neck stiffness, and cranial nerve defects. Infectious causes of meningitis/encephalitis include, but are not limited to Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, enteroviruses, herpes simplex virus, Cryptococcus, and Histoplasmosis.²

Indicate if the recipient developed infectious meningitis / encephalitis. If “yes” continue with question 56. If “no” continue with question 59.

 Questions 56-57: Meningitis/ encephalitis: Organism(s)

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the meningitis / encephalitis reported in question 55. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 56 and specify the organism in question 57. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 56-57 and specify the other organism(s). Continue with question 58.

Question 58: If meningitis/ encephalitis was present, was it a prominent feature of ID?

If meningitis / encephalitis was present, indicate if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 59.

Question 59: Pneumonia

Pneumonia is a respiratory condition due to lung infection. Symptoms may include fever, cough, and difficulty breathing. Infectious causes of pneumonia include, but are not limited to pneumocystic jirovecii (PCP, PJP), cytomegalovirus, and adenovirus.

Indicate “yes” if the recipient developed infectious pneumonia and continue with question 60. If the recipient did not have pneumonia, indicate “no” and continue with question 63.

Questions 60-61: Pneumonia: Organism(s)

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the pneumonia reported in question 59. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 60 and specify the organism in question 61. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 60-61 and specify the other organism(s). Continue with question 62.

Question 62: If pneumonia was present, was it a prominent feature of ID?

If pneumonia was present, indicate if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 63.

Question 63: Severe or protracted diarrhea

Protracted diarrhea (>10g/kg/24hrs) refers to three or more loose stools per day lasting longer than fourteen days. Indicate whether the recipient had severe or protracted diarrhea. If “yes” continue with question 64. If “no” continue with question 67.

Questions 64-65: Diarrhea: Organism(s)

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the diarrhea reported in question 63. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 64 and specify the organism in question 65. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were

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3 Guandalini S. Diarrhea. Medscape. Updated 4/10/14
identified, add additional instances for questions 64-65 and specify the other organism(s). Continue with question 66.

**Question 66: If diarrhea was present, was it a prominent feature of ID?**

If diarrhea was present, indicate if it was a prominent feature of ID. A prominent feature is generally well documented, closely followed, and treated. Continue with question 67.

**Question 67: Systemic infection**

A systemic infection is an infection isolated at 3 or more sites. Indicate whether the recipient had systemic infection. If “yes” continue with question 68. If “no” continue with question 71.

**Questions 68-69: Systemic infection: Organism(s)**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the systemic infection reported in question 67. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 68 and specify the organism in question 69. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 68-69 and specify the other organism(s). Continue with question 70.

**Question 70: If systemic infection was present, was it a prominent feature of ID?**

If systemic infection was present, indicate if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 71.

**Question 71: Other infection**

Indicate if the recipient had an infection other than reported in questions 51-70. If “yes” continue with question 72. If “no” continue with question 76.

**Questions 72-73: Other infection: Organism(s)**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the infection reported in question 71. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 72 and specify the organism in question 73. If no organism was
identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 72-73 and specify the other organism(s). Continue with question 74.

**Question 74: Specify other infection site**

Specify the site of the infection reported in question 71. Continue with question 75.

**Question 75: If other infection was present, was it a prominent feature of ID?**

If other infection was present, indicate if it was a prominent feature of ID. A prominent feature is generally well documented, closely followed, and treated. Continue with question 76.

**Clinical Status between Diagnosis and the Preparative Regimen**

**Questions 76-115: Did the recipient experience any of the following clinical features (between diagnosis and prior to the preparative regimen)?**

Depending on the immune deficiency, differing clinical features may be present. Indicate “yes” if the recipient has any of the clinical features listed on the form between diagnosis and the start of the preparative regimen and specify the feature in questions 77-115. Do not leave any feature blank. If the recipient does not have any of the clinical features listed, select “no” and continue with question 116.

<table>
<thead>
<tr>
<th>Q</th>
<th>Feature</th>
<th>Is the feature present?</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>Autoimmune hemolytic anemia</td>
<td>Autoimmune hemolytic anemia results in a decrease in circulating healthy red blood cells due to the development of immunity against and subsequent destruction of one’s own red blood cells.</td>
</tr>
<tr>
<td>79</td>
<td>Bone abnormalities</td>
<td>Short bones may be found in certain immune deficiencies such as cartilage hair hypoplasia (CHH). Lesions on bones may also be present as a result of infection.</td>
</tr>
<tr>
<td>81</td>
<td>Edema</td>
<td>Swelling caused by excess fluid in tissue.</td>
</tr>
<tr>
<td>83</td>
<td>Eosinophilia</td>
<td>Higher than normal eosinophils in the peripheral blood. &gt; 500 cells/µL</td>
</tr>
<tr>
<td>85</td>
<td>Failure to thrive (weight &lt;5th percentile)</td>
<td>Failure to thrive describes a weight that is below the 5th percentile per age or corrected age for premature infants &lt; 12 months</td>
</tr>
<tr>
<td>87</td>
<td>Graft-versus-host disease due to blood transfusion</td>
<td>Transfusion associated GVHD occurs when blood transfusion derived T cells attack host cells. Immunocompromised individuals are at higher risk for TA-GVHD because their immune system cannot destroy donor T cells.</td>
</tr>
<tr>
<td>89</td>
<td>Graft-versus-host</td>
<td>Occurs when maternally engrafted T cells attack the host cells.</td>
</tr>
<tr>
<td>Disease/Feature</td>
<td>Definition/Description</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>------------------------</td>
<td></td>
</tr>
<tr>
<td>Growth hormone deficiency</td>
<td>Growth Hormone (GH) is a hormone that stimulates cellular reproduction and growth. Deficiencies in GH are often diagnosed by pediatric endocrinologists.</td>
<td></td>
</tr>
<tr>
<td>Growth retardation (height &lt;5th percentile)</td>
<td>Growth retardation is characterized by a height below the 5th percentile for age or corrected age for premature infants &lt; 12 months.</td>
<td></td>
</tr>
<tr>
<td>Hepatosplenomegaly</td>
<td>Enlargement of the liver and/or spleen.</td>
<td></td>
</tr>
<tr>
<td>Hypoproteinemia</td>
<td>Abnormally low levels of protein in peripheral blood.</td>
<td></td>
</tr>
<tr>
<td>Lymphoproliferative disease</td>
<td>Lymphoproliferative diseases are characterized by excessive production of lymphocytes.</td>
<td></td>
</tr>
<tr>
<td>Maternal T-cell engraftment</td>
<td>Maternal T-cell engraftment is characterized by the presence of circulating maternal T-cells in the patient’s blood, which may cause GVHD, though GVHD is not always a feature of engrafted maternal T-cells.</td>
<td></td>
</tr>
<tr>
<td>Microcephaly</td>
<td>Microcephaly is characterized by a head circumference that is significantly small for age (≥ 3 standard deviations below mean for age/sex). Motor function and developmental delays may result.</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>ANC &lt; 1.0 × 10⁹/L</td>
<td></td>
</tr>
<tr>
<td>Skin rash</td>
<td>Rashes of the skin may be occur for a variety of reason, including but not limited to: GVHD, infection, or autoimmune conditions.</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia (&lt; 100 × 10⁹/L)</td>
<td>Platelets &lt; 100 × 10⁹/L</td>
<td></td>
</tr>
<tr>
<td>Warts</td>
<td>Warts are caused by infection by Human Papilloma Virus</td>
<td></td>
</tr>
<tr>
<td>Other clinical features</td>
<td>Other clinical features may include, but are not limited to: deafness, lung or liver manifestations, and cardiac issues when linked to the immune deficiency</td>
<td></td>
</tr>
</tbody>
</table>

**Is [the clinical feature] prominent?**

A prominent feature is generally well documented, closely followed, and treated. Select “yes” if the clinical feature that was reported as present was a prominent part of their disease.
Q116-191: Pre-HCT Therapy for Immune Deficiency

Question 116: Was treatment given (between diagnosis and prior to the preparative regimen)?

Since immune deficiencies are non-malignant diseases caused by genetic mutations, hematopoietic stem cell transplant is the main curative treatment at this time. Other treatments such as gene therapy are promising.

The questions below regarding prophylactic anti-infection and immunosuppressant drugs, refer to supportive therapy used to treat or prevent the sequelae (or condition as a result of the disease) such as infections, autoimmune issues, GVHD, etc. Additional questions ask about gene therapy or other significant treatments given to the recipient following the anti-infection and immunosuppresion therapy questions.

Indicate if the recipient received therapy between diagnosis and prior to the preparative regimen, including gene therapy, anti-infection drugs, immunosuppressive drugs, or any other significant and/or experimental therapies. If “yes,” continue with question 117. If “no,” continue with 176.

Questions 117-125: Prophylactic Drugs

Prophylactic drugs are used to prevent infection by a virus, bacteria, fungus, or parasite. Drugs started as a result of infection should not be reported as prophylactic drugs.

Indicate “yes” or “no” for each of the drug categories listed. If “yes,” continue with the subsequent questions regarding the stoppage of the prophylactic drug. If the drug was stopped, indicate “yes” and report the date the drug was stopped.

Drug

Antifungal drugs are used to prevent fungal infections. Common prophylactic antifungal drugs include fluconazole, caspofungin, voriconazole, etc.

Antiviral drugs are used to prevent viral infections. Common prophylactic antiviral drugs include acyclovir, ganciclovir, foscarnet, etc.

Co-trimoxazole (Bactrim, Septra) is a prophylactic drug used to prevent Pneumocystis jirovecii, a protozoan (i.e., parasitic) infection that colonizes the lungs of those with compromised immune systems.
**Prophylactic drug stopped?**
Indicate if the prophylactic drugs in each category were stopped. Prophylactic drugs stopped for a period of time shorter than one week should not be considered as "stopped." For example, if any of the prophylactic drugs are held during the preparative regimen and restarted shortly thereafter, they would not be reported as stopped.

**Date stopped**
Report the date the last prophylactic drug in each category was stopped. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Questions 126-170: Therapies**
Pre-transplant therapies for immune deficiencies may include immunosuppressive therapies to prevent or treat GVHD (maternal or transfusion associated), autoimmune conditions, etc.

Indicate "yes" or "no" for each of the drugs listed. If "yes," continue with the subsequent questions regarding the stoppage of the therapy. If the drug was stopped, indicate "yes" and report the date the drug was stopped.

**Therapy**
Each of the drugs in questions 126-170 have immunosuppressive properties.

Corticosteroids may be given topically or systemically. Budesonide, which is ingested orally, is considered a topical drug.

If the recipient is given a monoclonal antibody, select "yes" for question 141 and specify the monoclonal antibody in questions 142-157. If the monoclonal antibody is not listed, specify the drug in question 160.

If the recipient is given an immunosuppressant that is not listed, select "yes" for question 167 and specify the other immunosuppressant in question 170.

**Therapy stopped?**
Indicate if the therapy was stopped. Therapy that is stopped for a period of time shorter than one week should not be considered as “therapy stopped.”
For example, if any of the therapies are held during the preparative regimen and restarted shortly thereafter, they would not be reported as stopped.

**Date stopped**
Report the date the therapy was stopped. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Question 171: Was gene therapy performed (between diagnosis and prior to the preparative regimen)?**

Gene therapy is the process by which a faulty gene is replaced by a healthy one. This process uses a virus which is manipulated to include a functioning version of the gene. The recipient’s cells are “treated” with the functioning-gene-containing virus with the intention of the functioning rather than faulty gene proliferating.

**Question 172: Specify date of infusion of gene therapy**

Indicate the date the treated cells were infused to the recipient. If the recipient received several infusions, report the first date of infusion.

**Question 173: Was the recipient considered to have failed gene therapy?**

Gene therapy is considered a success if the healthy gene replaces the faulty one and the immune system begins to function normally. In the opinion of the physician, was the gene therapy considered a failure? If so, select “yes” and continue with question 174.

**Questions 174-175: Did the recipient receive any other significant treatment(s) (between diagnosis and prior to the preparative regimen)?**

Recipients with immune deficiency may receive treatments other than what is listed above. Treatments may include enzyme replacement therapy such as PEG-ADA. Each immune deficiency may have their own unique treatments, including interferon, growth factors, enzyme replacement, or other therapies.

If the recipient had any other significant treatments between diagnosis and prior to the preparative regimen, select “yes” and specify the treatments in question 175. If the recipient did not have additional significant treatments, select “no” and continue with question 176.

**Question 176: Did the recipient receive parenteral nutrition (between diagnosis and prior to the preparative regimen)?**

Parenteral nutrition is given to the recipients intravenously rather than through the digestive system. Parenteral nutrition contains the carbohydrates, proteins, fats, electrolytes, and other components needed for survival. The use of parenteral nutrition to deliver all required nutrients is called total parenteral nutrition (TPN).

Indicate “yes” if the recipient received parenteral nutrition between diagnosis and the start of the preparative regimen. If the recipient did not receive parenteral nutrition, select “no.”
**Question 177: Did the recipient receive mechanical ventilation (between diagnosis and prior to the preparative regimen)?**

Mechanical ventilation can occur as both an endotracheal tube and ventilator, or as a BIPAP machine with a tight fitting mask in continuous use. The one exception to BIPAP is CPAP used for sleep apnea, which generally involves overnight use only for patients with documented sleep apnea. Therefore, do not report a CPAP used for sleep apnea, as it does not have the same implications as other forms of mechanical ventilation.

Indications for mechanical ventilation include, but are not limited to:

- Apnea with respiratory arrest (excludes sleep apnea)
- Acute lung injury
- Vital capacity < 15 mL/kg
- Chronic obstructive pulmonary disease (COPD)
- Clinical deterioration
- Respiratory muscle fatigue
- Obtundation or coma
- Hypotension
- Tachypnea or bradypnea

If the recipient was placed on mechanical ventilation at any time after diagnosis but before the preparative regimen check “yes.” If the recipient does not have a history of mechanical ventilation during the time period, check “no.”

**Question 178-191: Were any biologic specimens collected for this recipient (between diagnosis and prior to the preparative regimen)?**

Indicate whether biologic specimens were collected for this recipient. Biologic specimens may be collected for more in-depth analyses and for research purposes. Different types of cells, for example B cells and T cells, can be isolated from whole blood and viral-transformed to establish permanent cell lines.

If “yes” continue with questions 179-191 and specify which specimens were collected and are available for future use. If “no” or “unknown” continue with “Signature Lines.”
2131: ID Post-HCT

The Immune Deficiency Post-HCT Data Form is one of the Comprehensive Report Forms. This form captures ID-specific post-HCT data such as: laboratory studies post-HCT, clinical features assessed post-HCT, Post-HCT treatment, and status of hematologic engraftment.

This form must be complete for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Disorders of the Immune System and specified as:

- Adenosine deaminase (ADA) deficiency / severe combined immunodeficiency (SCID)
- Absence of T and B cells SCID
- Absence of T, normal B cell SCID
- Omenn syndrome
- Reticular dysgenesis
- Bare lymphocyte syndrome
- Other SCID
- SCID, not otherwise specified
- Ataxia telangiectasia
- HIV infection
- DiGeorge anomaly
- Common variable immunodeficiency
- Leukocyte adhesion deficiencies, including GP180, CD-18, LFA, and WBC adhesion deficiencies
- Kostmann agranulocytosis (congenital neutropenia)
- Neutrophil actin deficiency
- Cartilage-hair hypoplasia
- CD40 ligand deficiency
- Other Immunodeficiencies
- Immune deficiency, not otherwise specific

The Immune Deficiency Post-HCT Data Form (Form 2131) must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, 2300). The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200, between the date of contact for the six-month follow up and the date of contact for the one-year follow up for Form 2200, etc.).

- Q1-43: Laboratory Studies Post-HCT
- **Q44-94: Clinical Features Assessed Post-HCT**
- **Q95-166: Post-HCT Treatment for Immune Deficiency**
- **Q167-172: Status of Hematologic Engraftment**

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
<tr>
<td>8/29/16</td>
<td>2131: ID Post-HCT</td>
<td>Add</td>
<td>Added information box under question 25: If CD56+ cells were not tested, centers may report CD16+ results in these data fields.</td>
</tr>
<tr>
<td>8/26/16</td>
<td>2131: ID Post-HCT</td>
<td>Add</td>
<td>Added information box under question 24: If CD20+ cells were not tested, centers may report CD19+ results in these data fields.</td>
</tr>
<tr>
<td>2/9/16</td>
<td>2131: ID Post-HCT</td>
<td>Add</td>
<td>Added CD15+ cells to the text in question 171: Myeloid subsets may be reported as CD15+ or CD33+ on the laboratory report.</td>
</tr>
<tr>
<td>8/28/15</td>
<td>2031/2131: Immune Deficiencies</td>
<td>Add</td>
<td>Published new manual for 2031 &amp; 2131 Pre- and Post-HCT Immune Deficiencies Data</td>
</tr>
</tbody>
</table>
Q1-43: Laboratory Studies Post-HCT

To be completed in conjunction with a form 2100 – 100 Days Post-HCT Data, 2200 – Six Months to Two Years Post-HCT Data, or Form 2300 – Yearly Follow-Up for Greater than Two Years Post-HCT Data. Information reported here should reflect the date of last contact as reported in the post-HCT data collection form, or immediately prior to death.

Report the most recent findings since the date of the last report. For questions 1-3 and 6-7, also report CBC results in the Form 2100 – 100 Days Post-HCT Data, or in the Form 2200 – Six Months to Two Years Post-HCT Data.

**Question 1: Date of most recent hematologic testing**

Report the date of the most recent hematologic testing since the date of last report. Continue with question 2.

**Question 2: WBC**

Report the white blood cell (WBC) count and unit of measure as documented on the laboratory report. If the WBC was not tested, leave the count and unit fields blank and select “WBC not tested.” Continue with question 3.

**Question 3: Lymphocytes**

Report the percentage of lymphocytes as documented on the laboratory report. If lymphocytes were not tested, leave the count field blank and select “Lymphocytes not tested.” Continue with question 4.

**Question 4: Eosinophils**

Report the percentage of eosinophils as documented on the laboratory report. If eosinophils were not tested, leave the count field blank and select “Eosinophils not tested.” Continue with question 5.

**Question 5: Polymorphonuclear leukocytes (PMN)**

Polymorphonuclear leukocytes are white blood cells containing cytoplasmic granules. PMNs are also referred to as granulocytes and include neutrophils, basophils, and eosinophils; however, this question refers to neutrophils. Report the percentage of neutrophils. If neutrophils were not tested, leave the count field blank and select “Polymorphonuclear leukocytes (PMN) not tested.” Continue with question 6.
Question 6: Hemoglobin

Report the hemoglobin count and the unit of measure as documented on the laboratory report. If the hemoglobin was not tested, leave the count and unit fields blank and indicate “Hemoglobin not tested.”

Indicate if red blood cells (RBC) were transfused ≤ 30 days from date of test. Continue with question 7.

Question 7: Platelets

Report the platelet count and unit of measure as documented on the laboratory report. If the platelet count was not tested, leave the count and unit fields blank and indicate “Platelets not tested.”

Indicate if platelets were transfused ≤ 7 days from date of test. Continue with question 8.

Immunoglobulin Analysis

Specify the most recent Immunoglobulin assessment measured since the date of the last report.

Question 8: IgG

Report the IgG level and the unit of measure documented on the laboratory report. Continue with question 9. If IgG was not tested, leave the value and unit fields blank and indicate “IgG not tested,” and continue with question 10.

Question 9: Date Tested: IgG

Report the date of IgG testing and continue with question 10.

Question 10: IgM

Report the IgM level and the unit of measure documented on the laboratory report. Continue with question 11. If IgM was not tested, leave the value and unit fields blank and indicate “IgM not tested,” and continue with question 12.
**Question 11: Date Tested: IgM**

Report the date of IgM testing and continue with question 12.

**Question 12: IgA**

Report the IgA level and the unit of measure documented on the laboratory report. Continue with question 13. If IgA was not tested, leave the value and unit fields blank and indicate “IgA not tested,” and continue with question 14.

**Question 13: Date Tested: IgA**

Report the date of IgA testing and continue with question 14.

**Question 14: IgE**

Report the IgE level in international units per milliliter (IU/ml). Continue with question 15. If IgE was not tested, leave the value field blank and indicate “IgE not tested,” and continue with question 16.

**Question 15: Date Tested: IgE**

Report the date of IgE testing and continue with question 16.

**Question 16: Did the recipient receive supplemental intravenous immunoglobulins (IVIG) since the date of the last report?**

IVIG is a product made from pooled human plasma that primarily contains IgG. It is used to provide immune-deficient recipients with antibodies to help prevent infection.

Indicate whether the recipient received IVIG since the date of last report. If “yes” continue with question 17. If “no” or “unknown” continue with question 18.

**Question 17: Was therapy ongoing within one month of immunoglobulin testing?**

Indicate whether the recipient received IVIG within one month prior to immunoglobulin testing. If IVIG is given within one month of immunoglobulin testing, the IgG level would not represent the recipient’s native IgG. Continue with question 18.

**Lymphocyte Analysis**

Specify the most recent lymphocyte assessment measured since the date of the last report.
**Question 18: Were lymphocyte analyses performed?**

Lymphocyte analyses include quantifying specific types of T cells, B Cells, and natural killer (NK) cells. Cells can be identified by cell-specific surface molecules using the clusters of differentiation (CD) nomenclature. For example, T cells can be classified as helper (CD4+) or cytotoxic (CD8+) cells depending on their cell surface markers designated with CD notation.

Indicate if lymphocyte analyses were performed. If “yes” continue with question 19. If “no” continue with question 28.

**Question 19: Date of most recent testing performed**

Report the date of most recent lymphocyte testing since the date of the last report. Continue with question 20.

**Question 20: Absolute lymphocyte count**

Report the absolute lymphocyte count in cells per microliter (cells/µL). Continue with question 21.

**Question 21: CD3 (T cells)**

T cells are a type of lymphocyte that can be characterized by CD3. If the laboratory quantifies CD3 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD3 cells as an absolute value, then report the value in the count field and specify the count units. If CD3 cells were not tested, select the “CD3 (T cells) not tested” option. Continue with question 22.

**Question 22: CD4 (T helper cells)**

T helper cells are a subset of T cells characterized by CD4, sometimes reported as CD3+CD4+. If the laboratory quantifies CD4 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4 cells as an absolute value, then report the value in the count field and specify the count units. If CD4 cells were not tested, select the “CD4 (T cells) not tested” option. Continue with question 23.

**Question 23: CD8 (cytotoxic T cells)**

Cytotoxic T cells are a subset of T cells characterized by CD8, sometimes reported as CD3+CD8+. If the laboratory quantifies CD8 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD8 cells as an absolute value, then report the value in the count field and specify the count units. If CD8 cells were not tested, select the “CD8 (T cells) not tested” option. Continue with question 24.
Question 24: CD20 (B lymphocyte cells)

B cells are a type of lymphocyte that can be characterized by CD20. If the laboratory quantifies CD20 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD20 cells as an absolute value, then report the value in the count field and specify the count units. If CD20 cells were not tested, select the “CD20 (B lymphocyte cells) not tested” option. Continue with question 25.

If CD20+ cells were not tested, centers may report CD19+ results in these data fields.

Question 25: CD56 (natural killer (NK) cells)

NK cells are a type of lymphocyte that can be characterized by CD56. If the laboratory quantifies CD56 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD56 cells as an absolute value, then report the value in the count field and specify the count units. If CD56 cells were not tested, select the “CD56 (natural killer (NK) cells) not tested” option. Continue with question 26.

If CD56+ cells were not tested, centers may report CD16+ results in these data fields.

Question 26: CD4+ / CD45RA+ (naïve T cells)

Naïve T cells are a type of T cell that can be characterized by CD4+/CD45RA+. T cells are considered naïve prior to encountering an antigen. If the laboratory quantifies CD4+/CD45RA+ cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4+/CD45RA+ cells as an absolute value, then report the value in the count field and specify the count units. If CD4+/CD45RA+ cells were not tested, select the “CD4+/CD45RA+ (naïve T cells) not tested” option. Continue with question 27.

Question 27: CD4+ / CD45RO+ (memory T cells)

Memory T cells are a type of T cell that can be characterized by CD4+/CD45RO+. If the laboratory quantifies CD4+/CD45RO+ cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4+/CD45RO+ cells as an absolute value, then report the value in the count field and specify the count units. If CD4+/CD45RO+ cells were not tested, select the “CD4+/CD45RO+ (memory T cells) not tested” option. Continue with question 28.
**Antibody Response**

The immune system produces antibodies in response to antigens. Tests that measure the antibody response to different antigens help determine if the immune system is properly functioning. Specify the most recent antibody responses measured since the date of the last report.

**Question 28: Date antibody responses were assessed**

Specify the most recent antibody responses measured since the date of the last report.

**Questions 29-36: Antibody response assessment**

For each of the antigens in questions 29-36, indicate if the antibody response was “Absent”, “Low”, “Normal”, or “Not Tested” based on normal values from the laboratory.

**Unconjugated pneumococcal polysaccharide**

The term unconjugated indicates that the pneumococcal capsule contains polysaccharides without the modification of proteins added to the surface to enhance the immune response.

Specify the number of serotypes producing a protective level out of the total serotypes tested from the vaccine. For example, if the Pneumococcal 23-valent vaccine was used for the test, then report the number of reactive serotypes out of the 23 serotype total.

**Conjugated pneumococcal polysaccharide**

The term conjugated indicates that the pneumococcal capsule contains polysaccharides that have been conjugated with proteins to enhance the immune response.

Specify the number of serotypes producing a protective level out of the total serotypes tested from the vaccine.

**Lymphocyte Function**

Lymphocyte function tests assess immune function by measuring immune cell responses to antigens and mitogens relative to control responses.

**Question 37: Date lymphocyte function was assessed**

Specify the date of the most recent lymphocyte function assessment since the date of last report in question 37.
Questions 38-43: Lymphocyte analysis assessment

For each of the lymphocyte function tests listed in questions 38-43, indicate whether the lymphocyte response was “Absent” (<10% of control), “Low (10-30% of control),” “Normal” (>30% of control) or “Not tested.”
Q44-94: Clinical Features Assessed Post-HCT

Infections Identified Post-HCT

Specify the presence of all clinically significant infections identified since the date of the last report. Only report an organism once, even if it was identified at the same site in subsequent infections.

Question 44: Hepatitis

Hepatitis refers to inflammation (acute or chronic) of the liver with infectious or noninfectious etiologies. Hepatitis symptoms can include abdominal pain, jaundice, nausea, and vomiting. Laboratory tests such as aminotransferase (ALT/AST) and bilirubin measurements may be performed to monitor hepatic function. These lab values are frequently elevated in patients with hepatitis. Infectious causes of hepatitis in children with immune deficiencies include, but are not limited to hepatitis A virus, hepatitis B virus, hepatitis C virus, and adenovirus.¹

Indicate if the recipient developed infectious hepatitis. If “yes” continue with question 45. If “no” continue with question 48.


Questions 45-46: Hepatitis: Organism(s)

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the hepatitis reported in question 44. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 45 and specify the organism in question 46. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 45-46 and specify the other organism(s). Continue with question 47.

Question 47: If hepatitis was present, was it a prominent feature of ID?

If infectious hepatitis was present, indicate “yes” if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 48.
**Question 48: Meningitis / encephalitis**

Meningitis is an inflammation of the meninges, membranes encasing the central nervous system. Encephalitis is inflammation of the brain tissue itself. Meningitis and encephalitis may co-occur as meningoencephalitis. Common symptoms include headache, lethargy, confusion, fever, neck stiffness, and cranial nerve defects. Infectious causes of meningitis/encephalitis include, but are not limited to Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, enteroviruses, herpes simplex virus, Cryptococcus, and Histoplasmosis.

Indicate if the recipient developed infectious meningitis / encephalitis. If “yes” continue with question 49. If “no” continue with question 52.

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**Questions 49-50: Meningitis/ encephalitis: Organism(s)**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the meningitis / encephalitis reported in question 48. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 49 and specify the organism in question 50. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 49-50 and specify the other organism(s). Continue with question 51.

**Question 51: If meningitis/ encephalitis was present, was it a prominent feature of ID?**

If meningitis / encephalitis was present, indicate “yes” if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 52.

**Question 52: Pneumonia**

Pneumonia is a respiratory condition due to lung infection. Symptoms may include fever, cough, and difficulty breathing. Infectious causes of pneumonia include, but are not limited to pneumocystic jirovecii (PCP, PJP), cytomegalovirus, and adenovirus.

Indicate “yes” if the recipient developed infectious pneumonia and continue with question 53. If the recipient...
did not have pneumonia, indicate “no” and continue with question 56.

**Questions 53-54: Pneumonia: Organism(s)**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the pneumonia reported in question 52. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 53 and specify the organism in question 54. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 53-54 and specify the other organism(s). Continue with question 55.

**Question 55: If pneumonia was present, was it a prominent feature of ID?**

If pneumonia was present, indicate “yes” if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 56.

**Question 56: Severe or protracted diarrhea**

Protracted diarrhea (>10g/kg/24hrs) refers to three or more loose stools per day lasting longer than fourteen days. Indicate whether the recipient had severe or protracted diarrhea. If “yes” continue with question 57. If “no” continue with question 60.

3 Guandalini S. Diarrhea. Medscape. Updated 4/10/14

**Questions 57-58: Diarrhea: Organism(s)**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the diarrhea reported in question 56. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 57 and specify the organism in question 58. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 57-58 and specify the other organism(s). Continue with question 59.

**Question 59: If diarrhea was present, was it a prominent feature of ID?**

If diarrhea was present, indicate “yes” if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 60.
**Question 60: Systemic infection**

A systemic infection is an infection isolated at 3 or more sites. Indicate whether the recipient had systemic infection. If “yes” continue with question 61. If “no” continue with question 64.

**Questions 61-62: Systemic infection: Organism(s)**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the systemic infection reported in question 60. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 61 and specify the organism in question 62. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 61-62 and specify the other organism(s). Continue with question 63.

**Question 63: If systemic infection was present, was it a prominent feature of ID?**

If systemic infection was present, indicate “yes” if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 64.

**Question 64: Other infection**

Indicate if the recipient had an infection other than reported in questions 44-63. If “yes” continue with question 65. If “no” continue with question 69.

**Questions 65-66: Other infection: Organism(s)**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the infection reported in question 64. If the organism was identified but is not listed, select “other chlamydia, specify,” “other mycobacterium, specify,” “other bacteria, specify,” “other fungus, specify,” “other aspergillus, specify,” “other virus, specify,” or “other parasite, specify” as appropriate for question 65 and specify the organism in question 66. If no organism was identified select the “No organism identified” option from the bottom of the list. If multiple organisms were identified, add additional instances for questions 65-66 and specify the other organism(s). Continue with question 67.

**Question 67: Specify other infection site**

Specify the site of the infection reported in question 64. Continue with question 68.
Question 68: If other infection was present, was it a prominent feature of ID?

If other infection was present, indicate “yes” if it was a prominent feature of ID. A prominent feature is related to the immune deficiency, generally well documented, closely followed, and treated. Continue with question 69

Clinical Status Post-HCT

Question 69: Did the recipient experience any of the following clinical features (since the date of last report)?

Depending on the immune deficiency, differing clinical features may be present. Indicate “yes” if the recipient has had any of the clinical features listed on the form since the date of the last report and specify the feature in questions 70-92. Do not leave any feature blank. If the recipient does not have any of the clinical features listed, select “no” and continue with question 93.

<table>
<thead>
<tr>
<th>Q</th>
<th>Feature</th>
<th>Is the feature present?</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>Autoimmune hemolytic anemia</td>
<td>Autoimmune hemolytic anemia results in a decrease in circulating healthy red blood cells due to the development of immunity against and subsequent destruction of one’s own red blood cells.</td>
</tr>
<tr>
<td>72</td>
<td>Failure to thrive (weight &lt;5th percentile)</td>
<td>Failure to thrive describes a weight that is below the 5th percentile per age or corrected age for premature infants &lt;12 months</td>
</tr>
<tr>
<td>74</td>
<td>Acute graft-versus-host disease</td>
<td>Acute GVHD occurs when donor immune cells attack recipient tissues post-transplant. Typical presentations of acute GVHD are early post-transplant in the skin, liver, and gastrointestinal tract.</td>
</tr>
<tr>
<td>76</td>
<td>Chronic graft-versus-host disease</td>
<td>Chronic GVHD occurs when donor cells attack recipient tissues post-transplant with features distinct from acute GVHD. Affected tissues include, but are not limited to: skin, liver, mouth, eyes, lungs, etc.</td>
</tr>
<tr>
<td>78</td>
<td>Growth hormone deficiency</td>
<td>Growth Hormone (GH) is a hormone that stimulates cellular reproduction and growth. Deficiencies in GH are often diagnosed by pediatric endocrinologists.</td>
</tr>
<tr>
<td>80</td>
<td>Growth retardation (height &lt;5th percentile)</td>
<td>Growth retardation is characterized by a height below the 5th percentile for age or corrected age for premature infants &lt;12 months.</td>
</tr>
<tr>
<td>82</td>
<td>Lymphoproliferative disease</td>
<td>Lymphoproliferative diseases are characterized by excessive production of lymphocytes.</td>
</tr>
<tr>
<td>84</td>
<td>Thrombotic thrombocytopenic purpura (TTP)</td>
<td>TTP is a coagulation disorder in which clots form in the small vessels. It is characterized by microangiopathic hemolysis, thrombocytopenia, and neurological changes.</td>
</tr>
</tbody>
</table>
| 86 | Veno-occlusive                               | Veno-occlusive disease, or sinusoidal occlusive syndrome occur when the veins of
VOD consists of endothelial damage, micro thrombosis of the hepatic venules and sinusoidal fibrosis.

Warts are caused by infection by Human Papilloma Virus.

Other clinical features may include, but are not limited to: deafness, lung or liver manifestations, and cardiac issues when linked to the immune deficiency.

Is [the clinical feature] prominent?

A prominent feature is generally well documented, closely followed, and treated. Select "yes" if the reported clinical feature was a prominent part of their immune deficiency.

Question 93: Did the recipient receive parenteral nutrition (since the date of last report)?

Parenteral nutrition is given to the recipients intravenously rather than through the digestive system. Parenteral nutrition contains the carbohydrates, proteins, fats, electrolytes, and other components needed for survival. The use of parenteral nutrition to deliver all required nutrients is called total parenteral nutrition (TPN).

Indicate “yes” if the recipient received parenteral nutrition since the date of the last report. If the recipient did not receive parenteral nutrition, select “no.”

Question 94: Did the recipient receive mechanical ventilation (since the date of last report)?

Mechanical ventilation can occur as both an endotracheal tube and ventilator, or as a BIPAP machine with a tight fitting mask in continuous use. The one exception to BIPAP is CPAP used for sleep apnea, which generally involves overnight use only for patients with documented sleep apnea. Therefore, do not report a CPAP used for sleep apnea, as it does not have the same implications as other forms of mechanical ventilation.

Indications for mechanical ventilation include, but are not limited to:

- Apnea with respiratory arrest (excludes sleep apnea)
- Acute lung injury
- Vital capacity < 15 mL/kg
- Chronic obstructive pulmonary disease (COPD)
- Clinical deterioration
- Respiratory muscle fatigue
- Obtundation or coma
- Hypotension
- Tachypnea or bradypnea
If the recipient was placed on mechanical ventilation at any time since the date of the last report check “yes.” If the recipient does not have a history of mechanical ventilation during the time period, check “no.”
**Q95-166: Post-HCT Treatment for Immune Deficiency**

**Question 95: Was treatment given (since the date of last report)?**

The questions below regarding prophylactic anti-infection and immunosuppressant drugs, refer to supportive therapy used to treat or prevent the sequelae (or condition as a result of the disease) such as infections, autoimmune issues, GVHD, etc. Additional questions ask about other significant treatments given to the recipient following the anti-infection and immunosuppression therapy questions.

Indicate if the recipient received therapy since the date of the last report, including anti-infection drugs, immunosuppressive drugs, or any other significant and/or experimental therapies. If “yes,” continue with question 96. If “no,” continue with 167.

**Questions 96-104 Prophylactic Drugs**

**Drug**

Prophylactic drugs are used to prevent infection by a virus, bacteria, fungus, or parasite. Drugs started as a result of infection should not be reported as prophylactic drugs.

Indicate “yes” or “no” for each of the drug categories listed. If “yes,” continue with the subsequent questions regarding the stoppage of the prophylactic drug. If the drug was stopped, indicate “yes” and report the date the drug was stopped.

- **Antifungal drugs** are used to prevent fungal infections. Common prophylactic antifungal drugs include fluconazole, caspofungin, voriconazole, etc.

- **Antiviral drugs** are used to prevent viral infections. Common prophylactic antiviral drugs include acyclovir, ganciclovir, foscarnet, etc.

- **Co-trimoxazole (Bactrim, Septra)** is a prophylactic drug used to prevent Pneumocystis jirovecii, a protozoan (i.e., parasitic) infection that colonizes the lungs of those with compromised immune systems.

- **Prophylactic drug stopped?**

  Indicate if the prophylactic drugs in each category were stopped. Prophylactic drugs stopped for a period of time shorter than one week should not be considered as “stopped.”
**Date stopped**

Report the date the last prophylactic drug in each category was stopped. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Questions 105-164: Therapies**

Post-transplant therapies for immune deficiencies may include immunosuppressive therapies to prevent or treat GVHD (maternal-, transfusion-, or HCT-associated), autoimmune conditions, etc.

Indicate “yes” or “no” for each of the drugs listed. If “yes,” continue with the subsequent questions regarding the stoppage of the therapy. If the drug was stopped, indicate “yes” and report the date the drug was stopped.

**Therapy**

Each of the drugs in questions 105-164 have immunosuppressive properties.

Corticosteroids may be given topically or systemically. Budesonide, which is ingested orally, is considered a topical drug.

If the recipient is given a monoclonal antibody, select “yes” for question 120 and specify the monoclonal antibody in questions 121-142. If the monoclonal antibody is not listed, specify the drug in question 142.

If the recipient is given an immunosuppressant that is not listed, select “yes” for question 161 and specify the other immunosuppressant in question 164.

**Therapy stopped**

Indicate if the therapy was stopped. Therapy that is stopped for a period of time shorter than one week should not be considered as “therapy stopped.”

**Date stopped**

Report the date the therapy was stopped. If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

**Questions 165-166: Did the recipient receive any other significant treatment(s) (since the date of last report)?**

Recipients with immune deficiency may receive treatments other than what is listed above. Treatments may include enzyme replacement therapy such as PEG-ADA. Each immune deficiency may have their own unique treatments, including interferon, growth factors, enzyme replacement, or other therapies.
If the recipient had any other significant treatments since the date of last report, select “yes” and specify the treatments in question 166. If the recipient did not have additional significant treatments, select “no” and continue with question 167.
Q167-172: Status of Hematologic Engraftment

This section refers to quantitative analysis utilizing discriminating DNA markers. Peripheral blood cells must undergo separation or sorting into T, B, or lymphoid vs. myeloid populations to perform this determination. If RFLP analysis indicate only donor type hematopoiesis, mark T-cell, B-cell, and myeloid as “predominantly or completely donor.”

Also, report chimerism in the Form 2100 – 100 days Post-HCT Data or Form 2200 – Six Months to Two Years Post-HCT Data.

Questions 167-168: What is the current status of T-cell engraftment?

Reporting the T-cell engraftment requires that the sample is separated into sub-sets for chimerism analysis. T-cell subsets may be reported as CD3+ or CD4+ cells on the laboratory report.

If a T-cell chimerism was performed during the reporting period, indicate if the results showed:

- Predominantly or completely donor (≥80% donor chimerism)
- Mixed chimerism (5-80% donor)
- Only host cells detected (<5% donor)

Report the date of sample collection for the most recent T-cell chimerism in question 168.

If a T-cell chimerism was not performed during the reporting period, report “unknown” and continue with question 169.

Questions 169-170: What is the current status of B-cell engraftment?

Reporting the B-cell engraftment requires that the sample is separated into sub-sets for chimerism analysis. B-cell subsets may be reported as CD19+ or CD20+ cells on the laboratory report.

If a B-cell chimerism was performed during the reporting period, indicate if the results showed:

- Predominantly or completely donor (≥80% donor chimerism)
- Mixed chimerism (5-80% donor)
- Only host cells detected (<5% donor)
Report the date of sample collection for the most recent B-cell chimerism in question 170.

If a B-cell chimerism was not performed during the reporting period, report “unknown” and continue with question 171.

**Questions 171-172: What is the current status of myeloid engraftment?**

Reporting myeloid engraftment requires that the sample is separated into sub-sets for chimerism analysis. Myeloid subsets may be reported as CD15+ or CD33+ on the laboratory report.

If a myeloid chimerism was performed during the reporting period, indicate if the results showed:

- Predominantly or completely donor (≥80% donor chimerism)
- Mixed chimerism (5-80% donor)
- Only host cells detected (<5% donor)

Report the date of sample collection for the most recent myeloid chimerism in question 172.

If a myeloid chimerism was not performed during the reporting period, report “unknown” and continue with the signature lines.
Wiskott-Aldrich syndrome (WAS) is a rare X-linked recessive immunodeficiency affecting 1 to 10 of every 1 million male newborns. It is characterized by microthrombocytopenia and defective lymphocyte function. The decreased numbers and reduced size of platelets (microthrombocytopenia) in the blood often result in bruising, bloody diarrhea, and potentially severe internal bleeding. Defective lymphocyte function can manifest with recurrent infections such as otitis media and pneumonia, autoimmune disorders, and malignancies.¹

The WAS gene encodes the WASp protein which has important roles in hematopoietic cellular function. Patients with Wiskott-Aldrich syndrome contain a WAS gene variant and altered WASp expression leading to a range of clinical presentations. A WAS scoring system was developed to categorize WAS-associated symptoms into three distinct groups (X-linked Neutropenia, X-linked Thrombocytopenia, and Classic WAS). See table below. Patients with microthrombocytopenia and only mild, transient eczema or minor infections are classified with X-linked thrombocytopenia (XLT). Those with treatment-resistant eczema and recurrent infections, or an autoimmune disease or malignancy receive the WAS classification. The spectrum of clinical manifestations underscores the complex role of WASp in cellular function.²³⁴

### Table: Scoring System to Define Clinical Phenotypes Associated with WAS mutations⁵

<table>
<thead>
<tr>
<th></th>
<th>XLN</th>
<th>iXLT</th>
<th>XLT</th>
<th>Classic WAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>0</td>
<td>&lt;1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>-</td>
<td>Intermittent</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Small Platelets</td>
<td>-</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Eczema</td>
<td>-</td>
<td>-</td>
<td>Mild, transient</td>
<td>Persistent but therapy-responsive</td>
</tr>
<tr>
<td>Immunodeficiency</td>
<td>Absent or mild</td>
<td>-</td>
<td>Absent or mild</td>
<td>Mild</td>
</tr>
<tr>
<td>Infections</td>
<td>Absent or mild</td>
<td>-</td>
<td>-</td>
<td>Mild, infrequent without sequelae</td>
</tr>
<tr>
<td>Autoimmunity</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
and/or Malignancy

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Congenital Neutropenia</td>
<td>Present</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myelodysplasia</td>
<td>Possible myelodysplasia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

XLN: X-linked Neutropenia, iXLT: Intermittent X-linked Thrombocytopenia, XLT: X-linked Thrombocytopenia, WAS: Wiskott-Aldrich Syndrome


- 2033: WAS Pre-HCT
- 2133: WAS Post-HCT
2033: WAS Pre-HCT

The Wiskott-Aldrich Syndrome Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures WAS-specific pre-HCT data such as: the recipient’s clinical and genetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HCT treatments administered, and disease manifestations prior to the preparative regimen.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Wiskott-Aldrich syndrome under “disorders of the immune system.”

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype, and this baseline disease insert has not been completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1. If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than Wiskott-Aldrich syndrome), begin at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, check the indicator box and continue with question 67.

- Q1-13: Disease Assessment at Diagnosis
- Q14-41: Laboratory Studies at Diagnosis
- Q42-130: Clinical Features Assessed between Diagnosis and the Start of the Preparative Regimen

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/ 24/ 17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
<tr>
<td>9/</td>
<td>2033/2133:</td>
<td>Add</td>
<td>Published new manual for 2033 &amp; 2131 WAS Pre- and Post-HCT.</td>
</tr>
<tr>
<td>11/15</td>
<td>Wiskott Aldrich Syndrome</td>
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</tbody>
</table>
**Q1-13: Disease Assessment at Diagnosis**

**Question 1: What was the date of diagnosis?**

Wiskott-Aldrich syndrome (WAS) is characterized by multiple clinical, laboratory, and genetic features, rather than distinct pathological characteristics. Examples of testing done to confirm a diagnosis of WAS include peripheral blood sample analyses that can determine if there are fewer than 70,000 platelets/mm$^3$ and if the platelets are abnormally small in size (low platelet volume). Lymphocyte studies, including mRNA assays and protein studies, are performed to determine gene expression and the presence or absence of functional WASp protein. In addition, genetic tests can detect WAS gene mutations. Since multiple assessments are used to diagnose a patient with WAS, the date of diagnosis should be the date of sample collection of last assessment used to establish a diagnosis of WAS. If there is a strong family history of WAS and no testing is done to confirm the diagnosis, report the recipient date of birth.

**Question 2: Specify the WAS defining (diagnostic) criteria?**

Depending on the criteria used to diagnose WAS select one of three options: Definitive, Probable, or Possible (see table below).

| Definitive | Male patient with congenital thrombocytopenia (<70,000 platelets/mm$^3$), small platelets, and ≥1 one of the following:  
| | • mutation in WASp  
| | • absent WASp mRNA on northern blot analysis of lymphocytes  
| | • absent WASp protein in lymphocytes  
| | • maternal cousins, uncles, or nephews with small platelets and thrombocytopenia |
| Probable | Male patient with congenital thrombocytopenia (<70,000 platelets/mm$^3$), small platelets, and ≥1 one of the following:  
| | • eczema  
| | • abnormal antibody response to polysaccharide antigens  
| | • Autoimmune disease(s)  
| | • lymphoma / leukemia |
| Possible | Male patient with congenital thrombocytopenia (<70,000 platelets/mm$^3$) and small platelets  
| OR |  
| Possible | Male patient with splenectomy for thrombocytopenia* and ≥1 one of the following:  
| | • eczema  
| | • abnormal antibody response to polysaccharide antigens  
| | • Autoimmune disease(s)  
| | • lymphoma / leukemia |
*Destruction of platelets in the spleen is thought to play an important role in thrombocytopenia because corrections of platelet count and size have been reported after splenectomy.¹

**Questions 3-6: Specify all additional criteria for definitive WAS diagnosis**

For a definitive WAS diagnosis at least one of the criteria from questions 3-6 must be true. For a probable or possible WAS diagnosis skip to question 7.

**Question 3: Mutation in WASp?**

WAS is an inherited disorder; for that reason, genetic testing may be performed as part of the diagnostic workup. If there is a known family history of WAS, or the mother is a known carrier, genetic testing may be done prior to the onset of symptoms or even prenatally using techniques like chorionic villus sampling or amniocentesis.

Indicate whether a genetic mutation was identified. Continue with question 4.

**Question 4: Absent WASp mRNA on northern blot analysis of lymphocytes?**

Northern blotting is a technique used to study gene expression by detecting mRNA. The absence of WASp mRNA reflects a lack of gene expression. Without mRNA, protein translation cannot occur.

Indicate “yes” if WASp mRNA was absent on northern blot analysis of lymphocytes. Indicate “no” if a northern blot analysis of lymphocytes was performed and detected WASp mRNA. Continue with question 5.

**Question 5: Absent WASp protein in lymphocytes?**

After RNA is transcribed from a gene’s DNA, the RNA is translated into protein. Lack of WASp protein is consistent with a definitive WAS diagnosis. WASp protein may be detected by performing tests on lymphocytes isolated from whole blood, including Western blotting and enzyme-linked immunosorbent assays (ELISA).

Indicate “yes” if WASp protein was absent from lymphocytes. Indicate “no” if WASp protein was detected in lymphocytes.

**Question 6: Maternal cousins, uncles, or nephews with small platelets and thrombocytopenia?**

X-linked patterns of inheritance are caused by genetic mutations carried on the X chromosome. Males normally carry one copy of the X chromosome and one copy of the Y chromosome. For this reason, a faulty X chromosome will affect all men who carry it. Females carry two copies of the X chromosome. This means they will be carriers for x-linked recessive traits, but will rarely be symptomatic since they will generally have
a normal X chromosome that is expressed. (For x-linked dominant patterns of inheritance, only a single mutated X chromosome is necessary for symptomatic expression. Therefore, x-linked dominant patterns of inheritance affect both males and females).

WAS follows an x-linked recessive pattern of inheritance. Indicate whether the patient has maternal cousins, uncles, or nephews with small platelets and thrombocytopenia. Continue with question 11.

Questions 7-10: Specify all additional criteria for probable / possible WAS diagnosis

For a probable or possible WAS diagnosis at least one of the criteria from questions 7-10 must be selected.

Question 7: Eczema?

Eczema is a skin disorder with an immunologic basis. It is characterized by itchy, dry skin, as well as thickening of the skin (lichenification) and may be indicative of the immune dysfunction associated with WAS.

Indicate “yes” if the patient has eczema, otherwise indicate “no.” Continue with question 8.

Question 8: Abnormal antibody response to polysaccharide antigens?

The surface of many bacterial species is covered by polysaccharides (antigens). Immunity (antibodies) against these surface antigens confers protection against the disease. Since WAS can affect the function of both T cells and B cells, the antibody response to polysaccharide antigens may be impaired. Examples of tests performed to detect antibody response include the enzyme-linked immunosorbent assay (ELISA) and quantitative PCR.

Indicate “yes” if an abnormal antibody response to polysaccharide antigens was detected. Indicate “no” if the antibody response to polysaccharide antigens was normal. Continue with question 9.

Question 9: Autoimmune disease(s)?

Autoimmune diseases are frequently observed in the Wiskott Aldrich syndrome. The most common manifestations are hemolytic anemia, arthritis, cutaneous vasculitis, and nephropathy. Other autoimmune manifestations include inflammatory bowel disease, idiopathic thrombocytopenic purpura (ITP), and neutropenia. Multiple autoimmune manifestations may present at the same time in patients with WAS.

Indicate whether the patient has an autoimmune disease(s) and continue with question 10.
**Question 10: Lymphoma / Leukemia?**

Lymphoma (often Epstein-Barr virus positive) and leukemia are the most frequently WAS-associated malignancies. Indicate if the patient had lymphoma or leukemia. Continue with question 11.

**Question 11: Was a WAS gene mutation identified?**

WAS is an inherited disorder; for that reason, genetic testing may be done to confirm the diagnosis. If there is a known family history of WAS, or the mother is a known carrier, genetic testing may be done prior to the onset of symptoms or even prenatally using techniques like chorionic villus sampling or amniocentesis. Indicate “yes” if testing revealed a mutation in the WAS gene and continue with question 12; indicate “no” if testing was done but did not reveal a WAS gene mutation and continue with question 13.

**Question 12: Specify gene mutation identified**

A gene is a linear sequence of nucleotides compromising a segment of DNA from which RNA is synthesized. Nucleotides are categorized by type of nitrogenous base: adenine (A), guanine (G), cytosine (C), uracil (U), and thymine (T). Nucleotides are given a number based on their location. After DNA has been transcribed into RNA, the RNA is translated into amino acids to form protein. Amino acids have distinct names which are abbreviated with a unique letter and are also assigned numbers based on their location.

Genetic mutations may be identified by the affected nucleotides or by predicted changes in amino acids. Indicate the type of gene mutation identified in question 11. Select either “nucleotides affected (e.g., 361C>T)” or “predicted amino acid change (e.g., W14R).”

**Question 13: Was a WASp protein expressed?**

WASp protein may be detected using tests such as Western blotting or an enzyme-linked immunosorbent assay (ELISA). Indicate whether WASp protein was expressed. Continue with question 14.


Q14-41: Laboratory Studies at Diagnosis

Report findings at the time of diagnosis; if multiple studies were performed prior to the institution of therapy, or if time elapsed between diagnosis and treatment, report the latest values prior to any first treatment of Wiskott-Aldrich syndrome, such as IL-2 therapy or gene therapy.

**Question 14: Date CBC tested**

Report the date of CBC testing done within 6 weeks of diagnosis. Continue with question 15.

**Question 15: WBC**

Report the white blood cell (WBC) count and unit of measure as documented on the laboratory report. If the WBC is unknown leave the count and unit fields blank and select “WBC not tested.” Continue with question 19.

**Question 16: Lymphocytes**

Report the percentage of lymphocytes. If lymphocytes were not tested leave the count field blank and select “Lymphocytes not tested.” Continue with question 17.

**Question 17: Eosinophils**

Report the percentage of eosinophils. If eosinophils were not tested leave the count field blank and select “Eosinophils not tested.” Continue with question 18.

**Question 18: Polymorphonuclear leukocytes (PMN)**

Polymorphonuclear leukocytes are white blood cells containing cytoplasmic granules. PMNs are also referred to as granulocytes and include neutrophils, basophils, and eosinophils; however, this question refers to **neutrophils**. Report the percentage of neutrophils. If neutrophils were not tested leave the count field blank and select “Polymorphonuclear leukocytes (PMN) not tested.” Continue with question 19.

**Transfusions**

Currently there is an error on the Form 2033 regarding transfusion history. The form should read: “transfused RBC less than or equal to 30 days from date of most current testing” and “transfused platelets less than or equal to 7 days from date of most current testing.”
Question 19: Hemoglobin

Report the hemoglobin count and the unit of measure as documented on the laboratory report. If the hemoglobin was not tested leave the count and unit fields blank and indicate “Hemoglobin not tested.”

Indicate if red blood cells (RBC) were transfused ≤ 30 days from date of test. Continue with question 20.

Question 20: Platelets

Report the platelet count and unit of measure as documented on the laboratory report. If the platelet count was not tested leave the count and unit fields blank and indicate “Platelets not tested.”

Indicate if platelets were transfused ≤ 7 days from date of test. Continue with question 21.

Question 21: Mean platelet volume

Report the mean platelet volume in femtoliters (fl). If the mean platelet volume was not tested leave the count field blank and indicate “Mean platelet volume not tested.” Continue with question 22.

Immunoglobulin Analysis

Specify the following quantitative immunoglobulins measured at the time of diagnosis; if multiple studies were performed prior to the institution of therapy, report the latest values prior to any first treatment of Wiskott-Aldrich syndrome.

Question 22: IgG

Report the IgG level and the unit of measure documented on the laboratory report. Continue with question 23. If IgG was not tested leave the value and unit fields blank and indicate “IgG not tested,” and continue with question 24.

Question 23: Date tested

Report the date of IgG testing and continue with question 24.

Question 24: IgM

Report the IgM level and the unit of measure documented on the laboratory report. Continue with question 25. If IgM was not tested leave the value and unit fields blank and indicate “IgM not tested,” and continue with question 26.
Question 25: Date tested
Report the date of IgM testing and continue with question 26.

Question 26: IgA
Report the IgA level and the unit of measure documented on the laboratory report. Continue with question 27. If IgA was not tested leave the value and unit fields blank and indicate “IgA not tested,” and continue with question 28.

Question 27: Date tested
Report the date of IgA testing and continue with question 28.

Question 28: IgE
Report the IgE level in international units per milliliter (IU/ml). Continue with question 29. If IgE was not tested leave the value field blank and indicate “IgE not tested,” and continue with question 30.

Question 29: Date tested
Report the date of IgE testing and continue with question 30.

Question 30: Did the recipient receive supplemental intravenous immunoglobulins (IVIG) prior to any first treatment of WAS?
IVIG is a product made from pooled human plasma that primarily contains IgG. It is used to provide immune-deficient recipients with antibody function to help prevent infection.

Indicate whether the recipient received IVIG prior to any first treatment of WAS. If “yes” continue with question 31. If “no” or “unknown” continue with question 32.

Question 31: Was therapy ongoing within one month of immunoglobulin testing?
Indicate whether the recipient received IVIG within one month prior to the immunoglobulin testing done at diagnosis. Patients exhibiting signs of a compromised or dysfunctional immune system may have received IVIG prior to a diagnosis being made. If IVIG is given within one month of immunoglobulin testing, the IgG level would not represent the recipient’s native IgG. Continue with question 32.

Lymphocyte Analysis
Specify the following lymphocyte analyses performed at the time of diagnosis; if multiple studies were
performed prior to the institution of therapy, report the latest values prior to any first treatment of Wiskott-Aldrich syndrome.

**Question 32: Were lymphocyte analyses performed?**

Lymphocyte analyses include quantifying specific types of T cells, B Cells, and natural killer (NK) cells. Cells can be identified by cell-specific surface molecules using the clusters of differentiation (CD) nomenclature. For example, T cells can be classified as helper (CD4+) or cytotoxic (CD8+) cells depending on their cell surface markers designated with CD notation.

Indicate if lymphocyte analyses were performed. If “yes” continue with question 33. If “no” continue with question 42.

**Question 33: Date of most recent testing performed**

Report the date of most recent lymphocyte testing performed prior to any disease treatment. Continue with question 34.

**Question 34: Absolute lymphocyte count**

Report the absolute lymphocyte count in cells per microliter (cells/µL). Continue with question 35.

**Question 35: CD3 (T cells)**

T cells are a type of lymphocyte that can be characterized by CD3. If the laboratory quantifies CD3 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD3 cells as an absolute value, then report the value in the count field and specify the count units. If CD3 cells were not tested, select the “CD3 (T cells) not tested” option. Continue with question 36.

**Question 36: CD4 (T helper cells)**

T helper cells are a subset of T cells characterized by CD4, sometimes reported as CD3+CD4+. If the laboratory quantifies CD4 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4 cells as an absolute value, then report the value in the count field and specify the count units. If CD4 cells were not tested, select the “CD4 (T cells) not tested” option. Continue with question 37.

**Question 37: CD8 (cytotoxic T cells)**

Cytotoxic T cells are a subset of T cells characterized by CD8, sometimes reported as CD3+CD8+. If the laboratory quantifies CD8 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD8 cells as an absolute value, then report the value in the count field and
specify the count units. If CD8 cells were not tested, select the “CD8 (T cells) not tested” option. Continue with question 38.

**Question 38: CD20 (B lymphocyte cells)**

B cells are a type of lymphocyte that can be characterized by CD20. If the laboratory quantifies CD20 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD20 cells as an absolute value, then report the value in the count field and specify the count units. If CD20 cells were not tested, select the “CD20 (B lymphocyte cells) not tested” option. Continue with question 39.

**Question 39: CD56 (natural killer (NK) cells)**

NK cells are a type of lymphocyte that can be characterized by CD56. If the laboratory quantifies CD56 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD56 cells as an absolute value, then report the value in the count field and specify the count units. If CD56 cells were not tested, select the “CD56 (natural killer (NK) cells) not tested” option. Continue with question 40.

**Question 40: CD4+/CD45RA+ (naïve T cells)**

Naïve T cells are a type of T cell that can be characterized by CD4+/CD45RA+. T cells are considered naïve prior to encountering an antigen. If the laboratory quantifies CD4+/CD45RA+ cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4+/CD45RA+ cells as an absolute value, then report the value in the count field and specify the count units. If CD4+/CD45RA+ cells were not tested, select the “CD4+/CD45RA+ (naïve T cells) not tested” option. Continue with question 41.

**Question 41: CD4+/CD45RO+ (memory T cells)**

Memory T cells are a type of T cell that can be characterized by CD4+/CD45RO+. If the laboratory quantifies CD4+/CD45RO+ cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4+/CD45RO+ cells as an absolute value, then report the value in the count field and specify the count units. If CD4+/CD45RO+ cells were not tested, select the “CD4+/CD45RO+ (memory T cells) not tested” option. Continue with question 42.
Q42-130: Clinical Features Assessed between Diagnosis and the Start of the Preparative Regimen

Infections identified between Diagnosis and the Start of the Preparative Regimen

Specify the presence of all clinically significant infections identified between diagnosis and the start of the preparative regimen. For the purposes of this form, clinically significant infections are those that require treatment such as antibiotics, antivirals, etc. Only report an organism once, even if it was identified at the same site in subsequent infections.

Question 42: Hepatitis

Hepatitis refers to inflammation (acute or chronic) of the liver with infectious or noninfectious etiologies. Hepatitis symptoms can include abdominal pain, jaundice, nausea, and vomiting. Laboratory tests such as aminotransferase (ALT/AST) and bilirubin measurements may be performed to monitor hepatic function. These lab values are frequently elevated in patients with hepatitis.

Indicate if the recipient developed infectious hepatitis. If “yes” continue with question 43. If “no” continue with question 46.

Question 43: Organism

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the hepatitis reported in question 42. If no organism was identified select the “No organism identified” option from the bottom of the list. If the organism was identified but is not listed, select the corresponding “Other, specify” option (i.e. other Chlamydia, other mycobacterium, other bacteria, etc.). Specify the organism in the open field provided in question 44. If multiple organisms were identified, add additional instances for questions 43-44 and specify the other organism(s). Continue with question 45.

Question 45: If hepatitis was present, was it a prominent feature of WAS?

If infectious hepatitis was present, indicate if it was a prominent feature of WAS. A prominent feature is generally well documented, closely followed, and treated. Continue with question 46.
**Question 46: Meningitis / encephalitis**

Meningitis is an inflammation of the meninges, membranes encasing the central nervous system. Encephalitis is inflammation of the brain tissue itself. Meningitis and encephalitis may co-occur as meningoencephalitis. Common symptoms include headache, lethargy, confusion, fever, neck stiffness, and cranial nerve defects.

Indicate if the recipient developed infectious meningitis / encephalitis. If “yes” continue with question 47. If “no” continue with question 50.

**Question 47: Organism**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the meningitis / encephalitis reported in question 46. If no organism was identified select the “No organism identified” option from the bottom of the list. If the organism was identified but is not listed, select the corresponding “Other, specify” option (i.e. other Chlamydia, other mycobacterium, other bacteria, etc.). Specify the organism in the open field provided in question 48. If multiple organisms were identified, add additional instances for questions 47-48 and specify the other organism(s). Continue with question 49.

**Question 49: If meningitis / encephalitis was present, was it a prominent feature of WAS?**

If meningitis / encephalitis was present, indicate if it was a prominent feature of WAS. A prominent feature is generally well documented, closely followed, and treated. Continue with question 50.

**Question 50: Pneumonia**

Pneumonia is a respiratory condition due to lung infection. Symptoms may include fever, cough, and difficulty breathing. Indicate “yes” if the recipient developed infectious pneumonia and continue with question 51. If the recipient did not have pneumonia, indicate “no” and continue with question 54.

**Question 51: Organism**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the pneumonia reported in question 50. If no organism was identified select the “No organism identified” option from the bottom of the list. If the organism was identified but is not listed, select the corresponding “Other, specify” option (i.e. other Chlamydia, other mycobacterium, other bacteria, etc.). Specify the organism in the open field provided in question 52. If multiple organisms were identified, add additional instances for questions 51-52 and specify the other organism(s). Continue with question 53.
**Question 53: If pneumonia was present, was it a prominent feature of WAS?**

If pneumonia was present, indicate if it was a prominent feature of WAS. A prominent feature is generally well documented, closely followed, and treated. Continue with question 54.

**Question 54: Severe or protracted diarrhea**

Protracted diarrhea (>10g/kg/24hrs) refers to three or more loose stools per day lasting longer than fourteen days. Indicate whether the recipient had severe or protracted diarrhea. If “yes” continue with question 55. If “no” continue with question 58.

1 Guandalini S. Diarrhea. Medscape. Updated 4/10/14

**Question 55: Organism**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the diarrhea reported in question 54. If no organism was identified select the “No organism identified” option from the bottom of the list. If the organism was identified but is not listed, select the corresponding “Other, specify” option (i.e. other Chlamydia, other mycobacterium, other bacteria, etc.). Specify the organism in the open field provided in question 56. If multiple organisms were identified, add additional instances for questions 55-56 and specify the other organism(s). Continue with question 57.

**Question 57: If diarrhea was present, was it a prominent feature of WAS?**

If diarrhea was present, indicate if it was a prominent feature of WAS. A prominent feature is generally well documented, closely followed, and treated. Continue with question 58.

**Question 58: Systemic infection**

A systemic infection is an infection isolated at 3 or more sites. Indicate whether the recipient had systemic infection. If “yes” continue with question 59. If “no” continue with question 62.

**Question 59: Organism**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the systemic infection reported in question 58. If no organism was identified select the “No organism identified” option from the bottom of the list. If the organism was identified but is not listed, select the corresponding “Other, specify” option (i.e. other Chlamydia, other mycobacterium, other bacteria, etc.). Specify the organism in the open field provided in question 60. If multiple organisms were identified, add additional instances for questions 59-60 and specify the other organism(s). Continue with question 61.
**Question 61: If systemic infection was present, was it a prominent feature of WAS?**

If systemic infection was present, indicate if it was a prominent feature of WAS. A prominent feature is generally well documented, closely followed, and treated. Continue with question 62.

**Question 62: Other infection**

Indicate if the recipient had an infection other than reported in questions 42-61. If “yes” continue with question 63. If “no” continue with question 67.

**Question 63: Organism**

Select the identified or suspected infectious organism as reported on the microbiology report, laboratory report, or other physician documentation causing the infection reported in question 62. If no organism was identified select the “No organism identified” option from the bottom of the list. If the organism was identified but is not listed, select the corresponding “Other, specify” option (i.e. other Chlamydia, other mycobacterium, other bacteria, etc.). Specify the organism in the open field provided in question 64. If multiple organisms were identified, add additional instances for questions 63-64 and specify the other organism(s). Continue with question 65.

**Question 65: Specify other infection site**

Specify the site of the infection reported in question 62. Continue with question 66.

**Question 66: If other infection was present, was it a prominent feature of WAS?**

If other infection was present, indicate if it was a prominent feature of WAS. A prominent feature is generally well documented, closely followed, and treated. Continue with question 67.

**Clinical Status between Diagnosis and the Preparative Regimen**

**Question 67: Did the recipient undergo a splenectomy (between diagnosis and prior to the preparative regimen)?**

Destruction of platelets in the spleen is thought to play an important role in thrombocytopenia because corrections of platelet count and size have been reported after splenectomy.²

Indicate if the recipient underwent a splenectomy after diagnosis but prior to the preparative regimen. If “yes” continue with question 68. If “no” or “unknown” continue with question 70.
Question 68: Specify the date the splenectomy was performed

Indicate the date of splenectomy and continue with question 69.

Question 69: Platelets (after splenectomy)

Report the platelet count and unit of measure after splenectomy as documented on the laboratory report. Indicate if platelets were transfused ≤ 7 days from the date of testing. If the platelet count was not tested leave the count and unit fields blank and indicate “Platelets not tested.” Continue with question 70.

Question 70: Were thrombocytopenia (<100 × 10^9/L) and small platelets present without any other symptoms, clinical findings, or laboratory abnormalities attributable to WAS (between diagnosis and prior to the preparative regimen)?

Indicate if the recipient had microthrombocytopenia without any other symptoms, findings, or abnormalities attributable to WAS. This would occur in the setting of X-linked thrombocytopenia (XLT). Continue with question 71.

Question 71: Was eczema present as a clinical feature (between diagnosis and prior to the preparative regimen)?

Eczema is a skin disorder with an immunologic basis. It is characterized by itchy, dry skin, as well as thickening of the skin (lichenification) and may be indicative of the immune dysfunction associated with WAS.

Indicate if eczema was present as a clinical feature after diagnosis but prior to the preparative regimen. If “yes” continue with question 72. If “no” continue with question 73.

Question 72: Specify severity of eczema

Indicate the eczema severity based on its documented persistence and manageability in the opinion of the physician by selecting one of the following options: “mild, transient” “persistent but manageable” or “difficult to control.”

“Mild, transient” can be controlled with intermittent steroids, “persistent but manageable” with chronic topical steroid use, and “difficulty to control” requires systemic steroids, multiple topical therapies, or is refractory to treatment.

Question 73: Was a coexisting malignancy present (between diagnosis and prior to the preparative
regimen)?

Indicate if the recipient had a coexisting malignancy after diagnosis but prior to the preparative regimen. If “yes” continue with question 74, if “no” or “unknown” continue with question 75.

**Question 74: Specify malignancy**

Specify the coexisting malignancy. Also, report the malignancy in the pre-TED Form 2400.

**Question 75: Did the recipient experience any of the following types of bleeding episodes (between diagnosis and prior to the preparative regimen)?**

Bleeding episodes are frequently observed due to WAS-associated thrombocytopenia. If nasal bleeds, gastrointestinal hemorrhage, hemarthrosis (bleeding into joints), hematuria (blood in the urine), intracranial hemorrhage, oral bleeding, subcutaneous bleeding, subdural hematoma, or other bleeding occurred after diagnosis but prior to the preparative regimen indicate “yes” and continue with question 76. If “no” continue with question 97.

**Question 76: Is epistaxis present?**

Indicate if epistaxis, bleeding from the nose, is present. If “yes” continue with question 77. If “no” continue with question 78.

**Question 77: Is epistaxis prominent?**

Indicate if epistaxis is prominent. A prominent feature is generally well documented, closely followed, and treated. Epistaxis may be recurrent, life-threatening, or require a transfusion. Continue with question 78.

**Question 78: Is upper GI hemorrhage present?**

Hemorrhage in the upper gastrointestinal tract includes bleeding that occurs above the duodenojejunal juncture of the small intestines. Signs of upper GI hemorrhage include vomiting blood (hematemesis) and black “tarry” stool (melena). As with other sources of blood loss, symptoms can include light headedness and fainting, weight loss, jaundice, and pain. Indicate if upper GI hemorrhage is present. If “yes” continue with question 79. If “no” continue with question 80.

**Question 79: Is upper GI hemorrhage prominent?**

Indicate if upper GI hemorrhage is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 80.
**Question 80: Is lower GI hemorrhage/rectal bleeding present?**

Hemorrhage in the lower gastrointestinal tract includes bleeding that occurs below the duodenojejunal juncture of the small intestines. Signs of lower GI hemorrhage include bright red blood in stool (hematochezia) and spontaneous rectal bleeding without defecation. Lower GI hemorrhage presents with symptoms similar to those associated with upper GI hemorrhage. Depending on the location and severity of hemorrhage, upper and lower GI bleeds may have similar presentations. Indicate if there is lower GI hemorrhage/rectal bleeding present. If “yes” continue with question 81. If “no” continue with question 82.

**Question 81: Is lower GI hemorrhage/rectal bleeding prominent?**

Indicate if lower GI hemorrhage/rectal bleeding is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 82.

**Question 82: Is hemarthrosis present?**

Hemarthrosis refers to bleeding into joint spaces leading to swelling and pain. Suspected hemarthrosis is often confirmed with a joint aspiration. Indicate if hemarthrosis is present. If “yes” continue with question 83. If “no” continue with question 84.

**Question 83: Is hemarthrosis prominent?**

Indicate if bleeding into joint spaces is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 84.

**Question 84: Is hematuria present?**

Hematuria refers to blood in the urine and can be further specified as gross hematuria or microscopic hematuria. Gross hematuria is visibly noticeable while microscopic hematuria is only apparent when examined with a microscope. Hematuria may either be asymptomatic or be associated with symptoms such as painful urination and changes in urination frequency. Indicate if hematuria is present. If “yes” continue with question 85. If “no” continue with question 86.

**Question 85: Is hematuria prominent?**

Indicate if blood in the urine is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 86.

**Question 86: Is intracranial hemorrhage present?**

Intracranial hemorrhage involves bleeding within the skull and may present with symptoms including nausea and vomiting, headache, and altered consciousness. CT scans and other imaging modalities are commonly
used to visualize intracranial bleeding. Indicate if intracranial hemorrhage is present. If "yes" continue with question 87. If "no" continue with question 88.

**Question 87: Is intracranial hemorrhage prominent?**

Indicate if intracranial hemorrhage is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 88.

**Question 88: Is oral bleeding present?**

Indicate if oral bleeding is present. If “yes” continue with question 89. If “no” continue with question 90.

**Question 89: Is oral bleeding prominent?**

Indicate if oral bleeding is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 90.

**Question 90: Is subcutaneous bleeding present?**

Indicate if there is bleeding under the skin, commonly identified by bruising (petechiae, purpura, ecchymosis). If “yes” continue with question 91. If “no” continue with question 92.

**Question 91: Is subcutaneous bleeding prominent?**

Indicate if bleeding under the skin is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 92.

**Question 92: Is subdural hematoma present?**

The dura mater is the outermost membrane that encloses the brain and spinal cord, keeping in the cerebrospinal fluid. A subdural hematoma is a collection of blood below the dura mater. Subdural hematoma symptoms include: headache, decreased consciousness, and motor deficits. CT scans are commonly used to visualize subdural bleeding. Indicate if a subdural hematoma is present. If “yes” continue with question 93. If “no” continue with question 94.

**Question 93: Is subdural hematoma prominent?**

Indicate if subdural hematoma is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 94.
followed, and treated. Continue with question 94.

**Question 94: Is other bleeding present?**

Indicate if bleeding other than listed in questions 76-93 is present. If “yes” continue with questions 95 and 96. If “no” continue with question 97.

**Question 95: Is other bleeding prominent?**

Indicate if other bleeding is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 96.

**Question 96: Specify other bleeding?**

Specify the type of other bleeding indicated in question 94. Continue with question 97.

**Question 97: Did the recipient experience any of the following autoimmune / inflammatory disorders (between diagnosis and prior to the preparative regimen)?**

Due to aberrant lymphocyte function associated with WAS, autoimmune and inflammatory disorders are common. Indicate “yes” if the recipient experienced autoimmune / inflammatory disorder(s) and continue with questions 98-129 to further specify the disorder(s). If “no” continue with question 130.

**Question 98: Is arthralgia present?**

Indicate if the recipient experienced joint pain. If “yes” continue with question 99. If “no” continue with question 100.

**Question 99: Is arthralgia prominent?**

Indicate if arthralgia is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 100.

**Question 100: Is chronic arthritis present?**

Chronic arthritis refers to persistent joint inflammation, leading to pain, swelling, and stiffness often with reduced movement. Indicate if chronic arthritis is present. If “yes” continue with question 101. If “no” continue with question 102.

**Question 101: Is chronic arthritis prominent?**

Indicate if chronic arthritis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 102.
**Question 102: Is autoimmune hemolytic anemia present?**

Autoimmune hemolytic anemia refers to the destruction (hemolysis) of red blood cells by the recipient’s own immune system. Anemia results when the recipient’s marrow is unable to sufficiently produce replacement red blood cells. Laboratory studies are the most common method of disease detection, usually involving a complete blood cell count and peripheral blood smear. Indicate if autoimmune hemolytic anemia is present. If “yes” continue with question 103. If “no” continue with question 104.

**Question 103: Is autoimmune hemolytic anemia prominent?**

Indicate if autoimmune hemolytic anemia is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 104.

**Question 104: Is idiopathic thrombocytopenic purpura (ITP) present?**

ITP refers to decreased platelet counts with normal bone marrow and the absence of other thrombocytopenia causes. Before reporting ITP, ensure that the thrombocytopenia is a result of an autoimmune process rather than representative of WAS. Indicate if ITP is present. If “yes” continue with question 105, if “no” continue with question 106.

**Question 105: Is idiopathic thrombocytopenic purpura (ITP) prominent?**

Indicate if ITP is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 106.

**Question 106: Is inflammatory bowel disease present?**

Inflammatory bowel disease (IBD) is a general term referring to inflammation anywhere along the lining of the gastrointestinal tract. Ulcerative colitis and Crohn’s disease are the two major types of IBD and commonly manifest with abdominal cramping and abnormal bowel movements including constipation, diarrhea, and the passage of mucus and/or blood. Complete blood counts, stool studies, and serologic studies can be performed to better characterize symptoms and exclude other disorders on the differential diagnosis. Imaging studies, especially endoscopies are used to diagnosis and monitor IBD. Indicate if inflammatory bowel disease is present. If “yes” continue with question 107. If “no” continue with question 108.

**Question 107: Is inflammatory bowel disease prominent?**

Indicate if inflammatory bowel disease is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 108.
**Question 108: Is juvenile rheumatoid arthritis present?**

Juvenile rheumatoid arthritis is a condition of autoimmune joint inflammation causing joint pain, swelling, and stiffness, with childhood onset. Indicate if juvenile rheumatoid arthritis is present. If “yes” continue with question 109. If “no” continue with question 110.

**Question 109: Is juvenile rheumatoid arthritis prominent?**

Indicate if juvenile rheumatoid arthritis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 110.

**Question 110: Is nephritis present?**

Nephritis refers to inflammation of the kidneys and may be further specified based on the area of kidney involvement and whether the inflammation is acute or chronic. Tests performed to assess and monitor kidney function include BUN and creatinine. In certain cases, a renal biopsy may be performed. Indicate if nephritis is present. If “yes” continue with question 111, if “no” continue with question 112.

**Question 111: Is nephritis prominent?**

Indicate if nephritis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 112.

**Question 112: Is neutropenia present?**

Neutropenia refers to a decreased number of neutrophils in the blood (ANC < 1.0 × 10^9/L). The risk of infection increases as the neutrophil count decreases. Indicate if the recipient is neutropenic. If “yes” continue with question 113, if “no” continue with question 114.

**Question 113: Is neutropenia prominent?**

Indicate if neutropenia is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 114.

**Question 114: Is sclerosing cholangitis present?**

Sclerosing cholangitis refers to inflammation and subsequent scarring and destruction of the bile ducts, eventually leading to liver damage. Imaging studies of the bile duct (cholangiography), as well as liver function tests such as aminotransferase and alkaline phosphatase are used to diagnose and monitor the disease. Indicate if sclerosing cholangitis is present. If “yes” continue with question 115, if “no” continue with question 116.
Question 115: Is sclerosing cholangitis prominent?

Indicate if sclerosing cholangitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 116.

Question 116: Is cerebral vasculitis present?

Vasculitis refers to inflammation of the vasculature, including both veins and arteries. Vasculitis may impact blood vessels of any size, from capillaries and arterioles to the great truncal vessels. It is typically caused by autoimmunity.

Cerebral vasculitis refers to inflammation involving vasculature of the brain. Indicate if the recipient had cerebral vasculitis. If “yes” continue with question 117, if “no” continue with question 118.

Question 117: Is cerebral vasculitis prominent?

Indicate if cerebral vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 118.

Question 118: Is coronary vasculitis present?

Coronary vasculitis refers to inflammation involving vasculature of the heart. Indicate if coronary vasculitis is present. If “yes” continue with question 119, if “no” continue with question 120.

Question 119: Is coronary vasculitis prominent?

Indicate if coronary vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 120.

Question 120: Is renal vasculitis present?

Renal vasculitis refers to inflammation involving vasculature of the kidney. Indicate if renal vasculitis is present. If “yes” continue with question 121, if “no” continue with question 122.

Question 121: Is renal vasculitis prominent?

Indicate if renal vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 122.

Question 122: Is skin vasculitis present?

Indicate if the recipient has inflammation involving vasculature of the skin. If “yes” continue with question 123, if “no” continue with question 124.
**Question 123: Is skin vasculitis prominent?**

Indicate if skin vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 124.

**Question 124: Is other vasculitis present?**

Indicate if other types of vasculitis are present than those listed in questions 116-123. If “yes” continue with question 125, if “no” continue with question 127.

**Question 125: Is other vasculitis prominent?**

Indicate if other vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 126.

**Question 126: Specify other vasculitis**

Specify the other vasculitis indicated in question 124. Continue with question 127.

**Question 127: Other disorder**

Indicate if the recipient had an autoimmune / inflammatory disorder not listed in questions 98-126. If “yes” continue with question 128, if “no” continue with question 130.

**Question 128: Is any other disorder prominent?**

Indicate if the other disorder from question 128 is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 129.

**Question 129: Specify other disorder**

Specify the other disorder indicated in question 127. Continue with question 130.

**Questions 130-143: Were any biologic specimens collected for this recipient (between the date of diagnosis and the preparative regimen)?**

Indicate whether biologic specimens were collected for this recipient. Biologic specimens may be collected for more in-depth analyses and for research purposes. Different types of cells, for example B cells and T cells, can be isolated from whole blood and viral-transformed to establish permanent cell lines.

If “yes” continue with questions 131-143 and specify which specimens were collected, if “no” or “unknown” continue with “Signature Lines.”
2133: WAS Post-HCT

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Wiskott-Aldrich Syndrome under “disorders of the immune system.” The Wiskott-Aldrich syndrome Post-HCT Data Form (Form 2133) must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, 2300) completed. The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200, between the date of contact for the six-month follow up and the date of contact for the one-year follow up for Form 2200, etc.)

- Q1-50: Laboratory Studies Post-HCT
- Q51-105: Clinical Status of Recipient Post-HCT
- Q106-167: Post-HCT Treatment for Wiskott-Aldrich Syndrome
- Q169-174: Status of Hematologic Engraftment

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
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<td>2/9/16</td>
<td>2133: WAS Post-HCT</td>
<td>Add</td>
<td>Added CD15+ cells to the text in question 173: Myeloid subsets may be reported as CD15+ or CD33+ on the laboratory report.</td>
</tr>
<tr>
<td>9/11/15</td>
<td>2033/2133: Wiskott Aldrich Syndrome</td>
<td>Add</td>
<td>Published new manual for 2033 &amp; 2131 WAS Pre- and Post-HCT.</td>
</tr>
</tbody>
</table>
Q1-50: Laboratory Studies Post-HCT

Report the most recent findings since the date of the last report. For questions 1-3 and 6-7, also report CBC results in the Form 2100 – 100 Days Post-HCT Data, or in the Form 2200 – Six Months to Two Years Post-HCT Data.

**Question 1: Date of most recent hematologic testing**

Report the date of the most recent hematologic testing since the date of last report. Continue with question 2.

**Question 2: WBC**

Report the white blood cell (WBC) count and unit of measure as documented on the laboratory report. If the WBC is unknown leave the count and unit fields blank and select “WBC not tested.” Continue with question 9.

**Question 3: Lymphocytes**

Report the percentage of lymphocytes. If lymphocytes were not tested leave the count field blank and select “Lymphocytes not tested.” Continue with question 4.

**Question 4: Eosinophils**

Report the percentage of eosinophils. If eosinophils were not tested leave the count field blank and select “Eosinophils not tested.” Continue with question 5.

**Question 5: Polymorphonuclear leukocytes (PMN)**

Polymorphonuclear leukocytes are white blood cells containing cytoplasmic granules. PMNs are also referred to as granulocytes and include neutrophils, basophils, and eosinophils; however, this question refers to **neutrophils**. Report the percentage of neutrophils. If neutrophils were not tested leave the count field blank and select “Polymorphonuclear leukocytes (PMN) not tested.” Continue with question 6.

**Transfusions**

Currently there is an error on the Form 2133 regarding transfusion history. The form should read: “transfused RBC less than or equal to 30 days from date of most current testing” and “transfused platelets less than or equal to 7 days from date of most current testing.”
**Question 6: Hemoglobin**

Report the hemoglobin count and the unit of measure as documented on the laboratory report. If the hemoglobin was not tested leave the count and unit fields blank and indicate “Hemoglobin not tested.”

Indicate if red blood cells (RBC) were transfused ≤ 30 days from date of test. Continue with question 7.

**Question 7: Platelets**

Report the platelet count and unit of measure as documented on the laboratory report. If the platelet count was not tested leave the count and unit fields blank and indicate “Platelets not tested.”

Indicate if platelets were transfused ≤ 7 days from date of test. Continue with question 8.

**Question 8: Mean platelet volume**

Report the mean platelet volume in femtoliters (fl). If the mean platelet volume was not tested leave the count field blank and indicate “Mean platelet volume not tested.” Continue with question 9.

**Question 9: What was the platelet size at the date of the most recent follow-up?**

Platelet size can be evaluated using platelet volume indices, including mean platelet volume and platelet deviation width. Indicate if the platelet size at the date of the most recent follow-up was “decreased,” “normal,” or “unknown.” Continue with question 10.

**Immunoglobulin Analysis**

Specify the following quantitative immunoglobulins measured since the date of the last report. Also report immunoglobulins and IVIG in the Form 2100 – 100 Days Post-HCT Data, or in the Form 2200 – Six Months to Two years Post-HCT Data.

**Question 10: IgG**

Report the IgG level and the unit of measure documented on the laboratory report. Continue with question 11. If IgG was not tested leave the value and unit fields blank and indicate “IgG not tested,” and continue with question 12.

**Question 11: Date tested**

Report the date of IgG testing and continue with question 12.
**Question 12: IgM**

Report the IgM level and the unit of measure documented on the laboratory report. Continue with question 13. If IgM was not tested leave the value and unit fields blank and indicate “IgM not tested,” and continue with question 14.

**Question 13: Date tested**

Report the date of IgM testing and continue with question 14.

**Question 14: IgA**

Report the IgA level and the unit of measure documented on the laboratory report. Continue with question 15. If IgA was not tested leave the value and unit fields blank and indicate “IgA not tested,” and continue with question 16.

**Question 15: Date tested**

Report the date of IgA testing and continue with question 16.

**Question 16: IgE**

Report the IgE level in international units per milliliter (IU/ml). Continue with question 17. If IgE was not tested leave the value field blank and indicate “IgE not tested,” and continue with question 18.

**Question 17: Date tested**

Report the date of IgE testing and continue with question 18.

**Question 18: Did the recipient receive supplemental intravenous immunoglobulins (IVIG) (since the date of the last report)?**

IVIG is a product made from pooled human plasma that primarily contains IgG. It is used to provide immune-deficient recipients with antibody function to help prevent infection.

Indicate whether the recipient received IVIG since the date of last report. If “yes” continue with question 19. If “no” or “unknown” continue with question 20.

**Question 19: Was therapy ongoing within one month of immunoglobulin testing?**

Indicate whether the recipient received IVIG within one month prior to the immunoglobulin testing. If IVIG is given within one month of immunoglobulin testing, the IgG level would not represent the recipient’s native IgG. Continue with question 20.
**Lymphocyte Analysis**

Specify the most recent lymphocyte assessment measured since the date of the last report. For questions 21 and 23-27, also report lymphocytes in the Form 2100 – 100 Days Post-HCT Data, or in the Form 2200 – Six Months to Two Years Post-HCT Data.

**Question 20: Were lymphocyte analyses performed?**

Lymphocyte analyses include quantifying specific types of T cells, B Cells, and natural killer (NK) cells. Cells can be identified by cell-specific surface molecules using the clusters of differentiation (CD) nomenclature. For example, T cells can be classified as helper (CD4+) or cytotoxic (CD8+) cells depending on their cell surface markers designated with CD notation.

Indicate if lymphocyte analyses were performed. If "yes" continue with question 21. If "no" continue with question 30.

**Question 21: Date of most recent testing performed**

Report the date of most recent lymphocyte testing since the date of the last report. Continue with question 22.

**Question 22: Absolute lymphocyte count**

Report the absolute lymphocyte count in cells per microliter (cells/µL). Continue with question 23.

**Question 23: CD3 (T cells)**

T cells are a type of lymphocyte that can be characterized by CD3. If the laboratory quantifies CD3 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD3 cells as an absolute value, then report the value in the count field and specify the count units. If CD3 cells were not tested, select the “CD3 (T cells) not tested” option. Continue with question 24.

**Question 24: CD4 (T helper cells)**

T helper cells are a subset of T cells characterized by CD4, sometimes reported as CD3+CD4+. If the laboratory quantifies CD4 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4 cells as an absolute value, then report the value in the count field and specify the count units. If CD4 cells were not tested, select the “CD4 (T cells) not tested” option. Continue with question 25.
Question 25: CD8 (cytotoxic T cells)

Cytotoxic T cells are a subset of T cells characterized by CD8, sometimes reported as CD3+CD8+. If the laboratory quantifies CD8 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD8 cells as an absolute value, then report the value in the count field and specify the count units. If CD8 cells were not tested, select the “CD8 (T cells) not tested” option. Continue with question 26.

Question 26: CD20 (B lymphocyte cells)

B cells are a type of lymphocyte that can be characterized by CD20. If the laboratory quantifies CD20 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD20 cells as an absolute value, then report the value in the count field and specify the count units. If CD20 cells were not tested, select the “CD20 (B lymphocyte cells) not tested” option. Continue with question 27.

Question 27: CD56 (natural killer (NK) cells)

NK cells are a type of lymphocyte that can be characterized by CD56. If the laboratory quantifies CD56 cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD56 cells as an absolute value, then report the value in the count field and specify the count units. If CD56 cells were not tested, select the “CD56 (natural killer (NK) cells) not tested” option. Continue with question 28.

Question 28: CD4+/CD45RA+ (naïve T cells)

Naïve T cells are a type of T cell that can be characterized by CD4+/CD45RA+. T cells are considered naïve prior to encountering an antigen. If the laboratory quantifies CD4+/CD45RA+ cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4+/CD45RA+ cells as an absolute value, then report the value in the count field and specify the count units. If CD4+/CD45RA+ cells were not tested, select the “CD4+/CD45RA+ (naïve T cells) not tested” option. Continue with question 29.

Question 29: CD4+/CD45RO+ (memory T cells)

Memory T cells are a type of T cell that can be characterized by CD4+/CD45RO+. If the laboratory quantifies CD4+/CD45RO+ cells as a percent of total lymphocytes, then report the value in the percentage field. If the laboratory quantifies CD4+/CD45RO+ cells as an absolute value, then report the value in the count field and specify the count units. If CD4+/CD45RO+ cells were not tested, select the “CD4+/CD45RO+ (memory T cells) not tested” option. Continue with question 30.
Questions 30-38: Antibody Response

The immune system produces antibodies in response to antigens. Tests that measure the antibody response to different antigens help determine if the immune system is properly functioning.

Specify the most recent antibody responses measured since the date of the last report. For each of the antigens in questions 31-36, indicate if the antibody response was “Absent”, “Low”, “Normal”, or “Not Tested.”

Unconjugated pneumococcal polysaccharide

The term unconjugated indicates that the pneumococcal capsule contains polysaccharides without the modification of proteins added to the surface to enhance the immune response.

Specify the number of serotypes producing a protective level out of the total serotypes tested from the vaccine. For example, if the Pneumococcal 23-valent vaccine was used for the test, then report the number of reactive serotypes out of the 23 serotype total.

Conjugated pneumococcal polysaccharide

The term conjugated indicates that the pneumococcal capsule contains polysaccharides that have been conjugated with proteins to enhance the immune response.

Specify the number of serotypes producing a protective level out of the total serotypes tested from the vaccine.

Questions 39-46: Lymphocyte function

Lymphocyte function tests assess immune function by measuring immune cell responses to antigens and mitogens relative to control responses.

Specify the date of the most recent lymphocyte function assessment since the date of last report at question 39.

For each of the lymphocyte function tests listed in questions 40-45, indicate whether the lymphocyte response was “Absent (<10% of control)” “Low (10-30% of control)” “Normal (>30% of control)” or “Not tested.”

Natural killer cell function can be assessed by quantifying cytolysis of NK-sensitive target cells, e.g. K562. At question 46, indicate if NK cell function is “absent (≤10% of control),” “decreased (11-50% normal response),” “normal,” or “unknown.” Continue with question 47.

Question 47: Did a new malignancy, lymphoproliferative or myeloproliferative disorder appear that is
different from the disease for which the HSCT was performed?

Indicate whether a new or secondary malignancy, lymphoproliferative disorder, or myeloproliferative disorder has developed. If “yes” continue with question 48, if “no” continue with question 51. Do not report recurrence, progression, or transformation of the recipient's primary disease (disease for which the transplant was performed), or relapse of a prior malignancy.

Also report malignancy in the Form 2100 – 100 Days Post-HCT Data, Form 2200 – Six Months to Two Years Post-HCT Data, or Form 2300 – Yearly Follow-Up for Greater Than Two Years Post-HSCT Data.

Add additional instances for questions 48-50 to report more than one secondary malignancy. If submitting a paper form copy questions 48-50 and check the box corresponding to “Check here if additional pages are attached.”

Question 48: Specify second malignancy

Specify if the second malignancy was an “EBV-associated lymphoproliferative disorder” “other second malignancy” or “unknown.” If other malignancy is selected continue with question 49, otherwise continue with question 50 to specify the date of second malignancy diagnosis.

Question 49: Specify other second malignancy

The following should not be reported as new malignancy:

- Recurrence of primary disease
- Relapse of malignancy from recipient’s pre-HSCT medical history
- Breast cancer found in other (i.e., opposite) breast
- Post-HSCT cytogenetic abnormalities associated with the pre-HSCT diagnosis
- Transformation of MDS to AML post-HSCT

Continue with question 50 to specify the date of second malignancy diagnosis.

Question 50: Specify the date of diagnosis

Indicate the date of second malignancy diagnosis.
Q51-105: Clinical Status of Recipient Post-HCT

Question 51: Did the recipient experience any types of bleeding (since the date of last report)?

Due to WAS-associated thrombocytopenia, bleeding episodes are frequently observed. Indicate whether the recipient experienced any types of bleeding since the date of last report. If “yes” continue with question 52. If “no” continue with question 73.

Question 52: Is epistaxis present?

Indicate if epistaxis, bleeding from the nose, is present. If “yes” continue with question 53. If “no” continue with question 54.

Question 53: Is epistaxis prominent?

Indicate if epistaxis is prominent. A prominent feature is generally well documented, closely followed, and treated. Epistaxis may be recurrent, life-threatening, or require a transfusion. Continue with question 54.

Question 54: Is upper GI hemorrhage present?

Hemorrhage in the upper gastrointestinal tract includes bleeding that occurs above the duodenojejunal juncture of the small intestines. Signs of upper GI hemorrhage include vomiting blood (hematemesis) and black “tarry” stool (melena). As with other sources of blood loss, symptoms can include light headedness and fainting, weight loss, jaundice, and pain. Indicate if upper GI hemorrhage is present. If “yes” continue with question 55. If “no” continue with question 56.

Question 55: Is upper GI hemorrhage prominent?

Indicate if upper GI hemorrhage is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 56.

Question 56: Is lower GI hemorrhage/rectal bleeding present?

Hemorrhage in the lower gastrointestinal tract includes bleeding that occurs below the duodenojejunal juncture of the small intestines. Signs of lower GI hemorrhage include bright red blood in stool (hematochezia) and spontaneous rectal bleeding without defecation. Lower GI hemorrhage presents with symptoms similar to those associated with upper GI hemorrhage. Depending on the location and severity of hemorrhage, upper and lower GI bleeds may have similar presentations. Indicate if there is lower GI
hemorrhage/rectal bleeding present. If “yes” continue with question 57. If “no” continue with question 58.

**Question 57: Is lower GI hemorrhage/rectal bleeding prominent?**

Indicate if lower GI hemorrhage/rectal bleeding is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 58.

**Question 58: Is hemarthrosis present?**

Hemarthrosis refers to bleeding into joint spaces leading to swelling and pain. Suspected hemarthrosis is often confirmed with a joint aspiration. Indicate if hemarthrosis is present. If “yes” continue with question 59. If “no” continue with question 60.

**Question 59: Is hemarthrosis prominent?**

Indicate if bleeding into joint spaces is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 60.

**Question 60: Is hematuria present?**

Hematuria refers to blood in the urine and can be further specified as gross hematuria or microscopic hematuria. Gross hematuria is visibly noticeable while microscopic hematuria is only apparent when examined with a microscope. Hematuria may either be asymptomatic or be associated with symptoms such as painful urination and changes in urination frequency. Indicate if hematuria is present. If “yes” continue with question 61. If “no” continue with question 62.

**Question 61: Is hematuria prominent?**

Indicate if blood in the urine is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 62.

**Question 62: Is intracranial hemorrhage present?**

Intracranial hemorrhage involves bleeding within the cranium and may present with symptoms including nausea and vomiting, headache, and altered consciousness. CT scans and other imaging modalities are commonly used to visualize intracranial bleeding. Indicate if intracranial hemorrhage is present. If “yes” continue with question 63. If “no” continue with question 64.

**Question 63: Is intracranial hemorrhage prominent?**

Indicate if intracranial hemorrhage is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 64.
Question 64: Is oral bleeding present?
Indicate if oral bleeding is present. If “yes” continue with question 65. If “no” continue with question 66.

Question 65: Is oral bleeding prominent?
Indicate if oral bleeding is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 66.

Question 66: Is subcutaneous bleeding present?
Indicate if there is bleeding under the skin, commonly identified by bruising (petechiae, purpura, ecchymosis). If “yes” continue with question 67. If “no” continue with question 68.

Question 67: Is subcutaneous bleeding prominent?
Indicate if bleeding under the skin is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 68.

Question 68: Is subdural hematoma present?
The dura mater is the outermost membrane that encloses the brain and spinal cord, keeping in the cerebrospinal fluid. A subdural hematoma is a collection of blood below the dura mater. Subdural hematoma symptoms include: headache, decreased consciousness, and motor deficits. CT scans are commonly used to visualize subdural bleeding. Indicate if a subdural hematoma is present. If “yes” continue with question 69. If “no” continue with question 70.

Question 69: Is subdural hematoma prominent?
Indicate if subdural hematoma is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 70.

Question 70: Is other bleeding present?
Indicate if bleeding other than listed in questions 52-69 is present. If “yes” continue with questions 71 and 72. If “no” continue with question 73.

Question 71: Is other bleeding prominent?
Indicate if other bleeding is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 72.
Question 72: Specify other bleeding?

Specify the type of other bleeding indicated in question 70. Continue with question 73.

Question 73: Did the recipient experience any of the following autoimmune / inflammatory disorders (since the date of the last report)?

Due to aberrant lymphocyte function associated with WAS, autoimmune and inflammatory disorders are common. Indicate “yes” if the recipient experienced autoimmune / inflammatory disorder(s) and continue with questions 74-105 to further specify the disorder(s). If “no” continue with question 106.

Question 74: Is arthralgia present?

Indicate if the recipient experienced joint pain. If “yes” continue with question 75. If “no” continue with question 76.

Question 75: Is arthralgia prominent?

Indicate if arthralgia is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 76.

Question 76: Is chronic arthritis present?

Chronic arthritis refers to persistent joint inflammation, leading to pain, swelling, and stiffness often with reduced movement. Indicate if chronic arthritis is present. If “yes” continue with question 77. If “no” continue with question 78.

Question 77: Is chronic arthritis prominent?

Indicate if chronic arthritis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 78.

Question 78: Is autoimmune hemolytic anemia present?

Autoimmune hemolytic anemia refers to the destruction (hemolysis) of red blood cells by the recipient’s own immune system. Anemia results when the recipient’s marrow is unable to sufficiently produce replacement red blood cells. Laboratory studies are the most common method of disease detection, usually involving a complete blood cell count and peripheral blood smear. Indicate if autoimmune hemolytic anemia is present. If “yes” continue with question 79. If “no” continue with question 80.

Question 79: Is autoimmune hemolytic anemia prominent?

Indicate if autoimmune hemolytic anemia is prominent. A prominent feature is generally well documented,
closely followed, and treated. Continue with question 80.

**Question 80: Is idiopathic thrombocytopenic purpura (ITP) present?**

ITP refers to decreased platelet counts with normal bone marrow and the absence of other thrombocytopenia causes. Indicate if ITP is present. If “yes” continue with question 81, if “no” continue with question 82.

**Question 81: Is idiopathic thrombocytopenic purpura (ITP) prominent?**

Indicate if ITP is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 82.

**Question 82: Is inflammatory bowel disease present?**

Inflammatory bowel disease (IBD) is a general term referring to inflammation anywhere along the lining of the gastrointestinal tract. Ulcerative colitis and Crohn’s disease are the two major types of IBD and commonly manifest with abdominal cramping and abnormal bowel movements including constipation, diarrhea, and the passage of mucus and/or blood. Complete blood counts, stool studies, and serologic studies can be performed to better characterize symptoms and exclude other disorders on the differential diagnosis. Imaging studies, especially endoscopies are used to diagnosis and monitor IBD. Indicate if inflammatory bowel disease is present. If “yes” continue with question 83. If “no” continue with question 84.

**Question 83: Is inflammatory bowel disease prominent?**

Indicate if inflammatory bowel disease is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 84.

**Question 84: Is juvenile rheumatoid arthritis present?**

Juvenile rheumatoid arthritis is a condition of autoimmune joint inflammation causing joint pain, swelling, and stiffness, with childhood onset. Indicate if juvenile rheumatoid arthritis is present. If “yes” continue with question 85. If “no” continue with question 86.

**Question 85: Is juvenile rheumatoid arthritis prominent?**

Indicate if juvenile rheumatoid arthritis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 86.

**Question 86: Is nephritis present?**

Nephritis refers to inflammation of the kidneys and may be further specified based on the area of kidney
involvement and whether the inflammation is acute or chronic. Tests performed to assess and monitor kidney function include BUN and creatinine. In certain cases, a renal biopsy may be performed. Indicate if nephritis is present. If “yes” continue with question 87, if “no” continue with question 88.

**Question 87: Is nephritis prominent?**

Indicate if nephritis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 88.

**Question 88: Is neutropenia present?**

Neutropenia refers to a decreased number of neutrophils in the blood (ANC < 1.0 × 10^9/L). The risk of infection increases as the neutrophil count decreases. Indicate if the recipient is neutropenic. If “yes” continue with question 89, if “no” continue with question 90.

**Question 89: Is neutropenia prominent?**

Indicate if neutropenia is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 90.

**Question 90: Is sclerosing cholangitis present?**

Sclerosing cholangitis refers to inflammation and subsequent scarring and destruction of the bile ducts, eventually leading to liver damage. Imaging studies of the bile duct (cholangiography), as well as liver function tests such as aminotransferase and alkaline phosphatase are used to diagnose and monitor the disease. Indicate if sclerosing cholangitis is present. If “yes” continue with question 91, if “no” continue with question 92.

**Question 91: Is sclerosing cholangitis prominent?**

Indicate if sclerosing cholangitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 92.

**Question 92: Is cerebral vasculitis present?**

Vasculitis refers to inflammation of the vasculature, including both veins and arteries. Vasculitis may impact blood vessels of any size, from capillaries and arterioles to the great truncal vessels. It is typically caused by autoimmunity.

Cerebral vasculitis refers to inflammation involving vasculature of the brain. Indicate if the recipient had cerebral vasculitis. If “yes” continue with question 93, if “no” continue with question 94.
**Question 93: Is cerebral vasculitis prominent?**

Indicate if cerebral vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 94.

**Question 94: Is coronary vasculitis present?**

Coronary vasculitis refers to inflammation involving vasculature of the heart. Indicate if coronary vasculitis is present. If “yes” continue with question 95, if “no” continue with question 96.

**Question 95: Is coronary vasculitis prominent?**

Indicate if coronary vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 96.

**Question 96: Is renal vasculitis present?**

Renal vasculitis refers to inflammation involving vasculature of the kidney. Indicate if renal vasculitis is present. If “yes” continue with question 97, if “no” continue with question 98.

**Question 97: Is renal vasculitis prominent?**

Indicate if renal vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 98.

**Question 98: Is skin vasculitis present?**

Indicate if the recipient has inflammation involving vasculature of the skin. If “yes” continue with question 99, if “no” continue with question 100.

**Question 99: Is skin vasculitis prominent?**

Indicate if skin vasculitis is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 100.

**Question 100: Is other vasculitis present?**

Indicate if other types of vasculitis are present than those listed in questions 92-99. If “yes” continue with question 101, if “no” continue with question 103.

**Question 101: Is other vasculitis prominent?**

Indicate if other vasculitis is prominent. A prominent feature is generally well documented, closely followed,
and treated. Continue with question 102.

**Question 102: Specify other vasculitis**

Specify the other vasculitis indicated in question 100. Continue with question 103.

**Question 103: Is any other disorder present?**

Indicate if the recipient had an autoimmune / inflammatory disorder not listed in questions 74-105. If “yes” continue with question 104, if “no” continue with question 106.

**Question 104: Is any other disorder prominent?**

Indicate if the other disorder from question 103 is prominent. A prominent feature is generally well documented, closely followed, and treated. Continue with question 105.

**Question 105: Specify other disorder**

Specify the other disorder indicated in question 103. Continue with question 106.
Q106-167: Post-HCT Treatment for Wiskott-Aldrich Syndrome

Question 106: Was any treatment given for relapsed, persistent, or progressive disease (since the date of last report)?

Following transplant, additional therapy may be given for relapsed, persistent, or progressive disease. Low lymphocyte counts, new or persistent autoimmunity, or thrombocytopenia may require additional therapy to start to treat these features of WAS.

Indicate if any treatment was given since the date of last report for relapsed, persistent, or progressive disease. If “yes” continue with question 107, if “no” go to question 169.

Report immunosuppressive medications given to prevent or treat GVHD in the corresponding questions on the Form 2000 – Recipient Baseline Data, Form 2100 – 100 days Post-HCT Data, Form 2200 – Six Months to Two Years Post-HCT Data, or Form 2300 – Yearly Follow-Up for Greater Than Two Years Post-HCT Data.

Questions 107-166: Treatments

Indicate whether each of the therapies listed in questions 107-168 were given for relapsed, persistent, or progressive disease since the date of last report. If a therapy was given, indicate if that therapy was stopped; if “yes” specify the stopping date. Therapy paused for < 1 week should not be considered as “Therapy Stopped.”

Question 167: Did the recipient receive any other significant treatment(s) for WAS (since the date of last report)?

Indicate whether the recipient received other significant treatment, such as those with IL-2, gene therapy, or clinical trial therapies, for WAS.
Q169-174: Status of Hematologic Engraftment

This section refers to quantitative analyses utilizing discriminating DNA markers. Peripheral blood cells must undergo separation or sorting into T, B, or lymphoid vs. myeloid populations to perform this determination. If RFLP analyses indicate only donor type hematopoiesis, mark T-cell, B-cell, and myeloid as “predominately or completely donor.”

Also report chimerism in the Form 2100 – 100 Days Post-HCT Data or Form 2200 – Six Months to Two Years Post-HCT Data.

Status of hematologic engraftment is particularly important for WAS because persistent thrombocytopenia is associated with mixed whole blood or lymphocyte chimerism.

Questions 169-170: What is the current status of T-cell engraftment?

Reporting the T-cell engraftment requires that the sample is separated into sub-sets for chimerism analysis. T-cell subsets may be reported as CD3+ and CD4+ cells on the laboratory report.

If a T-cell chimerism was performed during the reporting period, indicate if the results showed:
• Predominantly or completely donor (≥80% donor chimerism)
• Mixed chimerism (5-80% donor)
• Only host T-cells detected (<5% donor)

Report the sample collection date for the most recent T-cell chimerism in question 170.

If a T-cell chimerism was not performed during the reporting period, report “unknown” and continue with question 171.

Questions 171-172: What is the current status of B-cell engraftment?

Reporting the B-cell engraftment requires that the sample is separated into sub-sets for chimerism analysis. B-cell subsets may be reported as CD19+ and CD20+ cells on the laboratory report.

If a B-cell chimerism was performed during the reporting period, indicate if the results showed:
• Predominantly or completely donor (≥80% donor chimerism)
• Mixed chimerism (5-80% donor)
• Only host B-cells detected (<5% donor)

Report the sample collection date for the most recent B-cell chimerism in question 172.
If a B-cell chimerism was not performed during the reporting period, report “unknown” and continue with question 173.

**Questions 173-174: What is the current status of myeloid engraftment?**

Reporting myeloid engraftment requires that the sample is separated into sub-sets for chimerism analysis. Myeloid subsets may be reported as CD15+ or CD33+ on the laboratory report.

If a myeloid chimerism was performed during the reporting period, indicate if the results showed:
- Predominantly or completely donor (≥80% donor chimerism)
- Mixed chimerism (5-80% donor)
- Only host cells detected (<5% donor)

Report the sample collection date for the most recent myeloid chimerism in question 174.

If a myeloid chimerism was not performed during the reporting period, report “unknown” and continue with the signature lines.

Following question 174, continue with "Signature Lines."
X-linked lymphoproliferative syndrome, also known as XLP or Duncan’s syndrome, is a rare inherited immunodeficiency. It is characterized by severe immune dysregulation, which generally manifests as an exaggerated immune response to infection. XLP belongs to the group of familial hemophagocytic lymphohistiocytosis syndromes. Patients typically present in childhood or early adolescence, often following infection with Epstein-Barr virus (which causes what is commonly known as “mono,” or infectious mononucleosis); up to 90% of XLP patients are seropositive for Epstein-Barr virus. Following the response to the pathogen, the exaggerated proliferation of T-cells, B-cells, and macrophages may clinically manifest as hemophagocytic lymphohistiocytosis (HLH), dysgammaglobulinemia, and/or lymphoma.

XLP is divided into two specific types that are characterized by their clinical presentation and associated genetic abnormalities. XLP1 is defined by the \textit{SH2D1A} mutation, which affects the signaling lymphocyte activation molecule (SLAM)-associated protein (SAP). XLP1 patients are more likely to present with fulminant infectious mononucleosis (FIM) and/or HLH following EBV, dysgammaglobulinemia, and/or lymphoma. Mutations in \textit{BIRC4}, also known as x-linked apoptosis inhibitor protein (XIAP), define XLP2. Patients with XLP2 tend to present with colitis and/or splenomegaly; they may also present following EBV infection with or without subsequent HLH. The common presentation of HLH following EBV suggests there may be a functional or molecular link between the SAP and XIAP proteins.


The X-Linked Lymphoproliferative Syndrome Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures XLP-specific pre-HCT data such as: the recipient’s clinical and genetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HCT treatments administered, and disease manifestations prior to the preparative regimen.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as “disorders of the immune system” and question 628 as X-Linked Lymphoproliferative Syndrome. Additional disease insert forms will be required if the recipient had lymphoma at the time of their XLP diagnosis or prior to the start of the preparative regimen.

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1.

If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than X-Linked Lymphoproliferative Syndrome), begin at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, check the indicator box and continue with question 52.

Q1-23: Disease Assessment at Diagnosis
Q24-32: History of Epstein Barr Virus (EBV) Infection
Q33-51: Assessment of Immunologic Function at Diagnosis
Q52-104: Disease Assessment between Diagnosis and the Start of the Preparative Regimen
Q105-130: Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.
<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
</tbody>
</table>
Q1-23: Disease Assessment at Diagnosis

Question 1: Is this recipient a registered participant in the United States Immunodeficiency Network (USIDNET)?

The United States Immunodeficiency Network (USIDNET) is a research consortium studying primary immune deficiencies. They maintain a registry of primary immunodeficiency patients and act as a resource for clinical and laboratory research. Indicate if the recipient is a registered participant in the USIDNET. If “yes,” continue with question 2. If “no,” continue with question 3.

Question 2: USIDNET ID

Report the recipient’s USIDNET participant identification number.

Question 3: What was the date of diagnosis?

X-linked lymphoproliferative syndrome (XLP) is characterized by multiple clinical, laboratory, and genetic features, rather than distinct pathological characteristics. Examples of testing done to confirm a diagnosis of XLP include peripheral blood sample analysis to determine the presence or absence of functional SH2D1A or BIRC4 proteins, or molecular testing for SH2D1A or BIRC4 mutations. The date of diagnosis should be the date of sample collection of last assessment used to establish a diagnosis of XLP. If there is a strong family history of XLP and no testing is done to confirm the diagnosis, report the recipient date of birth.

Question 4: Was genetic testing used to confirm the diagnosis?

X-linked lymphoproliferative syndrome is known to be an inherited disorder; for that reason, genetic testing is often done to confirm the diagnosis. If there is known family history of XLP, or the mother is a known carrier, genetic testing may be done prior to the onset of symptoms or even prenatally. The presence of SH2D1A (XLP1/XLP) or BIRC4 (XLP2/XIAP) mutations are associated with XLP. Other gene mutations may be present and should be reported even if their clinical significance is uncertain. Indicate if genetic testing was performed.

If genetic testing was performed, check “yes” and continue with question 5. If genetic testing was not done or it is unknown if genetic testing was performed, indicate “no” or “unknown” and continue with question 10.

Questions 5-8: Specify genetic mutation(s) present at diagnosis

If question 4 indicates that genetic testing was performed, each of questions 5-7 must be answered. Indicate “yes” if testing revealed the specified gene mutation; indicate “no” if testing was done but did not reveal the specified gene mutation. If testing for the specified gene mutation was not done or it is unknown if testing
was performed, specify this. Do not leave any response blank. If a genetic mutation was found that is best classified as “other mutation,” specify in question 8.

**Question 9: Was documentation submitted to the CIBMTR? (e.g., pathology report)**

Indicate if a copy of the genetic testing report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the genetic report. Attaching a copy of the report may prevent additional queries.

**Question 10: Was X-linked inheritance demonstrated in the recipient's maternal family members?**

X-linked patterns of inheritance are caused by genetic mutations carried on the X chromosome, which is a sex chromosome (allosome). Males normally carry one copy of the X chromosome and one copy of the Y chromosome. For this reason, a faulty X chromosome will affect all men who carry it, since it is the only X chromosome they can express; men will be symptomatic for x-linked recessive patterns of inheritance. X-linked traits cannot be passed from father to son (since the father will supply the son's Y chromosome). Women carry two copies of the X chromosome. This means they will be carriers for x-linked recessive traits, but will rarely be symptomatic since they will generally have a normal X chromosome that is expressed. (For x-linked dominant patterns of inheritance, only a single mutated X chromosome is necessary for symptomatic expression. Therefore, x-linked dominant patterns of inheritance affect both men and women.)

XLP follows an x-linked recessive pattern of inheritance. Indicate if the patient's maternal family members exhibit evidence of x-linked recessive inheritance; this would be shown by a brother, male maternal cousin, maternal uncle, and/or maternal grandfather being affected by the disease. Do not report “yes” based only on known carrier status in female family members. Specify “no” if the recipient's brother(s) and/or male cousin(s) all exhibit normal X chromosome expression (no evidence of disease). Indicate “unknown” if information is not available about the recipient’s family history or if the recipient is the only male child and does not have male maternal cousins.

**Specify if the following disorders were present at diagnosis**

XLP typically presents following an exaggerated response to Epstein-Barr virus. Other common clinical presentations of XLP are dysgammaglobulinemia and/or lymphoproliferative processes. Additional clinical manifestations may include a lesser response to EBV or other pathogen, cytopenias including aplastic anemia, autoimmune processes including vasculitis or psoriasis, lymphoma, and/or colitis. Specify if the recipient had any of the following at the time of diagnosis.

**Question 11: Aplastic anemia**

Aplastic anemia is a hematologic condition defined by peripheral blood cytopenia(s) and markedly hypocellular marrow with pancytopenia. Indicate if the patient had aplastic anemia at the time of XLP diagnosis.
**Question 12: Colitis**

Colitis refers to inflammation of the large intestine, often manifesting as diarrhea, abdominal pain and bloating, and melena (black “tarry” feces) or hematochezia (passage of fresh blood in feces). Indicate if the patient had colitis at the time of XLP diagnosis.

**Question 13: Epstein-Barr Virus (EBV) infection with evidence of Hemophagocytic Lymphohistiocytosis (HLH)**

Epstein-Barr viral infection is ubiquitous and rarely causes life-threatening complications. EBV generally infects the B-lymphocytes; however, in rare circumstances it may infect natural killer (NK) cells and T-lymphocytes. This unusual event is associated with aggressive lymphoproliferative manifestations, including hemophagocytic lymphohistiocytosis (HLH). HLH leads to an abnormal proliferation of macrophages and histiocytes, leading to the phagocytosis of healthy circulating blood cells. Indicate if the patient had evidence of HLH secondary to EBV at the time of diagnosis.

**Question 14: EBV infection without HLH**

EBV sensitivity is a common characteristic of XLP. The majority of patients present after acute EBV infection has caused an exaggerated response of the immune system and subsequent excessive proliferation of lymphocytes. Indicate if the patient had evidence of an EBV infection *without* HLH prior to or at time of diagnosis.

**Question 15: Hypogammaglobulinemia**

Hypogammaglobulinemia is a condition in which the body does not make enough antibodies or immunoglobulins. It is generally due to decreased numbers of B-lymphocytes. Indicate if the patient had hypogammaglobulinemia at the time of XLP diagnosis.

**Question 16: Lymphoproliferative disorder**

Various lymphoproliferative disorders caused by clonal lymphocyte proliferation may present with XLP due to the exaggerated, dysfunctional immune response caused by the disease. Examples of lymphoproliferative disorders include large granular lymphocytic leukemia (LGL) and lymphoplasmacytic lymphoma (also known as Waldenström’s macroglobulinemia). Indicate if the patient had a lymphoproliferative disorder *other than lymphoma* at the time of XLP diagnosis.

**Question 17: Lymphoma**

XLP is associated with a higher incidence of lymphoma, which may be secondary to EBV infection; however, not all lymphomas in the setting of XLP exhibit EBV clonality. There is speculation that lymphoma risk is increased secondary to aberrant invariant natural killer T-cell (iNKT), NK cell, and T-cell cytotoxic
function. The majority of lymphomas seen in XLP patients are T-cell lymphomas. Indicate if the patient had lymphoma at the time of XLP diagnosis. If yes, also complete Form 2018, Hodgkin and Non-Hodgkin Lymphoma Pre-HCT Data.

**Question 18: Psoriasis**

Psoriasis is an immune-mediated skin condition characterized by dry, thick patches of skin that are primarily red with silver-white scaling. Indicate if the patient had psoriasis at the time of XLP diagnosis.

**Question 19: Vasculitis**

Vasculitis refers to inflammation of the vasculature (blood vessels), including both veins and arteries. Vasculitis may impact blood vessels of any size, from capillaries and arterioles to the great truncal vessels. It is typically caused by autoimmunity. Indicate if the patient had vasculitis (any presentation) at the time of XLP diagnosis. If “yes,” continue with questions 20-23. Answer each of questions 20-22 and do not leave any response blank. If “no,” continue with question 24.

**Question 20: Central nervous system**

CNS vasculitis refers to inflammation of the vasculature of the brain and/or spinal cord. Indicate if the patient had CNS vasculitis.

**Question 21: Pulmonary system**

Pulmonary vasculitis involves inflammation of pulmonary vasculature. This can range from the great vessels, such as the pulmonary arteries, to the small alveolar capillaries. Indicate if the patient had pulmonary vasculitis.

**Question 22: Other vasculitis involvement**

Indicate if the patient had other vasculitis involvement. Specify involvement in question 23. Examples include systemic vasculitis, urticarial vasculitis, or gastrointestinal vasculitis.
Q24-32: History of Epstein Barr Virus (EBV) Infection

**Question 24: Is there a history of EBV infection?**

Epstein-Barr virus (EBV) is one of the human herpes viruses (Herpesviridae family). It is the virus that causes infectious mononucleosis, commonly referred to as “mono.” XLP may present as an exaggerated immune response to EBV; up to 90% of XLP patients have previously had an EBV exposure. Indicate if the recipient has a history of EBV infection, as identified by any method of detection. If the patient has not had exposure to EBV or did not have an evaluation of previous exposure, continue with question 33.

**Questions 25-27: Specify results used for diagnosis of EBV**

In situ hybridization refers to the use of a labeled viral probe to detect virus nucleic acids in tissue. Polymerase chain reaction (PCR) amplifies viral DNA to determine if the patient has a current primary infection or reactivation infection. Serologic testing may be used to determine the presence of EBV antigen or antibodies to EBV.

Report the method used to diagnose a current or latent EBV infection. Answer each of the questions 25-27 and do not leave any response blank. If serologic testing was used, continue with question 28. If serologic testing was not performed or was negative, continue with question 32.

**Questions 28-31: Specify [serologic] results**

Antibody titration to four EBV-specific markers can provide distinct information about whether a patient has a current primary or reactivated infection, recent infection, or past infection. Antibodies to EBV nuclear antigen (EBNA) are not seen during acute infection, but develop 2-4 months after the first presentation of infection and persist for life. Early antigen testing measures IgG antibodies to early antigen; this generally appears at acute onset and is only detectable for 3-6 months. Viral capsid IgG measures IgG antibodies to viral capsid antigen that appear 2-4 weeks after presentation and persist for life. Viral capsid IgM testing for IgM antibodies to viral capsid antigen indicates current or recent infection, as it is generally only detectable for 4-6 weeks following first presentation.

Specify each EBV serologic antibody test as “positive” or “negative” in questions 28-31. Do not leave any response blank unless testing failed, was inconclusive, or was not performed.

**Question 32: Was documentation submitted to the CIBMTR?**

Indicate if a copy of the EBV infection testing is attached. Use the Log of Appended Documents (Form
2800) to attach a copy of the laboratory report(s). Attaching a copy of the report may prevent additional queries.
Q33-51: Assessment of Immunologic Function at Diagnosis

Report findings from immune function studies at the time of diagnosis; if multiple studies were performed, report the initial values.

Question 33: NK cell function

Natural killer (NK) cells are cytotoxic lymphocytes implicated in viral response and tumor immunosurveillance. Patients with XLP often have normal numbers of NK cells, but the cells have functional defects. Indicate if the patient’s immune studies revealed absent (≤ 10% lower limit of normal), decreased (11-50% lower limit of normal), or normal (> 50% lower limit of normal) quantity of NK cells. If NK cell function was not assessed, indicate “not done.”

Questions 34-35: Invariant natural killer T-cells (iNKT)

Invariant natural killer T-cells (iNKT) are a subset of T-lymphocytes that have actions resembling mechanisms of both the innate and adaptive immune systems. They express T-cell receptors that act similarly to pattern-recognition receptors seen in the adaptive immune system. In terms of function, iNKT do not have a “memory” of previously seen antigens, similar to cells of the innate immune system. iNKT cells are absent in XLP patients with the SH2D1A mutation. Specify if iNKT quantification was “known” or “unknown.” If “known,” report the quantity of iNKT as cells/mm³ (or cells/µL) in question 35. If “unknown,” continue with question 36.

Questions 36-39: Mucosal-associated invariant T-cells (MAIT)

Mucosal-associated invariant T-cells (MAIT) are a subset of T-lymphocytes that act as part of the innate immune system. MAIT are decreased in XLP patients with the SH2D1A mutation. Specify if MAIT quantification was “known” or “unknown.” If “known,” report the quantity of MAIT as cells/mm³ (or cells/µL) in question 37; report the laboratory upper and lower limits of normal in questions 38-39 respectively. If “unknown,” continue with question 40.

Question 40: Signaling lymphocyte activation molecule (SLAM)-associated protein (SAP) expression

Signaling lymphocyte activation molecule-associated protein (SAP) is encoded for by SH2D1A and is expressed in T-cells and NK cells. SAP is implicated in the development of iNKT cells, as well as in the regulation of NK and T-lymphocytes. Indicate if SAP was or was not expressed. If protein expression was not evaluated, report “not done.”
Question 41: XIAP protein expression

X-linked inhibitor of apoptosis (XIAP) is encoded for by *BIRC4* and is part of an apoptosis inhibitor protein family. It is believed to be one of the more powerful inhibitors of apoptosis through its action blocking certain apoptosis cascade enzymes. Indicate if XIAP was or was not expressed. If protein expression was not evaluated, report “not done.”

Question 42: Did the recipient receive supplemental intravenous immunoglobulins (IVIG)?

IVIG is a product made from pooled human plasma that primarily contains IgG. It is used to provide immune-deficient recipients with antibody function to prevent infection.

Indicate whether the recipient received IVIG at diagnosis. If “yes,” continue with question 43. If “no,” continue with question 44.

Question 43: Was therapy ongoing within three months of immunoglobulin testing?

Indicate whether the recipient received IVIG within three months prior to the immunoglobulin testing done at diagnosis. Patients exhibiting signs of a compromised or dysfunctional immune system may have received IVIG prior to a diagnosis being made. If IVIG is given within three months of immunoglobulin testing, the IgG level would not represent the recipient’s native IgG.

Questions 44-45: IgG

Indicate whether IgG level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 45. If “unknown,” continue with question 46.

Questions 46-47: IgM

Indicate whether IgM level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 47. If “unknown,” continue with question 48.

Questions 48-49: IgA

Indicate whether IgA level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 49. If “unknown,” continue with question 50.

Questions 50-51: IgE

Indicate whether IgE level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value in question 51. If “unknown,” continue with question 52.
Q52-104: Disease Assessment between Diagnosis and the Start of the Preparative Regimen

Question 52: Was HLH present?

HLH is an abnormal proliferation of macrophages and histiocytes that leads to the phagocytosis of healthy circulating blood cells. Indicate if the patient developed HLH at any time after diagnosis but prior to the start of the preparative regimen; include HLH persisting from diagnosis. If “yes,” continue with question 53. If “no,” continue with question 89.

Question 53: Was the HLH triggered by an acute EBV infection?

HLH may present as an exaggerated response to EBV infection. Epstein-Barr viral infection is ubiquitous and rarely causes life-threatening complications. EBV generally infects the B-lymphocytes; however, in rare circumstances it may infect natural killer (NK) cells and T-lymphocytes. This unusual event is associated with aggressive lymphoproliferative manifestations, including hemophagocytic lymphohistiocytosis (HLH). Indicate if the patient’s HLH was associated with EBV infection. If “yes,” continue with question 63. If “no” or “unknown,” continue with question 54.

Question 54: Was the HLH triggered by any other known condition(s)?

HLH may also present as a response to malignancy or pathogen other than EBV. Indicate if the patient’s HLH was associated with another known condition. If “yes,” continue with question 55. If “no” or “unknown,” continue with question 63.

Questions 55-62: Specify other known condition(s)

Report condition or conditions believed to have triggered HLH. Each of the questions 55-58 and 61 must be answered as “yes” or “no”; do not leave any response blank. If the HLH was in response to a viral infection other than EBV, specify the virus in question 59. If it was a response to a virus not listed, specify in question 60. Questions 59-60 may be repeated to report multiple viral triggers. If the cause of HLH response is best classified as “other,” specify in question 62.

Questions 63-69: Specify site(s) where HLH was present

Indicate “yes” or “no” for each site specified in questions 63-68. Do not leave any response blank. If “yes” is indicated for “other site,” specify the site in question 69. At least one of questions 63-68 must be answered.
“yes.”

**Question 70: Was therapy given for HLH?**

Indicate if the recipient received treatment for HLH after the diagnosis and before the start of the preparative regimen. If “yes,” continue with question 71. If “no,” continue with question 89.

**Questions 71-72: Date therapy started**

Indicate “known” if the therapy start date is documented and specify the first date of therapy in question 72. If the date is unknown, indicate this and continue with question 73.

**Questions 73-74: Date therapy stopped**

Indicate “known” if the therapy stop date is documented and specify the date therapy stopped using question 74. If the patient received systemic therapy in cycles, specify the first day of the last cycle of systemic therapy. If the patient received a single line or single administration, indicate the last day therapy was administered.

If the date is unknown, indicate this and continue with question 75.

**Questions 75-88: Specify therapeutic agents**

Allogeneic stem cell transplant is considered the only curative treatment for XLP. However, therapeutic agents may be given in settings where allogeneic HCT is not a viable treatment option or to maintain the patient in the pre-transplant period. Therapy may vary depending on disease presentation. Most therapeutic agents given in the setting of XLP are intended to suppress the patient’s over-responsive, dysfunctional immune system. There is some evidence that cytotoxic therapy, particularly etoposide, may be beneficial in controlling lymphocyte proliferation. B-cell therapy, such as rituximab, may be given to treat EBV infection, since it generally infects B-lymphocytes. Other agents, such as IVIG, may be given to supplement the patient’s immune system and provide artificial immune response.

Indicate “yes” or “no” for each therapeutic agent listed. Do not leave any response blank. If the recipient received an agent that is not listed, check “yes” for “other systemic therapy” and use question 88 to specify the treatment.

**Question 89: Did colitis develop?**

Colitis refers to inflammation of the large intestine, often manifesting as diarrhea, abdominal pain and bloating, and melena or hematochezia. Indicate if the patient developed colitis at any time after diagnosis but prior to the start of the preparative regimen; include colitis persisting from diagnosis.
**Question 90: Did vasculitis develop?**

Vasculitis refers to inflammation of the vasculature, including both veins and arteries. Vasculitis may impact blood vessels of any size, from capillaries and arterioles to the great truncal vessels. It is typically caused by autoimmunity. Indicate if the patient had vasculitis (any presentation) at any time after diagnosis but prior to the start of the preparative regimen; include vasculitis persisting from diagnosis. If “yes,” continue with questions 91-94. Answer each of questions 91-93 and do not leave any response blank. If “no” or “unknown,” continue with question 95.

**Question 91: Central nervous system**

CNS vasculitis refers to inflammation of the vasculature of the brain and/or spinal cord. Indicate if the patient had CNS vasculitis at any time after diagnosis but prior to the start of the preparative regimen; include vasculitis persisting from diagnosis.

**Question 92: Pulmonary system**

Pulmonary vasculitis involves inflammation of pulmonary vasculature. This can range from the great vessels, such as the pulmonary arteries, to the small alveolar capillaries. Indicate if the patient had pulmonary vasculitis at any time after diagnosis but prior to the start of the preparative regimen; include vasculitis persisting from diagnosis.

**Question 93: Other vasculitis involvement**

Indicate if the patient had other vasculitis involvement. Specify involvement in question 94. Examples include systemic vasculitis, urticarial vasculitis, or gastrointestinal vasculitis at any time after diagnosis but prior to the start of the preparative regimen; include vasculitis persisting from diagnosis.

**Question 95: Did the recipient develop lymphoma?**

XLP is associated with a higher incidence of lymphoma, which may be secondary to EBV infection; however, not all lymphomas in the setting of XLP exhibit EBV clonality. There is speculation that lymphoma risk is increased secondary to aberrant iNKT, NK, and T-cell cytotoxic function. The majority of lymphomas seen in XLP patients are T-cell lymphomas. Indicate if the patient had lymphoma at any time after diagnosis but prior to the start of the preparative regimen. If the patient had lymphoma, continue with questions 96-98; also complete Form 2018, Hodgkin and Non-Hodgkin Lymphoma Pre-HCT Data.

**Question 96: Was the lymphoma associated with an EBV infection?**

Indicate if the patient’s lymphoma was associated with an EBV infection. If the patient’s EBV status was not assessed, indicate “unknown.”
Question 97: Is the tumor EBV positive?

If the patient’s lymphomatous tumor was evaluated for EBV clonality, indicate if it was or was not EBV positive. If the tumor was not evaluated for EBV clonality, indicate “unknown.”

Question 98: Was documentation submitted to the CIBMTR? (e.g., pathology report)

Indicate if a copy of the pathology report and/or immunohistochemistry results are attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the pathology and/or laboratory report(s). Attaching a copy of the report may prevent additional queries.

Question 99: Did the recipient develop hypogammaglobulinemia?

Hypogammaglobulinemia is a condition in which the body does not make enough antibodies or immunoglobulins. It is generally due to decreased numbers of B-lymphocytes. Indicate if the patient had hypogammaglobulinemia at any time after diagnosis but prior to the start of the preparative regimen; include hypogammaglobulinemia persisting from diagnosis.

Question 100: Did the recipient develop aplastic anemia?

Aplastic anemia is a hematologic condition defined by peripheral blood cytopenia(s) and markedly hypocellular marrow with pancytopenia. Indicate if the patient had aplastic anemia at any time after diagnosis but prior to the start of the preparative regimen; include aplastic anemia persisting from diagnosis.

Questions 101-104: Specify therapy given for aplastic anemia

Indicate therapies the recipient received for aplastic anemia after the time of diagnosis and before the start of the preparative regimen. Each of questions 101-103 should be answered as “yes” or “no”; do not leave any response blank. If therapy is best categorized as “other therapy,” specify in question 104.
**Q105-130: Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen**

**Question 105: Specify the status of HLH**

If the patient previously had HLH at any time during their disease course, specify if it was “active” or “inactive” (quiescent) at the last evaluation prior to the start of the preparative regimen. If the patient never had HLH at any time during their disease course, indicate “not applicable.”

**Question 106: Was colitis active?**

If the patient previously had colitis at any time during their disease course, specify if it was active at last evaluation prior to the start of the preparative regimen. If the colitis was inactive, status of colitis is unknown, or the patient never had colitis at any time during their disease course (not applicable), continue with question 108.

**Question 107: Was the recipient receiving therapy for colitis?**

Indicate if the patient was receiving treatment for active colitis at time of last evaluation prior to the start of the preparative regimen.

**Question 108: Was the CNS vasculitis active?**

If the patient previously had CNS vasculitis at any time during their disease course, specify if it was active at last evaluation prior to the start of the preparative regimen. If the CNS vasculitis was inactive, status of CNS vasculitis is unknown, or the patient never had CNS vasculitis at any time during their disease course (not applicable), continue with question 110.

**Question 109: Was the recipient receiving therapy for CNS vasculitis?**

Indicate if the patient was receiving treatment for active CNS vasculitis at time of last evaluation prior to the start of the preparative regimen.

**Question 110: Was pulmonary vasculitis active?**

If the patient previously had pulmonary vasculitis at any time during their disease course, specify if it was active at last evaluation prior to the start of the preparative regimen. If the pulmonary vasculitis was inactive, status of pulmonary vasculitis is unknown, or the patient never had pulmonary vasculitis at any time during their disease course (not applicable), continue with question 112.
**Question 111: Was the recipient receiving therapy for pulmonary vasculitis?**

Indicate if the patient was receiving treatment for active pulmonary vasculitis at time of last evaluation prior to the start of the preparative regimen.

**Question 112: Was the other vasculitis active?**

If the patient previously had other vasculitis at any time during their disease course, specify if it was active at last evaluation prior to the start of the preparative regimen. If the other vasculitis was inactive, status of other vasculitis is unknown, or the patient never had other vasculitis at any time during their disease course (not applicable), continue with question 114.

**Question 113: Was the recipient receiving therapy for other vasculitis?**

Indicate if the patient was receiving treatment for active other vasculitis at time of last evaluation prior to the start of the preparative regimen.

Specify the clinical and laboratory features assessed at last evaluation prior to the preparative regimen: These questions are intended to determine the immunological status of the recipient prior to the preparative regimen. Testing may be performed multiple times within the pre-transplant work-up period (approximately 30 days) prior to the start of the preparative regimen; report the most recent laboratory value. Laboratory values obtained on the first day of the preparative regimen may be reported as long as the sample was taken before any radiation or systemic therapy was administered.

**Questions 114-116: Serum ferritin**

Indicate whether serum ferritin level was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the value and unit of measure documented on the laboratory report in question 115; indicate the date sample was collected in question 116. If “unknown,” continue with question 117.

**Questions 117-119: Soluble interleukin-2 receptor (sIL-2R)**

Indicate whether soluble interleukin-2 receptor levels were “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the value and unit of measure documented on the laboratory report in question 118; indicate the date sample was collected in question 119. If “unknown,” continue with question 120.

**Questions 120-122: Triglycerides**

Indicate whether triglyceride levels were “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the value and unit of measure documented on the laboratory report
in question 121; indicate the date sample was collected in question 122. If “unknown,” continue with question 123.

Questions 123-125: Fibrinogen antigen assay (factor I; fibrinogen activity; functional fibrinogen; fibrinogen antigen)

Indicate whether fibrinogen antigen levels were “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the value and unit of measure documented on the laboratory report in question 124; indicate the date sample was collected in question 125. If “unknown,” continue with question 126.

Question 126: Bone marrow aspirate/biopsy evidence of hemophagocytosis

Bone marrow aspirate and biopsy evidence of hemophagocytosis typically includes hypercellularity with markedly increased histiocytes and cytotoxic T-cells. Indicate if the pathologist interpretation of the marrow indicated the presence or absence of findings consistent with hemophagocytosis. If bone marrow evaluation was not performed, indicate “not done.”

Questions 127-128: Specify the cerebrospinal fluid (CSF) findings

Indicate if protein and WBC count were elevated or normal in questions 127 and 128, respectively. If CSF evaluation was not performed, indicate “not done.”

Question 129: Was donor testing for XLP done prior to HCT?

Indicate if the donor was tested for XLP during their donor selection work-up. This is most applicable for related male donors. If the donor was tested, continue with question 130. If the donor was not tested for XLP or testing is not applicable because the donor is unrelated or female, continue with the signature section.

Question 130: Was there evidence of XLP?

Indicate if testing revealed evidence of XLP in the donor.
2134: XLP Post-HCT

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as “disorders of the immune system” and question 628 as X-Linked Lymphoproliferative Syndrome. The X-Linked Lymphoproliferative Syndrome Post-HCT Data Form (Form 2134) must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, 2300) completed. The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200, between the date of contact for the six-month follow up and the date of contact for the one-year follow up for Form 2200, etc.).

Q1-19: Disease Assessment Since the Date of Last Report
Q20-30: Current Assessment of Immunologic Function Post-HCT
Q31-41: Laboratory Studies at the Time of Evaluation for This Reporting Period

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/24/17</td>
<td>Comprehensive Disease-Specific Manuals</td>
<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
</tbody>
</table>
Q1-19: Disease Assessment Since the Date of Last Report

Question 1: Did the recipient have lymphoma at the time of HCT?

XLP is associated with a higher incidence of lymphoma, which may be secondary to EBV infection; however, not all lymphomas in the setting of XLP exhibit EBV clonality. There is speculation that lymphoma risk is increased secondary to aberrant invariant natural killer T-cell (iNKT), NK, and T-cell cytotoxic function. The majority of lymphomas seen in XLP patients are T-cell lymphomas.

Specify if the patient had lymphoma at the time of transplant. If “yes,” continue with question 3; if “no,” continue with question 2.

Question 2: Did the recipient develop lymphoma or have persistent disease since the date of last report?

Indicate if the patient developed lymphoma during the reporting period or had persistent lymphoma carrying over from a previous reporting period. If “yes,” continue with question 3. If “no,” continue with question 4.

Question 3: Specify current status of lymphoma

Report the status of the patient’s lymphoma at last assessment during the reporting period. Disease response criteria are defined in Table 1 below.

Table 1. Lymphoma Disease Response Definitions

<table>
<thead>
<tr>
<th>Disease Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Remission (CR)</td>
<td>Complete disappearance of all known disease for ≥ 4 weeks</td>
</tr>
<tr>
<td>Partial Remission (PR)</td>
<td>≥ 50% reduction in greatest diameter of all sites of known disease and no new sites of disease</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>&lt;50% reduction in greatest diameter of all sites of known disease</td>
</tr>
<tr>
<td>Progressive Disease (PD)</td>
<td>Increase in size of known disease or new sites of disease</td>
</tr>
<tr>
<td>Not Assessed</td>
<td>No assessment of patient’s disease during reporting period; this would indicate an absence of radiology or physical examination</td>
</tr>
<tr>
<td>-------------</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Unknown</td>
<td>Disease assessment was performed but is insufficient to determine disease status or results of evaluation(s) unknown or it is unknown if evaluations were performed</td>
</tr>
</tbody>
</table>

**Question 4: Did colitis persist or develop since the date of the last report?**

Colitis refers to inflammation of the large intestine, often manifesting as diarrhea, abdominal pain and bloating, and melena (black “tarry” feces) or hematochezia (passage of fresh blood in feces).

Specify if the patient had colitis develop during the reporting period or persist from a previous reporting period. If “yes,” continue with question 5. If “no” or “unknown,” continue with question 7.

**Question 5: What is the status of colitis?**

Specify if colitis was active at the last assessment during the reporting period.

**Question 6: Was the recipient receiving therapy for colitis?**

Indicate if the patient received treatment for colitis at any time during the reporting period.

**Question 7: Did vasculitis persist or develop since the date of the last report?**

Vasculitis refers to inflammation of the vasculature (blood vessels), including both veins and arteries. Vasculitis may impact blood vessels of any size, from capillaries and arterioles to the great truncal vessels. It is typically caused by autoimmunity. If “yes,” continue with question 8. If “no” or “unknown,” continue with question 18.

**Question 8: Central nervous system**

CNS vasculitis refers to inflammation of the vasculature of the brain and/or spinal cord.

Specify if the patient had CNS vasculitis develop during the reporting period or persist from a previous reporting period. If “yes,” continue with question 9. If “no,” continue with question 11.

**Question 9: What is the status of the CNS vasculitis?**

Specify if CNS vasculitis was active at the last assessment during the reporting period.

**Question 10: Was the recipient receiving therapy for CNS vasculitis?**

Indicate if the patient received treatment for CNS vasculitis at any time during the reporting period.
Question 11: Pulmonary system

Pulmonary vasculitis involves inflammation of pulmonary vasculature. This can range from the great vessels, such as the pulmonary arteries, to the small alveolar capillaries.

Specify if the patient had pulmonary vasculitis develop during the reporting period or persist from a previous reporting period. If “yes,” continue with question 12. If “no,” continue with question 14.

Question 12: What is the status of the pulmonary vasculitis?

Specify if pulmonary vasculitis was active at the last assessment during the reporting period.

Question 13: Was the recipient receiving therapy for pulmonary vasculitis?

Indicate if the patient received treatment for pulmonary vasculitis at any time during the reporting period.

Questions 14-15: Other vasculitis involvement

Indicate if the patient had other vasculitis involvement. Specify involvement in question 15.

Question 16: What is the status of other vasculitis?

Specify if other vasculitis was active at the last assessment during the reporting period.

Question 17: Was the recipient receiving therapy for other vasculitis?

Indicate if the patient received treatment for other vasculitis at any time during the reporting period.

Question 18: Did the recipient have hemophagocytic lymphohistiocytosis (HLH) prior to transplant or did it present since the date of last report?

HLH is an abnormal proliferation of macrophages and histiocytes that leads to the phagocytosis of healthy circulating blood cells.

Indicate if the patient had HLH prior to transplant or developed HLH during the reporting period. If “yes,” continue with question 19. If “no,” continue with question 20.

If the recipient had HLH in the previous reporting period, but there was no evidence of HLH during the current reporting period, select “no.”

Question 19: Specify the status of the HLH disease since the date of last report

Specify if HLH was active or inactive (quiescent) at the last assessment during the reporting period.
Q20-30: Current Assessment of Immunologic Function Post-HCT

Question 20: Did the recipient receive supplemental intravenous immunoglobulins (IVIG)?

IVIG is a product made from pooled human plasma that primarily contains IgG. It is used to provide immunodeficient recipients with antibody function to prevent infection.

Indicate whether the recipient received IVIG during the reporting period. If “yes,” continue with question 21. If “no,” continue with question 22.

Question 21: Was therapy ongoing within three months of immunoglobulin testing?

Indicate whether the recipient received IVIG within three months prior to the immunoglobulin testing done during the reporting period. If IVIG was given within three months of the immunoglobulin testing, the IgG level would not represent the recipient’s native IgG. If “yes,” continue with question 24. If “no,” continue with question 22.

Questions 22-23: IgG

Indicate whether IgG level was “known” or “unknown” during the reporting period. If “known,” report the laboratory value and unit of measure in question 23; if multiple tests were done, report the latest. If “unknown,” continue with question 24.

Questions 24-25: IgM

Indicate whether IgM level was “known” or “unknown” during the reporting period. If “known,” report the laboratory value and unit of measure in question 25; if multiple tests were done, report the latest. If “unknown,” continue with question 26.

Questions 26-27: IgA

Indicate whether IgA level was “known” or “unknown” during the reporting period. If “known,” report the laboratory value and unit of measure in question 27; if multiple tests were done, report the latest. If “unknown,” continue with question 28.

Questions 28-29: IgE

Indicate whether IgE level was “known” or “unknown” during the reporting period. If “known,” report the laboratory value in question 29; if multiple tests were done, report the latest. If “unknown,” continue with
question 30.

**Question 30: NK cell function**

Natural killer (NK) cells are cytotoxic lymphocytes implicated in viral response and tumor immunosurveillance. Patients with XLP often have normal numbers of NK cells, but the cells have functional defects. Indicate if the patient’s immune studies revealed absent (≤ 10% lower limit of normal), decreased (11-50% lower limit of normal), or normal quantity of NK cells (> 50% lower limit of normal); if multiple NK studies were performed during the reporting period, report the latest results. If NK cell function was not assessed during the reporting period, indicate “unknown.”
Q31-41: Laboratory Studies at the Time of Evaluation for This Reporting Period

Questions 31-32: Serum ferritin

Indicate whether serum ferritin level was “known” or “unknown” during the reporting period. If “known,” report the value and unit of measure documented on the laboratory report in question 32. If there are multiple values from the reporting period, report the latest. If “unknown,” continue with question 33.

Questions 33-34: Soluble interleukin-2 receptor (sIL-2R)

Indicate whether soluble interleukin-2 receptor levels were “known” or “unknown” during the reporting period. If “known,” report the value and unit of measure documented on the laboratory report in question 34. If there are multiple values from the reporting period, report the latest. If “unknown,” continue with question 35.

Questions 35-36: Triglycerides

Indicate whether triglyceride levels were “known” or “unknown” during the reporting period. If “known,” report the value and unit of measure documented on the laboratory report in question 36. If there are multiple values from the reporting period, report the latest. If “unknown,” continue with question 37.

Questions 37-38: Fibrinogen antigen assay (factor 1; fibrinogen activity; functional fibrinogen; fibrinogen antigen)

Indicate whether fibrinogen antigen levels were “known” or “unknown” during the reporting period. If “known,” report the value and unit of measure documented on the laboratory report in question 38. If there are multiple values from the reporting period, report the latest. If “unknown,” continue with question 39.

Question 39: Bone marrow aspirate/biopsy evidence of hemophagocytosis

Bone marrow aspirate and biopsy evidence of hemophagocytosis typically includes hypercellularity with markedly increased histiocytes and cytotoxic T-cells. Indicate if the pathologist interpretation of the marrow indicated the presence or absence of findings consistent with hemophagocytosis. If multiple evaluations were done during the reporting period, report the data from the latest. If bone marrow evaluation was not performed during the reporting period, indicate “not done.”

Questions 40-41: Specify the cerebrospinal fluid (CSF) findings

Indicate if protein and WBC count were elevated or normal in questions 40 and 41, respectively. If multiple
evaluations were done during the reporting period, report the data from the latest. If CSF evaluation was not performed during the reporting period, indicate “not done.”
Hemophagocytic Lymphohistiocytosis (HLH) is a rare condition characterized by immune dysregulation, which generally manifests as an exaggerated immune response to a trigger (such as infection). Based on genetics and family history, the disease is divided into “primary” and “secondary” HLH. Those with a genetic component or clear family history are classified as “primary” and have “familial hemophagocytic lymphohistiocytosis” (FHL). Subtypes of FHL are numbered one through five. They are often diagnosed in infancy with molecular, hematologic, and clinical assessments. Those who are diagnosed as older children or adults have “secondary” HLH and may not have a genetic component or family history of the disease. HLH may be triggered by an infection, malignancy, or other autoimmune condition. Manifestations of HLH include prolonged fever, hepatosplenomegaly, bleeding, skin rash, central nervous system (CNS) abnormalities (such as seizures), jaundice, cytopenia(s), coagulopathy, hyperlipidemia, hypofibrinogenemia, hyperferritinemia, transaminitis, hyperbilirubinemia, hypoalbuminemia, and hyponatremia.


2039: Hemophagocytic Lymphohistiocytosis Pre-HCT
2139: Hemophagocytic Lymphohistiocytosis Post-HCT
2039: HLH Pre-HCT

The Hemophagocytic Lymphohistiocytosis Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures HLH-specific Pre-HCT data such as the disease assessment, clinical and laboratory features at diagnosis, history of infection, pre-transplant therapy, and clinical and laboratory studies prior to the start of the preparative regimen.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as “histiocytic disorders” and question 635 as “hemophagocytic lymphohistiocytosis (HLH).”

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior HCT or prior HCT was autologous with no consent), select “no” and begin at question 1.

If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than HLH), select “no” and begin at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, select “yes” and continue with question 108.

Q1-22: Disease Assessment at Diagnosis
Q23-47: Clinical Features and Laboratory Studies at Diagnosis
Q48-58: Disease Assessment Between Diagnosis and the Start of the Preparative Regimen
Q59-74: History of Infection at Any Time Prior to the Preparative Regimen
Q75-107: Pre-HCT Therapy
Q108-127: Clinical Features and Laboratory Studies At Last Evaluation Prior to the Start of the Preparative Regimen

Manual Updates:
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Q1-22: Disease Assessment at Diagnosis

**Question 1: Is this recipient a registered participant in the United States Immunodeficiency Network (USIDNET)?**

The United States Immunodeficiency Network (USIDNET) is a research consortium studying primary immune deficiencies. They maintain a registry of primary immunodeficiency patients and act as a resource for clinical and laboratory research. Indicate if the recipient is a registered participant in the USIDNET. If “yes,” continue with question 2. If “no,” continue with question 3.

**Question 2: USIDNET ID:**

Report the recipient's USIDNET participant identification number.

**Question 3: What was the date of diagnosis?**

Diagnosis is based on molecular OR diagnostic criteria below:\(^1\)\(^2\)

**Molecular Diagnosis**

A diagnosis consistent with HLH:

- *PRF1*
- *UNC13D*
- *STX11*
- *STXBP2*
- *BIRC4*
- *ITK*

**OR**

**Diagnostic Criteria**

Meets diagnostic criteria for HLH (5 of 8 criteria below):

- Fever
- Splenomegaly
- Cytopenias (affecting ≥ 2 of 3 lineages in the peripheral blood)
- Hemoglobin < 90 g/L (9.0 g/dL) (in infants < 4 weeks: hemoglobin < 100 g/L (10.0 g/dL))
- Platelets < 100 \times 10^9/L
- Absolute neutrophil count < 1.0 \times 10^9/L
  - Hypertriglyceridemia and/or hypofibrinogenemia:
    - Fasting triglycerides ≥ 3.0 mmol/L (265 mg/dL)
    - Fibrinogen ≤ 1.5 g/L
  - Hemophagocytosis in bone marrow, spleen, or lymph nodes
  - Low or absent NK-cell activity (according to local laboratory reference)
  - Ferritin ≥ 500 μg/L
  - Soluble CD25 (soluble IL-2 receptor) ≥ 2,400 U/mL


HLH is characterized by multiple clinical, laboratory, and genetic features, rather than distinct pathological characteristics. Examples of testing done to confirm a diagnosis of HLH include molecular analysis to determine defects in PRF1, UNC13D, STX11, STXBP2, and ITK genes. In situations where molecular testing did not result in diagnosis, the date of diagnosis should be the date the sample was collected for the last assessment used to establish a diagnosis of HLH (i.e., the 5th criteria that establishes 5 of 8 diagnostic criteria are met, in the absence of molecular marker). If there is a strong family history of HLH and no testing was done to confirm the diagnosis, report the recipient's date of birth as the date of diagnosis.

**Questions 4-10: Is there a family history of hemophagocytic disorders?**

Indicate if there is a family history of hemophagocytic disorders. Family history includes the recipient’s biological aunts, uncles, cousins, and/or siblings. If there is a family history of hemophagocytic disorders, indicate “yes” and continue with questions 5-10. In questions 5-9, indicate the biological family member(s) that were affected by the hemophagocytic disorder. Indicate “yes” or “no” for each member listed, leaving no question blank. If a biological family relationship is not listed, select “other family member” in question 9 and specify the relationship in question 10.

If there is no family history of hemophagocytic disorders, select “no” and continue with question 11. If it is unknown if there is a family history of hemophagocytic disorders, indicate “unknown” and continue with question 11.
Question 11: Is there a family history of consanguinity (inter-familial marriage/descent from common ancestors)?

Consanguinity describes a relationship between people who share common ancestors (i.e., are “blood-relatives”). Indicate if the there is a family history of consanguinity in the direct ancestry of the recipient. This includes the recipient’s parents, grandparents, great-grandparents, etc. Indicate “yes” if there is a known history of consanguinity. Indicate “no” if there is no family history of consanguinity. Indicate “unknown” if the family history is not known.

Question 12: Was genetic testing used to confirm the diagnosis?

Genetic testing includes molecular methods to detect mutations characteristic of the disease. Genetic mutations for HLH include Perforin deficiency (PRF1) MUNC 13-4 (UNC13D), Syntaxin 11 (STX11), Munc 13-2 (STXBP2), and IL-2 inducible T-cell kinase (ITK). Indicate if genetic testing was performed to confirm the diagnosis. If “yes,” continue with question 13. If “no,” continue with question 20. If it is unknown if genetic testing was performed to confirm the diagnosis, indicate “unknown” and continue with question 20.

Questions 13-19: Specify genetic mutation(s) identified:

For each genetic mutation listed, indicate if the mutation was identified. If the genetic test was performed and the mutation was present, indicate “Yes.” If the genetic analysis was performed, but the mutation was absent, indicate “No.” If it is unknown if the test for the genetic mutation was performed or if the results are unknown, indicate “unknown.” If the test was not done for the genetic mutation, select “not done.” Do not leave any of the questions blank. If a test for a different mutation was performed, indicate the results of the test in question 18 and specify the other mutation in question 19. If no testing was done for mutations other than those already listed, select “not done” for question 18.

Question 20: Were central nervous system (CNS) abnormalities found on computed tomography (CT or CAT) or magnetic resonance imaging (MRI) scans?

Indicate if radiology (CT, CAT, and/or MRI) performed on the recipient detected any abnormalities in the central nervous system (brain and spinal cord) at the time of diagnosis. CNS abnormalities may include lesions, leptomeningeal enhancements, or edema.\(^3\)

If the recipient did have CNS abnormalities found on imaging at diagnosis, select “yes” and continue with question 21. If the recipient did not have CNS abnormalities detected by imaging, select “no” and continue with question 23. If it is unknown if the recipient had imaging done or if the results of imaging studies are not known, select “unknown” and continue with question 23.

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**Question 21: Date scan was performed:**

Enter the date the radiological assessment was performed.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

**Question 22: Was documentation submitted to the CIBMTR?**

Indicate if a copy of the CT, CAT, or MRI scan(s) is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of CT, CAT, or MRI report(s). Attaching a copy of the report may prevent additional queries.
Q23-47: Clinical Features and Laboratory Studies at Diagnosis

Question 23: Anemia (Hgb < 9 g/dL):
Indicate if the recipient had anemia at diagnosis or prior to the start of treatment for HLH. Anemia is defined as hemoglobin less than 9 g/dL. Select “yes,” “no,” or “unknown.”

Question 24: Degranulation assay of NK cells (as defined by local laboratory):
Degranulation in natural killer (NK) cells is the process by which NK cells release granules containing chemicals (perforin and granzymes) that are used to destroy targeted cells. In some subtypes of FHL (FHL3, 4, and 5), degranulation of NK cells is absent or abnormally low. A granule release assay (GRA) can be used to assess the degranulation indirectly by measuring the expression of CD107a on the cell surface following stimulation. ¹ This expression is only detectable when the granules fuse with the cell membrane, thus the absence of CD107a by GRA would indicate a defect in some part of NK degranulation. Indicate if the results of the degranulation assay of NK cells were “normal,” “abnormal,” or “unknown” at diagnosis.


Question 25: Fever (> 38.5° C or > 101.3° F for > 7 days within 1 week of diagnosis):
Indicate if the recipient had fever at diagnosis for HLH. The fever should last more than 7 days and be within 1 week of diagnosis. Fever is defined as a temperature above 38.5° C (101.3° F) for more than 7 days within 1 week of diagnosis. Select “yes,” “no,” or “unknown.”

Question 26: Hepatomegaly (liver edge palpable > 3 cm below right costal margin):
Indicate if the recipient had hepatomegaly (enlargement of the liver) at diagnosis or prior to the start of treatment for HLH. Hepatomegaly is defined by the palpability of the liver edge 3 cm or more below the right costal margin. Indicate “yes,” “no,” or “unknown.”
Questions 27-28: Serum ferritin:
Indicate if the serum ferritin level was known at diagnosis or prior to the start of treatment for HLH. If “known,” indicate the value in question 28. If “unknown,” continue with question 29.

Questions 29-30: Triglycerides:
Indicate if the triglyceride level was known at diagnosis or prior to the start of treatment for HLH. If “known,” indicate the value in question 30. If “unknown,” continue with question 31.

Questions 31-32: Fibrinogen antigen assay (factor I; fibrinogen activity; functional fibrinogen; fibrinogen antigen):
Fibrinogen levels may be low in patients with HLH. Indicate if a fibrinogen antigen assay (factor I; fibrinogen activity; functional fibrinogen; fibrinogen antigen) level was known at diagnosis or prior to the start of treatment for HLH. If “known,” indicate the value (and corresponding unit) in question 32. If “unknown,” continue with question 33.

Question 33: NK cell function:
NK cell function is measured by a cytotoxicity assay. NK cell function (cytotoxicity) may be absent or reduced in those with HLH. Indicate the NK cell function at diagnosis or prior to the start of treatment for HLH; select “absent (≤ 10% lower limit of normal),” “decreased (11-50% lower limit of normal),” “normal,” or “unknown.”

Question 34: Neutropenia (ANC < 1.0 × 10^9/L):
Indicate if the recipient was neutropenic at diagnosis or prior to the start of therapy for HLH. Neutropenia is defined as an absolute neutrophil count (ANC) less than 1.0 × 10^9/L. Indicate “yes,” “no,” or “unknown.”

Question 35: Soluble interleukin-2 receptor alpha chain (sCD25): (As defined by local laboratory)
The presence of soluble interleukin-2 receptors (soluble IL-2R, sCD25) in the plasma indicates the activation of T cells. Elevated soluble IL-2R is indicative of prolonged T-cell activation, indicating a protracted immune response. Levels of soluble IL-2R differ based on age, so using age-based reference ranges is helpful to identify abnormal results. Indicate the soluble IL-2R alpha chain level at diagnosis or prior to the start of therapy for HLH. The results of the test should be reported as defined by the local laboratory. Indicate if the soluble IL-2R alpha chain level was “normal,” “elevated,” or “unknown.”

Question 36: Splenomegaly (spleen palpable > 3 cm below left costal margin):

Indicate if the recipient had splenomegaly (enlargement of the spleen) at diagnosis or prior to the start of treatment for HLH. Splenomegaly is defined by the palpability of the spleen edge 3 cm or more below the left costal margin. Indicate “yes,” “no,” or “unknown.”

Question 37: Thrombocytopenia (platelets < 100 × 10^9/L):

Indicate if the recipient was thrombocytopenic at diagnosis or prior to the start of therapy for HLH. Thrombocytopenia is defined as a platelet count less than 100 × 10^9/L. Indicate “yes,” “no,” or “unknown.”

Question 38: Neopterin level:

The measurement of neopterin in the cerebrospinal fluid (CSF) is useful to determine immune system activity. Indicate the neopterin level in the CSF at diagnosis or prior to the start of therapy for HLH. Indicate “normal” or “elevated.” “Elevated” indicates levels above the upper limit of normal for the laboratory processing the specimen. If an assessment of neopterin levels in the CSF was not done at diagnosis or prior to the start of therapy for HLH, select “not done.”

Question 39: Protein:

Indicate the protein level in the cerebrospinal fluid (CSF) at diagnosis or prior to the start of therapy for HLH. Indicate “normal” or “elevated.” “Elevated” indicates levels above the upper limit of normal for the laboratory processing the specimen. If an assessment of protein levels in the CSF was not done at diagnosis or prior to the start of therapy for HLH, select “not done.”

Question 40: WBC count:

Indicate the WBC count in the cerebrospinal fluid (CSF) at diagnosis or prior to the start of therapy for HLH. Indicate “normal” if there were less than or equal to 5 cells/μL in the CSF. Indicate “elevated” if there were greater than 5 cells/μL in the CSF. If an assessment of WBC count in the CSF was not done at diagnosis or prior to the start of therapy for HLH, select “not done.”

Questions 41-47: Specify the site(s) where hemophagocytosis was documented at diagnosis:

Indicate the site(s) where hemophagocytosis was present at diagnosis or prior to the start of any therapy for HLH. Hemophagocytosis is the process in which a phagocyte engulfs red blood cells, white blood cells, or platelets. Hemophagocytosis is a characteristic of HLH, but does not need to be present for diagnosis; it is one of eight criteria of which five must be met. Select “yes” or “no” for each question, ensure that no question is left blank. If a site is not listed but hemophagocytosis was present, select “yes” for question 46.
(“other site”) and specify the site using question 47.
Q48-58: Disease Assessment Between Diagnosis and the Start of the Preparative Regimen

Question 48: Were central nervous system (CNS) abnormalities found on computed topography (CT or CAT) or magnetic resonance imaging (MRI) scans?

Indicate if radiology (CT, CAT, and/or MRI) performed on the recipient between diagnosis and the start of the preparative regimen detected any abnormalities in the CNS (brain and spinal cord). CNS abnormalities may include lesions, leptomeningeal enhancements, or edema.

If CNS abnormalities were detected on the radiological examination, select “yes” and continue with question 49. If no CNS abnormalities were detected on the radiological examination, select “no” and continue with question 50. If it is unknown if abnormalities were present or if no CT/CAT/MRIs were performed, select “unknown” and continue with question 50.

Question 49: Date scan was performed:

Enter the date the radiological assessment was performed.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 50: Were there any clinical neurologic abnormalities present?

Based on a clinical neurologic assessment, indicate if there were any clinical neurological abnormalities between diagnosis and the start of the preparative regimen. Neurologic abnormalities include abnormal gait, cranial nerve palsies, developmental delay, motor weakness, seizures, and sensory deficits. If clinical neurological abnormalities were present between diagnosis and the start of the preparative regimen, select “yes” and continue with question 51. If no clinical neurologic abnormalities were present, select “no” and continue with question 59. If it is not known if clinical abnormalities were present, select “unknown.”

Questions 51-58: Specify neurologic abnormalities:

Indicate the clinical neurological abnormalities present between diagnosis and prior to the start of the preparative regimen. Select “yes” or “no” for each question and ensure that no question is left blank. If a neurological abnormality is not listed but was present, select “yes” for question 57 (“other neurologic abnormality”) and specify the abnormality using question 58.
Q59-74: History of Infection at Any Time Prior to the Preparative Regimen

Specify documented infection(s) associated with HLH.

Question 59: Was an infection documented?

Indicate if an infection associated with HLH was present at any time prior to the start of the preparative regimen. If the recipient developed an infection associated with HLH prior to the start of the preparative regimen, select “yes” and continue with question 60. If there is no documentation of an infection associated with HLH, select “no” and continue with question 75.

Question 60: Cytomegalovirus (CMV):

Cytomegalovirus (CMV), also known as human herpesvirus 5 (HHV5), is one of the human herpes viruses (Herpesviridae family) and is very common, with an estimated 50-80% of individuals in the United States being infected by age 40. In healthy individuals, infection with CMV may not lead to any symptoms; however, the virus will lay dormant in the body after initial infection and can reoccur. In immunocompromised patients, such as immunosuppressed transplant recipients or HIV/AIDS patients, the virus can have serious consequences such as pneumonia, liver failure, and death.

If the recipient has a documented history of CMV associated with HLH, select “yes” and continue with question 61. If the recipient does not have a documented history of CMV, select “no” and continue with question 62.

Question 61: Specify the test method used for diagnosis of CMV:

Indicate the method used to diagnosis the CMV infection. The antigen method detects PP65 CMV proteins in leukocytes using an immunofluorescence assay. A PCR test is a molecular method to quantify the copies of CMV virus present in the sample. The shell vial test is performed by inoculating a culture within a shell vial with the specimen, incubating the culture, and staining to detect CMV. Indicate if the method used to diagnose CMV infection was “antigen,” “PCR,” or “shell vial test.”

Question 62: Epstein-Barr virus (EBV):

Epstein-Barr Virus (EBV) is one of the human herpes viruses (Herpesviridae family). EBV infection may cause infectious mononucleosis, particularly in young adults. Infectious mononucleosis symptoms include fever, sore throat, lymphadenopathy, and fatigue. After initial infection, the virus will lay dormant in the body and can reoccur; recurrence of EBV is often subclinical. Late events associated with prior EBV infection
include Burkitt’s Lymphoma and nasopharyngeal carcinoma.

If the recipient has a documented history of EBV associated with HLH, select “yes” and continue with question 63. If the recipient does not have a documented history of EBV, select “no” and continue with question 71.

**Question 63: In situ hybridization:**

*In situ* hybridization refers to the use of labeled viral probes to detect virus nucleic acids in tissue. Specify if the results of the *in situ* hybridization were “positive,” “negative,” or “not done” for EBV.

**Question 64: Polymerase chain reaction (PCR):**

Polymerase chain reaction (PCR) amplifies viral DNA to determine if the patient has a current primary infection or reactivated infection. Specify if the results of the PCR were “positive,” “negative,” or “not done” for EBV.

**Question 65: Serology:**

Serologic testing may be used to determine the presence of EBV antigen or antibodies to EBV. Specify if the results of the serology(s) were “positive,” “negative,” or “not done” for EBV. If “positive,” continue with question 66. If “negative” or “not done,” continue with question 70.

**Questions 66-69: Specify titers:**

Antibody titration to four EBV-specific markers can provide distinct information about whether a patient has a current primary or reactivated infection, recent infection, or past dormant infection. Antibodies to EBV nuclear antigen (EBNA) are not seen during acute infection, but develop 2-4 months after the first presentation of infection and persist for life. Early antigen testing measures IgG antibodies to early antigen; this generally appears at acute onset and is only detectable for 3-6 months. Viral capsid IgG measures IgG antibodies to viral capsid antigen that appear 2-4 weeks after presentation and persist for life. Viral capsid IgM testing for IgM antibodies to viral capsid antigen indicates current or recent infection, as it is generally only detectable for 4-6 weeks following first presentation.

Specify each EBV serologic antibody test as “positive” or “negative” in questions 66-69. Do not leave any response blank, unless testing failed, was inconclusive, or was not performed. If a validation error occurs due to the blank field, override the error.

**Question 70: Was documentation submitted to the CIBMTR?**

Indicate if a copy of the EBV results are attached. Use the Log of Appended Documents (Form 2800) to attach a copy of EBV result report(s). Attaching a copy of the report may prevent additional queries.
Question 71: Other infection:

Indicate if the recipient had an infection other than CMV or EBV associated with HLH at any time prior to the preparative regimen. If the recipient had an infection other than CMV or EBV, select “yes” and continue with question 72. If the recipient had no other documented infections associated with HLH, select “no” and continue with question 75.

Questions 72-74: Organism and Site:

For each infection, report the organism and site. Copy questions 72-74 for each infection.

72. Other Infection:
Specify the other viral, bacterial, fungal, or parasitic infection.

73. Organism:
From the list “Codes for Commonly Reported Organisms,” select the code corresponding to the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. Report the code in the boxes provided. If the specific organism is not listed, use the “other, specify” code (198 – bacteria, 209 – Candida, 219 – Aspergillus, 259 – fungus, 329 – virus, 409 – parasite) and report the name of the organism in the space provided. If the source of the infection is not determined, use code 509.

74. Site:
From the list “Codes for Common Sites of Infection,” select the code corresponding to the site of the infection.

If three or more sites are infected with the same organism, enter code 2 (Disseminated – generalized, isolated at 3 or more distinct sites).

* Disseminated Infections
The CIBMTR acknowledges that a discrepancy exists between the CIBMTR definition (3 or more sites) and the BMT-CTN definition (2 or more sites) for disseminated infections. For the purposes of this form, please use “disseminated” when the same organism is isolated at three or more distinct sites.
Q75-107: Pre-HCT Therapy

Copy questions 76-107 to report more than one line of therapy.

**Question 75: Was therapy given?**

Indicate if the recipient received therapy for HLH between diagnosis and the start of the preparative regimen. If the recipient received therapy, select “yes” and continue with question 76. If the recipient did not receive therapy, select “no” and continue with question 108.

**Question 76: Specify the purpose of therapy:**

Induction therapies are the initial lines of therapy given to a recipient to bring them into remission. Maintenance therapies are designed to keep the recipients in remission; for some patients with HLH, maintenance is used as an ongoing treatment until a suitable donor can be found for an HCT. If HLH reactivates or relapses following induction therapy or during maintenance therapy, additional therapy is given to treat the reactivation/relapse. Indicate if the line of therapy being reported is “induction,” “maintenance,” or “treatment for disease relapse/reactivation.”

**Questions 77-78: Date therapy started:**

Indicate if the therapy start date is “known” or “unknown.” If the therapy start date is known, use question 78 to enter the date the recipient began this line of therapy.

**Questions 79-90: Specify therapy given:**

Systemic treatments vary based on protocol and in many cases are administered in the outpatient setting. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. Indicate “yes” or “no” for each therapy regimen or drug administered for the line of therapy being reported. Do not leave any responses blank. If the recipient received a therapy that is not listed, check “yes” for “other therapy” and specify the treatment in question 90. Report the generic name of the agent, not the brand name.

**Question 91: Was this therapy given following the HLH-94/HLH 2004 protocol of the Histiocyte Society?**

Indicate if the therapy followed the HLH-94/HLH 2004 protocol of the Histiocyte Society. These protocols are meant to bring the recipient into remission, and then maintain their remission until an HCT can be performed. HLH-94 is a protocol that consists of 8 weeks of induction therapy with Etoposide and Dexamethasone followed by continuation therapy with etoposide, dexamethasone, and cyclosporine until transplant or reactivation of disease. Intrathecal methotrexate may be used in patients who have
progressive neurological symptoms or CSF abnormalities. HLH 2004 is a protocol that adds cyclosporine to the induction therapy phase and proceeds similarly to HLH-94. For the purposes of this form, the induction and continuation phases of these protocols can be reported as one line of therapy. Prior to transplant, the patient receives a preparative regimen that is separate from these protocols and should be reported on the Form 2000, but should not be included on this form as a line of therapy.


**Question 92: Was CNS disease inactive?**

Following this line of therapy, indicate if the recipient’s CNS disease was inactive. Indicate “yes” or “no” and continue with question 93 to report specific response(s). If “unknown,” continue with question 97.

**Question 93: Normal or stable CT or MRI of CNS:**

Based on CT or MRI of the central nervous system, indicate if previous CNS abnormalities have normalized or stabilized in response to this line of therapy. If the results of the CT or MRI are normal or stable, select “yes.” If there was evidence of new, recurrent, or progressive CNS abnormality, indicate “no.” If the response of CNS abnormalities assessed by CT or MRI is unknown, or if CT or MRI was not performed following the line of therapy, indicate “unknown.”

**Question 94: Neopterin level:**

Indicate the neopterin level in the cerebrospinal fluid (CSF) following this line of therapy. Indicate “normal” or “elevated.” If an assessment of neopterin levels in the CSF was not done following this line of therapy, select “not done.”

**Question 95: Protein level:**

Indicate the protein level in the cerebrospinal fluid (CSF) following this line of therapy. Indicate “normal” or “elevated.” If an assessment of protein levels in the CSF was not done following this line of therapy, select “not done.”

**Question 96: WBC level:**

Indicate the WBC count in the cerebrospinal fluid (CSF) following this line of therapy. Indicate “normal” if there were less than or equal to 5 cells/μL in the CSF. Indicate “elevated” if there were greater than 5 cells/μL in the CSF. If an assessment of WBC count in the CSF was not done following this line of therapy, select “not done.”
**Question 97: Was systemic disease inactive?**

Indicate if systemic disease consistent with the recipient’s disease was inactive. Assessments of systemic disease include neutrophil count, hemoglobin level, hepatomegaly and splenomegaly evaluation, fibrinogen levels, triglyceride levels, and platelet counts. If the recipient’s systemic disease was inactive following this line of therapy, indicate “yes” and continue with question 98. If the recipient’s systemic disease was not inactive following this line of therapy, continue with 98. If the status of the recipient’s systemic disease was unknown following this line of therapy, select “unknown” and continue with question 105.

**Question 98: ANC > 1.0 × 10⁹/L (without growth factor support):**

Indicate if the recipient’s absolute neutrophil count (ANC) was greater than 1.0 ×10⁹/L following this line of therapy, without the use of growth factors (e.g., filgrastim). Indicate “yes,” “no,” or “unknown.”

**Question 99: Hemoglobin ≥ 9 g/dL without transfusion:**

Indicate if the recipient’s hemoglobin level was equal to or greater than 9 g/dL without the use of red blood cell transfusions (within 30 days before test) following this line of therapy. Indicate “yes,” “no,” or “unknown.”

**Question 100: Hepatomegaly resolved (≤ 3 cm below costal margin):**

Indicate if hepatomegaly was no longer present on physical examination following this line of therapy. Indicate “yes,” “no,” or “unknown.”

**Question 101: Normal fibrinogen:**

Indicate if the fibrinogen level (factor I; fibrinogen activity; functional fibrinogen; fibrinogen antigen) returned to normal following this line of therapy. Indicate “yes,” “no,” or “unknown.”

**Question 102: Normal triglycerides:**

Indicate if the triglyceride level has returned to normal following this line of therapy. Indicate “yes,” “no,” or “unknown.”

**Question 103: Platelets > 100 × 10⁹/L without transfusion:**

Indicate if the recipient’s platelet count was greater than 100 ×10⁹/L without the use of platelet transfusions (within 7 days before test) following this line of therapy. Indicate “yes,” “no,” or “unknown.”

**Question 104: Splenomegaly resolved (≤ 3 cm below costal margin):**

Indicate if splenomegaly was no longer present on physical examination following this line of therapy.
Question 105: Were there any signs of disease relapse/reactivation?

Indicate if there were any signs of relapsed or reactivated disease following this line of therapy. These signs may be present in the central nervous system and detected on radiology (CT/MRI) or clinical neurologic exam, or based on systemic disease assessments. If there were any signs of disease relapse or reactivation following this line of therapy, select “yes” and continue with question 106. If there was no evidence of disease relapse or reactivation following this line of therapy, select “no” and continue with question 108.

Question 106: Specify the date of the relapse / reactivation:

Indicate the date that relapse or reactivation was detected. Use the date of the radiological exam where relapse/reactive was determined, the date of the clinical neurologic exam, or the date the sample was collected for systemic disease assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 107: Specify the site of the relapse/reactivation:

Indicate if the site of relapse was CNS, systemic, or CNS and systemic. CNS disease is limited to findings in the central nervous system by radiology (CT or MRI) or features specific to the CNS in the clinical neurologic exam. Systemic disease includes findings in the blood counts, triglycerides, ferritin, fibrinogen, and hepatosplenomegaly evaluations.
Q108-127: Clinical Features and Laboratory Studies At Last Evaluation Prior to the Start of the Preparative Regimen

Question 108: Anemia (Hgb < 9 g/dL):
Indicate if the recipient had anemia at the last evaluation prior to the start of the preparative regimen. Anemia is defined as hemoglobin less than 9 g/dL. Select “yes,” “no,” or “unknown.”

Question 109: Degranulation assay of NK cells (as defined by local laboratory):
Degranulation in natural killer (NK) cells is the process by which NK cells release granules containing chemicals (perforin and granzymes) that are used to destroy targeted cells. In some subtypes of FHL (FHL3, 4, and 5), degranulation of NK cells is absent or abnormally low. A granule release assay (GRA) can be used to assess the degranulation indirectly by measuring the expression of CD107a on the cell surface following stimulation. This expression is only detectable when the granules fuse with the cell membrane, thus the absence of CD107a by GRA would indicate a defect in some part of NK degranulation. Indicate if the results of degranulation assay of NK cells were “normal,” “abnormal,” or “unknown” at the last evaluation prior to the start of the preparative regimen.

Question 110: Fever (> 38.5° C or > 101.3° F for > 7 days):
Indicate if the recipient had fever at the last evaluation prior to the start of the preparative regimen. Fever is defined as a temperature above 38.5° C (101.3° F) for more than 7 days. Select “yes,” “no,” or “unknown.”

Question 111: Hepatomegaly (liver edge palpable > 3 cm below right costal margin):
Indicate if the recipient had hepatomegaly (enlargement of the liver) at the last evaluation prior to the start of the preparative regimen. Hepatomegaly is defined by the palpability of the liver edge 3 cm or more below the right costal margin. Indicate “yes,” “no,” or “unknown.”

Questions 112-113: Serum ferritin:
Indicate if the serum ferritin level was known at the last evaluation prior to the start of the preparative regimen. If “known,” indicate the value in question 113. If “unknown,” continue with question 114.

Questions 114-115: Triglycerides:
Indicate if the triglyceride level was known at the last evaluation prior to the start of the preparative regimen.
If “known,” indicate the value in question 115. If “unknown,” continue with question 116.

**Questions 116-117: Fibrinogen antigen assay (factor I; fibrinogen activity; functional fibrinogen; fibrinogen antigen):**

Fibrinogen levels may be low in those with HLH. Indicate if a fibrinogen antigen assay (factor I; fibrinogen activity; functional fibrinogen; fibrinogen antigen) level was known at the last evaluation prior to the start of the preparative regimen. If “known,” indicate the value (and corresponding unit) in question 117. If “unknown,” continue with question 118.

**Question 118: NK cell function:**

NK cell function is measured by a cytotoxicity assay.

NK cell function (cytotoxicity) may be absent or reduced in those with HLH. Indicate the NK cell function at the last evaluation prior to the start of the preparative regimen. Select “absent (≤ 10% lower limit of normal),” “decreased (11-50% lower limit of normal),” “normal,” or “unknown.”

**Question 119: Neutropenia (ANC < 1.0 × 10^9/L):**

Indicate if the recipient was neutropenic at the last evaluation prior to the start of the preparative regimen. Neutropenia is defined as an absolute neutrophil count (ANC) less than 1.0 × 10^9/L. Indicate “yes,” “no,” or “unknown.”

**Question 120: Soluble interleukin-2 receptor alpha chain (sCD25) (as defined by local laboratory):**

The presence of soluble interleukin-2 receptors (soluble IL-2R, sCD25) in the plasma indicates the activation of T cells. Elevated soluble IL-2R is indicative of prolonged T-cell activation, indicating a protracted immune response. Levels of soluble IL-2R differ based on age, so using age-based reference ranges is helpful to identify abnormal results. Indicate the soluble IL-2R alpha chain level at diagnosis or prior to the start of therapy for HLH. The results of the test should be reported as defined by the local laboratory. Indicate if the soluble IL-2R alpha chain level was “normal,” “elevated,” or “unknown.”


**Question 121: Splenomegaly (spleen palpable > 3 cm below left costal margin):**

Indicate if the recipient had splenomegaly (enlargement of the spleen) at the last evaluation prior to the start
of the preparative regimen. Splenomegaly is defined by the palpability of the spleen edge 3 cm or more below the left costal margin. Indicate “yes,” “no,” or “unknown.”

**Question 122: Thrombocytopenia (platelets < 100 \times 10^9/L):**

Indicate if the recipient was thrombocytopenic at the last evaluation prior to the start of the preparative regimen. Thrombocytopenia is defined as a platelet count less than 100 \times 10^9/L. Indicate “yes,” “no,” or “unknown.”

**Question 123: Neopterin level:**

The measurement of neopterin in the CSF is useful to determine immune system activity. Indicate the neopterin level in the cerebrospinal fluid (CSF) at the last evaluation prior to the start of the preparative regimen. Indicate “normal” or “elevated.” If an assessment of neopterin levels in the CSF was not done at the last evaluation prior to the start of the preparative regimen, select “not done.”

**Question 124: Protein:**

Indicate the protein level in the cerebrospinal fluid (CSF) at the last evaluation prior to the start of the preparative regimen. Indicate “normal” or “elevated.” If an assessment of protein levels in the CSF was not done at the last evaluation prior to the start of the preparative regimen, select “not done.”

**Question 125: WBC count:**

Indicate the WBC count in the cerebrospinal fluid (CSF) at the last evaluation prior to the start of the preparative regimen. Indicate “normal” if there were less than or equal to 5 cells/μL in the CSF. Indicate “elevated” if there were greater than 5 cells/μL in the CSF. If an assessment of WBC count in the CSF was not done at the last evaluation prior to the start of the preparative regimen, select “not done.”

**Question 126: Were central nervous system (CNS) abnormalities found on computed tomography (CT or CAT) or magnetic resonance imaging (MRI) scans?**

Indicate if radiology (CT, CAT, and/or MRI) detected any abnormalities in the central nervous system (brain and spinal cord) at the time of assessment prior to the preparative regimen. CNS abnormalities may include lesions, leptomeningeal enhancements, or edema.

If CNS abnormalities were detected on radiological examination, select “yes” and continue with question 127. If no CNS abnormalities were detected on radiological examination, select “no” and continue with the signature lines. If it is unknown if abnormalities were present or if no CT/CAT/MRIs were performed, select “unknown” and continue with the signature lines.
Question 127: Specify date scan was performed:

Enter the date the radiological assessment was performed.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.
2139: HLH Post-HCT

The Hemophagocytic Lymphohistiocytosis Post-HCT Data Form is one of the Comprehensive Report Forms. This form captures HLH-specific Post-HCT data such as the disease assessment since the date of the last report.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as “histiocytic disorders” and question 635 as “hemophagocytic lymphohistiocytosis (HLH).” The HLH Post-HCT Data (Form 2118) must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, and 2300) completed. The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100; between day 100 and the six-month date of contact for six-month follow-up Form 2200; and between the date of contact for the six-month follow-up Form 2200 and the date of contact for the one-year follow-up Form 2200, etc.).

Q1-32: Disease Assessment Since the Date of Last Report

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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<th>Description</th>
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<td>Modify</td>
<td>Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400)</td>
</tr>
</tbody>
</table>
Q1-32: Disease Assessment Since the Date of Last Report

Indicate which of the following clinical features and laboratory findings were present on the most recent evaluation since the date of the last report. For values assessed multiple times since the date of the last report, report the most recent results.

**Question 1: Anemia (Hgb < 9 g/dL):**

Indicate if the recipient had anemia on the most recent evaluation since the date of the last report. Anemia is defined as hemoglobin less than 9 g/dL. Select “yes,” “no,” or “unknown.”

**Question 2: Degranulation assay of NK cells:**

Degranulation in natural killer (NK) cells is the process by which NK cells release granules containing chemicals (perforin and granzymes) that are used to destroy targeted cells. In some subtypes of FHL (FHL3, 4, and 5), degranulation of NK cells is absent or abnormally low. A granule release assay (GRA) can be used to assess the degranulation indirectly by measuring the expression of CD107a on the cell surface following stimulation. This expression is only detectable when the granules fuse with the cell membrane, thus the absence of CD107a by GRA would indicate a defect in some part of NK degranulation. Indicate if the degranulation assay of NK cells was “normal,” “abnormal,” or “unknown” on the most recent evaluation since the date of the last report.

**Question 3: Fever:**

Indicate if the recipient had fever on the most recent evaluation since the date of the last report. Fever is defined as a temperature above 38.5° C (>101.3° F) for more than 7 days. Select “yes,” “no,” or “unknown.”

**Question 4: Hepatomegaly (liver edge palpable > 3 cm below right costal margin):**

Indicate if the recipient had hepatomegaly (enlargement of the liver) on the most recent evaluation since the date of the last report. Hepatomegaly is defined by the palpability of the liver edge 3 cm or more below the right costal margin. Indicate “yes,” “no,” or “unknown.”

**Questions 5-6: Serum ferritin:**

Indicate if the serum ferritin level was tested since the date of the last report. If “known,” indicate the most recent value in question 6. If “unknown,” continue with question 7.
Questions 7-8: Triglycerides:
Indicate if the triglyceride level was tested since the date of the last report. If “known,” indicate the most recent value in question 8. If “unknown,” continue with question 9.

Questions 9-10: Fibrinogen antigen assay (factor I; fibrinogen activity; functional fibrinogen; fibrinogen antigen):
Fibrinogen levels may be low in patients with HLH. Indicate if a fibrinogen antigen assay (factor 1; fibrinogen activity; functional fibrinogen; fibrinogen antigen) level was tested since the date of the last report. If “known,” indicate the most recent value (and corresponding unit) in question 10. If “unknown,” continue with question 11.

Question 11: NK cell function:
NK cell function is measured by a cytotoxicity assay.

NK cell function may be absent or reduced in those with HLH. Indicate the NK cell function on the most recent evaluation since the date of the last report; select “absent (≤ 10% lower limit of normal),” “decreased (11-50% lower limit of normal),” “normal,” or “unknown.”

Question 12: Neutropenia (ANC < 1.0 × 10^9/L):
Indicate if the recipient was neutropenic on the most recent evaluation since the date of the last report. Neutropenia is defined as an absolute neutrophil count (ANC) less than 1.0 × 10^9/L. Indicate “yes,” “no,” or “unknown.”

Question 13: Soluble interleukin-2 receptor alpha chain (sCD25): (As defined by local laboratory)
Indicate the soluble interleukin-2 receptor alpha chain (soluble IL-2R, sCD25) level on the most recent evaluation since the date of the last report. The results of the test should be reported as defined by the local laboratory. Indicate if the soluble IL-2R alpha chain level was “normal,” “elevated,” or “unknown.”

Question 14: Splenomegaly (spleen palpable > 3 cm below left costal margin):
Indicate if the recipient had splenomegaly (enlargement of the spleen) on the most recent evaluation since the date of the last report. Splenomegaly is defined by the palpability of the spleen edge 3 cm or more below the left costal margin. Indicate “yes,” “no,” or “unknown.”

Question 15: Thrombocytopenia (platelets < 100 × 10^9/L):
Indicate if the recipient was thrombocytopenic on the most recent evaluation since the date of the last
report. Thrombocytopenia is defined as a platelet count less than $100 \times 10^9$/L. Indicate “yes,” “no,” or “unknown.”

**Question 16: Neopterin level:**

The measurement of neopterin in the cerebrospinal fluid (CSF) is useful to determine immune system activity. Indicate the neopterin level in the CSF on the most recent evaluation since the date of the last report. Indicate “normal” or “elevated.” “Elevated” indicates levels above the upper limit of normal for the laboratory processing the specimen. If an assessment of neopterin levels in the CSF was not done since the date of the last report, select “not done.”

**Question 17: Protein:**

Indicate the protein level in the cerebrospinal fluid (CSF) on the most recent evaluation since the date of the last report. Indicate “normal” or “elevated.” “Elevated” indicates levels above the upper limit of normal for the laboratory processing the specimen. If an assessment of protein levels in the CSF was not done since the date of the last report, select “not done.”

**Question 18: WBC count:**

Indicate the WBC count in the cerebrospinal fluid (CSF) on the most recent evaluation since the date of the last report. Indicate “normal” if there were less than or equal to 5 cells/μL in the CSF. Indicate “elevated” if there were greater than 5 cells/μL in the CSF. If an assessment of WBC count in the CSF was not done since the date of last report, select “not done.”

**Question 19: Were central nervous system (CNS) abnormalities found on a computed tomography (CT or CAT) or magnetic resonance imaging (MRI) scan since the date of the last report?**

Indicate if radiology (CT, CAT, and/or MRI) performed on the recipient since the date of the last report detected any abnormalities in the CNS. CNS abnormalities may include lesions, leptomeningeal enhancements, or edema.

If CNS abnormalities were detected on the radiological examination at the most recent evaluation since the date of the last report, select “yes” and continue with question 20. If no CNS abnormalities were detected on the radiological examination, select “no” and continue with question 21. If it is unknown if abnormalities were present or if no CT/CAT/MRIs were performed, select “unknown” and continue with question 21.

**Question 20: Was documentation submitted to the CIBMTR?**

Indicate if a copy of the CNS radiography results is attached. Use the Log of Appended Documents (Form 2800) to attach a copy. Attaching a copy of the report may prevent additional queries.
**Question 21: Did any clinical neurologic abnormalities persist or develop?**

Based on a clinical neurologic assessment, indicate if there were any clinical neurological abnormalities that persisted or developed since the date of the last report. Neurologic abnormalities include abnormal gait, cranial nerve palsies, developmental delay, motor weakness, seizures, and sensory deficits. If clinical neurological abnormalities were present on the most recent evaluation since the date of the last report, select “yes” and continue with question 22. If no clinical neurologic abnormalities were present, select “no” and continue with question 30. If it is unknown if a clinical neurological exam was performed or if the results of the exam are not known, select “unknown” and continue with question 30.

**Questions 22-29: Specify neurologic abnormalities:**

Indicate the clinical neurologic abnormalities identified since the date of last report. Select “yes” or “no” for each question, ensuring that no question is left blank. If a neurological abnormality is not listed but was present, select “yes” for question 28 (“Other neurologic abnormality”) and use question 29 to specify the abnormality.

**Question 30: Were there any signs of disease relapse/reactivation?**

Indicate if there were any signs of new or recurrent disease since the date of the last report. These signs may be present in the central nervous system and detected on radiology (CT/MRI) or clinical neurologic exam, or based on systemic disease assessments. If there were any signs of disease relapse or reactivation since the date of the last report, select “yes” and continue with question 31. If there was no evidence of disease relapse or reactivation since the date of the last report, select “no” and continue with the signature lines.

**Question 31: Specify the date of the relapse/reactivation:**

Indicate the date that relapse or reactivation was detected. Use the date of the radiological exam, the date of the clinical neurologic exam, or the date the sample was collected for systemic disease assessment when relapse/reactive was determined.

If the exact date is not known, use the process for reporting partial or unknown dates as described in [General Instructions, Guidelines for Completing Forms](#).

**Question 32: Specify the site of the relapse/reactivation:**

Indicate if the site of relapse or reactivation was CNS, systemic, or CNS and systemic. CNS disease is limited to findings in the central nervous system by radiology (CT or MRI) or features specific to the CNS in the clinical neurologic exam. Systemic disease includes findings in the blood counts, triglycerides, ferritin, fibrinogen, and/or hepatosplenomegaly evaluations.
Cellular Therapy Manuals

The sections below provide explanatory text for instructions on completing the Cellular Therapy Essential Data Pre-Infusion Form (F4000), Cellular Therapy Product Form (F4003), Cellular Therapy Infusion Form (F4006), and Cellular Therapy Essential Data Follow-Up Form (F4100).

What cellular therapies to report and when:

1. Cellular therapy given in context of HCT (e.g. co-infusion, DLI/DCI): When a cellular therapy is given in context of a transplant, such as a co-infusion with an HCT or a DLI/DCI post-HCT, these infusions need to be reported to the CIBMTR. This includes both autologous and allogeneic products, such as cell stored prior to an allogeneic HCT used for treatment of graft failure.
2. Cellular therapy given with a prior HCT (e.g. CAR T-cell therapy for treatment of relapse): When a cellular therapy (e.g. CAR T-cell therapy) is given and there is a prior HCT, reporting these infusions are voluntary at this time.
3. Stand-alone cellular therapy (no prior HCT) (e.g. CAR T-cells): reporting these infusions are voluntary at this time*.

*Reporting of commercial products infusions (i.e. Kymriah, Yescarta) is strongly encouraged.

What infusions can be classified as a "DCI"?

An infusion can be classified as a “DCI" when:

- The intent is something other than to restore hematopoiesis
- The infusion must be post-HCT, often by the same donor as the HCT
- Indication is suboptimal donor chimerism, immune reconstitution, GVHD treatment, prevent or treat disease relapse (as reported on F4000)
- Composition of cells include un-manipulated lymphocytes, mesenchymal cells, peripheral blood mononuclear cells, NK cells, etc.

3500: Subsequent Neoplasms
4000: Cellular Therapy Essential Data Pre-Infusion
4003: Cellular Therapy Product
4006: Cellular Therapy Infusion
4100: Cellular Therapy Essential Data Follow-Up
**3500: Subsequent Neoplasms**

This form must be completed when a new malignancy is reported on a Cellular Therapy Essential Data Follow-Up Form (Form 4100). Reported new malignancies should be different than the disease / disorder for which cellular therapy was performed. Do not include relapse, progression or transformation of the same disease subtype.

New malignancies, lymphoproliferative disorders, and myeloproliferative disorders include but are not limited to:

- Skin cancers (basal, squamous, melanoma)
- New leukemia
- New myelodysplasia
- Solid tumors
- PTLD (post-transplant lymphoproliferative disorder) report as lymphoma or lymphoproliferative disease

The following should not be reported as new malignancy:

- Recurrence of primary disease (report as relapse or disease progression)
- Relapse of malignancy from recipient’s pre-cellular therapy medical history
- Breast cancer found in other (i.e., opposite) breast (report as relapse)
- Post-cellular therapy cytogenetic abnormalities associated with the pre-cellular therapy diagnosis (report as relapse)

A separate form 3500 must be submitted to report each new malignancy diagnosed since the date of last report. Reporting a new malignancy / disorder on a Form 4100 will make one Form 3500 due. If more than one new malignancy occurs during a reporting period, the Form 3500 can be made due on demand. Contact your CIBMTR CRC with any questions.

The submission of a pathology report or other supportive documentation for each reported new malignancy is strongly recommended.

**Links to sections of the form:**
Q1-23: New Malignancy, Lymphoproliferative or Myeloproliferative Disease/ Disorder
Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please [click here](#) or reference the retired manual section on the [Retired Forms Manuals](#) webpage.

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<td>Add</td>
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Q1-23: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder

Questions 1-3: Specify the new malignancy:

Indicate which new malignancy / disorder was diagnosed during the reporting period. If the new malignancy / disorder is not found in the list, select ‘other new malignancy’ and specify in question 2. Report the date of diagnosis in question 3, using the pathologic diagnosis date. If the original assessment confirming diagnosis is not available, report the date of diagnosis indicated in the progress notes.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 4 & 5: Was the new malignancy donor / cell product derived?

Indicate whether the new malignancy originated from the donor / cell product. If “yes,” indicate whether documentation was submitted to CIBMTR (e.g., cell origin evaluation (VNTR, cytogenetics, FISH)) in question 5.

For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 6: Was documentation submitted to the CIBMTR? (e.g. pathology report, autopsy report)

Indicate whether documentation of the new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was submitted to CIBMTR (e.g., pathology report, autopsy report).

For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Post-Transplant Lymphoproliferative Disorder

Questions 7-23 can only be answered if post-transplant lymphoproliferative disorder is selected in question 1.
**Question 7: Was there EBV reactivation in the blood?**

If reactivation in the blood was confirmed during the reporting period, report “yes” and continue with question 8. If reactivation did not occur during the reporting period report “no” and continue with question 13.

Indicate “unknown” if no EBV testing was performed during the reporting period and continue with question 13.

**Question 8-12: How was EBV reactivation diagnosed?**

Indicate the method of detection for EBV reactivation.

If reactivation was diagnosed by “qualitative PCR of blood,” continue with question 13.

If the diagnosis was made by “quantitative PCR of blood,” report the number of copies detected in question 10. Also, indicate whether repeat testing was performed during the reporting period in question 11. If repeat testing was performed, report the results of the most recent test performed during the reporting period in question 12.

If the diagnosis was made by “other method,” specify the method of detection in question 9 and then continue with question 13.

**Question 13: Was there lymphomatous involvement? (e.g., a mass)**

Indicate whether a mass or other lymphomatous involvement was detected during the reporting period. If there was lymphomatous involvement was confirmed during the reporting period, report “yes” and continue with question 14. If lymphomatous involvement was not confirmed during the reporting period, report “no” and continue with question 22.

**Question 14-21: Specify sites of PTLD involvement:**

For each site listed, indicate whether there was post-transplant lymphoproliferative disorder (PTLD) involvement. Sites may be identified by radiographic or pathologic methods. If there was PTLD involvement at a site not listed, report “other site” in question 20 and specify in question 21.

**Question 22 & 23: Was PTLD confirmed by biopsy?**

Indicate whether PTLD was confirmed by a biopsy. If PTLD was confirmed by a biopsy, report “yes” and indicate whether documentation was submitted to CIBMTR (e.g., pathology report) in question 23. If a biopsy did not confirm the diagnosis of PTLD, report “no”.
For further instructions on how to attach documents in FormsNet3\textsuperscript{SM}, refer to the Training Guide.
4000: Cellular Therapy Essential Data Pre-Infusion

This form must be completed for all recipients of cellular therapy (non-HCT) where it is the first indication for treatment (no prior hematopoietic cell transplant), when a cellular therapy event (e.g. DCI, CAR-T) is reported on an HCT follow up form, when cellular therapy (non-HCT) is reported as a new indication following a marrow toxic injury (RITN patient) / non-cellular therapy (e.g. chemotherapy, immunotherapy)

For recipients of hematopoietic cellular transplants, complete the pre-TED form 2400 and Disease Classification F2402.

This form reflects baseline recipient data and indication for a course of cellular therapy. All cellular therapies (non-HCT) are being collected on this form, including indications that reflect donor cellular infusions (DCI/DLI) done post-transplant, now referred to as “post-HCT cellular therapy”. A course of cellular therapy are all infusions given per protocol, or when multiple infusions are given for the same indication using the same product/donor (e.g. post-HCT cellular therapy (DCI/DLI)).

The use of cellular therapy is expanding. Treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g. cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g. CAR T-cells).

Links to sections of form:
Q1-13: Recipient Data
Q14-28: Cellular Therapy and HCT History
Q29-46: Product Identification
Q47-60: Indication for Cellular Therapy
Q61-67: Infection
Q68-93: Disease Assessment at Last Evaluation Prior to Cellular Therapy
Q94-249: Systemic Therapy Prior to Cellular Therapy
Q250-252: Functional Status
Q253-311: Comorbid Conditions

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference
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<td>Removed text (struck out below) and added text (in red below) to the instructions for question 49. If the indication for cellular therapy is relapsed, persistent or progressive disease (post-HCT), the indication should be the primary disease for which the cellular therapy is being given. If the recipient is receiving post-HCT cellular therapy (e.g. DCI/DLI) for relapsed, persistent, or progressive disease, the indication should be recorded as “malignant hematologic disorders” and complete a new F2402 for the disease that has relapsed/persisted/progressed.</td>
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<tr>
<td>2/13/18</td>
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<td>Remove</td>
<td>Removed the instruction below from section Q68-93: Disease Assessment at Last Evaluation Prior to Cellular Therapy. Specify the method(s) of disease detection below. For each method used, if the result was positive report the first date the disease was detected; if the result was negative report the last date the method was used prior to cellular therapy.</td>
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Forms Instruction Manual - 1
Q1-13: Recipient Data

**Recipient Ethnicity and Race**
For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2400 and F4000. To reduce the reporting burden, duplicated questions on the Cellular Therapy forms are disabled. This includes recipient ethnicity and race reported on F4000.

**Question 1: Ethnicity**

Indicate the recipient’s ethnicity. The United States Office of Management and Budget (OMB) has defined ethnicity as culturally or geographically determined. The distinction between Hispanic and non-Hispanic is for the purpose of the United States census. According to the OMB, “Hispanic” is an ethnic designation based upon where someone (his or her ancestors) was raised (e.g., “Latin America”). Hispanic people may be of any race. The CIBMTR recognizes regional differences with regard to the interpretation of ethnicity throughout the world.

If the recipient is not a resident of the USA, select “not applicable.”

If the recipient declines to provide this information or the recipient’s ethnicity is not documented, select “unknown.”

For more information regarding ethnicity, see Appendix I.

**Question 2: Race: (check all that apply)**

Indicate the recipient’s race. If this recipient has reported that they are more than one race, please select all options that apply. The race groups provided are specific to the United States.

For non-U.S. centers, select “not reported” if the rules/regulations of your country prohibit the collection or reporting of race data (or due to lack of documentation). If race is reported, it may be necessary to consult with the recipient to select the race group(s) with which they most closely identify.

If the recipient declines to provide this information, select “not reported.” If the recipient’s race is not documented, select “unknown.”

For more information regarding race, see Appendix I.
Question 3: Has the recipient signed an IRB / Ethics Committee-approved consent form for submitting research data to the CIBMTR?

To be compliant with Federal Regulations for human research subject protection, centers must obtain IRB-approved informed consent from recipients and donors (if applicable) to allow data submitted to the CIBMTR to be used for observational research. The NMDP/CIBMTR has written protocols and informed consent documents for the Observational Database. All centers must have local IRB approval for the Observational Database protocol. The NMDP IRB has approved these protocols and consent forms, and the documents are provided to participating sites to include with their local IRB submissions. International Centers must obtain consent of each patient participating in the Observational Database in a manner consistent with the laws and regulations of their country.

Reporting Consent Status for DCI
If this form is being completed for a DCI reported on a Post-TED Form (Form 2450) or Post-HCT Follow-Up Data Form (Form 2100), report “not applicable” for question 3. The consent status will be reported on the Pre-TED Form (Form 2400) and should not be re-reported here. If the recipient’s consent status has changed since the Pre-TED Form was completed, update the consent status on the Pre-TED Form.

When a recipient consents to participate in the Observational Database, their data are available in the CIBMTR’s Observational Research Database and may be used for research. The database includes recipient baseline and outcome data for related and unrelated allogeneic transplants from any cell source and for autologous transplants.

The primary purpose of the Observational Research Database is to have a comprehensive source of data that can be used to study hematopoietic cellular transplantation and cellular therapy. Studies using these data include:

- How well recipients recover from their infusions
- How recovery after infusion can be improved
- What the long-term outcomes are after transplantation and cellular therapies
- How access to transplantation for different groups of recipients can be improved
- How well donors recover from collection procedures
- The application and success of transplantation in the management of marrow toxic injuries
- Cellular therapy
- Better understand new complications seen with infusion of certain cellular therapy products
- Compare outcomes of transplantation and cellular therapies between each other and to other therapies
Indicate if the recipient has signed an IRB-approved consent form to participate in the Observational Research Database. If “yes (patient consented),” continue with question 4. If “no” (patient declined), “not approached”, or “not applicable” (post-HCT scenario) continue with question 5. If the patient declines consent, any data reported will not be used in observational studies.

**When to use the “Not Approached” option for the Research Database Consent**

CIBMTR expects all transplant centers to approach all patients for the Research Database consent. The “not approached” option should only be used in the rare event when the physician feels it would be in the best interest of the patient not to be consented.

**Question 4: Date form was signed:**

Report the date (YYYY-MM-DD) the research database consent form was signed by the recipient. Do not report the date that the witness or healthcare professional signed the consent form.

**Question 5: Is the recipient participating in a cellular therapy clinical trial?**

Indicate if the recipient is a registered participant with BMT-CTN, RCI-BMT, USIDNET, COG, a Corporate / Industry trial, EudraCT, UMIN, an investigator initiated trial and/or another clinical trial sponsor, regardless if that sponsor uses CIBMTR forms to capture outcomes data. If “yes,” continue with question 6 to report the sponsor. If “no,” continue with question 12. If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.

- BMT-CTN: Blood and Marrow Transplant Clinical Trials Network
- RCI-BMT: Resource for Clinical Investigation in Blood and Marrow Transplant
- USIDNET: United States Immunodeficiency Network
- COG: Children’s Oncology Group
- Corporate / Industry
- EudraCT: European Clinical Trials Database
- UMIN: University Hospital Medical Information Network Center
- Investigator initiated

**Questions 6-11 Reporting Participation in More Than One Study**

FormsNet3SM application: Complete questions 6-11 for each study the recipient is participating in by adding an additional instance in the FormsNet application. Paper form submission: Copy questions 6-11 and complete for each study the recipient is participating in.
**Question 6 – 11: Study sponsor:**

Select the study sponsor of the clinical trial the recipient is participating in. See question 5 for a link to more information about each organization.

If the study sponsor is reported as “BMT-CTN”, “COG”, “Investigator initiated”, “RCI-BMT”, or “USIDNET”, specify the ClinicalTrials.gov identification number in question 11. See links listed under question 5 for more information. Investigator initiated trials include those that are initiated and managed by a non-pharmaceutical/company researcher (e.g. individual physicians or cooperative groups) and center specific trials or multi-center trials. Continue with question 14.

If the recipient is participating in corporate / industry sponsored trial, indicate the study sponsor as “Corporate/Industry” in question 6, specify the name of the Corporate or Industry sponsor in question 7 and report the clinicaltrials.gov ID number in question 11. Corporate/Industry examples include, but are not limited to, Atara Biotherapeutics, Bellicum Pharmaceuticals, BlueBird Bio, Celgene, Juno Therapeutics, Kite Pharma, Mesoblast, and Novartis. Continue with question 14.

If the recipient is participating in a European Medicines Agency clinical trial, indicate the study sponsor as “EudraCT” in question 6 and specify the Study identification number in question 8 (not the recipient ID). The European Union Drug Regulating Authorities Clinical Trials is the European Clinical Trials Database of all clinical trials of investigational medicinal products with at least one site in the European Union commencing 1 May 2004 or later. See link listed under question 5 for more information. The EudraCT number has the format YYYY-NNNNNN-CC, where YYYY is the year in which the number is issued, NNNNNN is a six digit sequential number, and CC is a check digit. Continue with question 12.

If the recipient is participating in a study with UMIN, indicate the study sponsor as “UMIN” in question 6 and specify the alpha-numeric Study identification number in question 9 (not the recipient ID). UMIN was established in 1989 as a cooperative organization national medical school in Japan, sponsored by the Ministry of Education, Culture, Science, Sports and Technology (MEXT), Japan. See link listed under question 5 for more information. Continue with question 12.

If the recipient is participating in a clinical trial and the study sponsor is not listed, select “other sponsor” in question 6, specify the sponsor name in question 10, and report the ClinicalTrials.gov identification number in question 11. Continue with question 14.

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**ClinicalTrials.gov identification number**

All clinical trials are required to be registered on the clinicaltrials.gov website and will have an associated identification number. Report the number in question 11. It is not necessary to include the letters “NCT” that precede the digits.
Question 12: Is the recipient receiving cellular therapy outside of the context of a clinical trial?

Indicate “yes” if the recipient is receiving cellular therapy in the setting of “institutional guidelines/standard of care”, “hospital exemption”, or “compassionate use” and continue with question 13 (see below for definitions). If “no”, continue with question 14.

Question 13: Specify the reason for not being on a clinical trial: (check all that apply)

Institutional guidelines/standard of treatment: internal protocols at the center

Hospital exemption: applicable when giving cell therapy product without a clinical trial, the hospital that produces the cells must be the hospital that gives the cells.

Compassionate use: No protocol is available or approved by institution, the physician asks for a one-time use
Q14-28: Cellular Therapy and HCT History

Question 14: Is this the first application of cellular therapy (non-HCT)?

Indicate if this is the recipient's first cellular therapy application. “First application” is defined as the first application the recipient ever receives, not the first application the recipient receives at your facility. The intent is to capture the full picture of the recipient’s treatment history.

If “yes” or “unknown”, continue with question 23. If “no”, continue with question 15.

Question 15: Were all prior cellular therapies (non-HCT) reported to the CIBMTR?

This should include any/all infusions not performed at your center. If the recipient is a transfer patient, you will be able to see all past infusion dates in the Recipient Information Grid in FormsNet3SM. Contact your CIBMTR CRC if there are questions.

If “yes” or “unknown”, continue to question 23. If “no”, continue with question 16.

Question 16: Specify the number of prior cellular therapies:

Enter the number of prior cellular therapies for the recipient. A “cellular therapy event” is defined as the infusion or administration of a cellular therapy product for treatment of a specific indication(s). Each infusion or administration of a cellular product should be counted separately. Include all infusions the recipient received, even if they were not performed at your center. The intent is to capture the full picture of the recipient’s treatment history.

Questions 17-22 Reporting Prior Cellular Therapies

FormsNet3SM application: Complete questions 17-22 to report all prior cellular therapies that have not yet been reported to the CIBMTR by adding an additional instance in the FormsNet application.

Paper form submission: Copy questions 17-22 and complete for each prior cellular therapy that has not yet been reported to the CIBMTR.

Question 17: Date of the prior cellular therapy:

Report the date (YYYY-MM-DD) of the prior cellular therapy being reported in this instance. If the exact date is unknown and must be estimated, check the “date estimated” box.

For more information regarding reporting partial or unknown dates, see General Instructions, General.
Guidelines for Completing Forms.

**Question 18: Was the cellular therapy performed at a different institution?**

Indicate if the prior cellular therapy being reported in this instance was performed at another institution. If “yes”, report the name and address of the institution in question 19. If “no”, continue with question 20.

**Question 19: Specify the institution that performed the prior cellular therapy:**

Report the name, city, state, and country of the institution where the recipient’s prior cellular therapy being reported in this instance was performed. These data are used to identify and link the recipient’s existence in the database and, if necessary, obtain data from the other institution where the previous treatment was administered.

**Question 20 & 21: Specify the indication for the prior cellular therapy:**

Select the indication for the prior cellular therapy being reported in this instance. Any indication that is followed by “(post-HCT)” or “(with HCT)” requires that a prior HCT also be reported to CIBMTR.

If the indication for the prior cellular therapy is not listed, select “other indication” and specify the indication in question 21. If the indication for the prior cellular therapy is not documented, select “unknown”.

**Question 22: What was the cell source for the prior cellular therapy? (check all that apply)**

Indicate the cell source(s) for the prior cellular therapy being reported in this instance. If the product is “off the shelf” or a “third party donor” product obtained from pharmaceutical companies or other corporate entities, donor type should still be identified

- An autologous product has cells collected from the recipient for his/her own use.

- An unrelated donor (allogeneic, unrelated) is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or step-parents/children.

- A related donor (allogeneic or syngeneic, related) is a blood-related relative. This includes monozygotic (identical twins), non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc.

**Questions 23-28 HCT History**

For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2400 and F4000. To reduce the reporting burden, duplicated questions on the Cell Therapy forms are disabled. This includes HCT History.
Question 23: Has the recipient ever had a prior HCT?

Include all HCTs in the recipient’s history, even if the transplants were not performed at your center. The intent is to capture the full picture of the recipient’s treatment history.

If “yes” continue with question 24. If “no” or “unknown”, continue with question 29.

Question 24: Were all prior HCTs reported to the CIBMTR?

This should include any/all HCTs not performed at your center. If the recipient is a transfer patient, you will be able to see all past infusion dates in the Recipient Information Grid in FormsNet3SM. Contact your CIBMTR CRC if there are questions.

If “yes” or “unknown”, continue with question 29. If “no”, continue with question 25.

Question 25: Date of the prior HCT:

Report the date (YYYY-MM-DD) of the prior HCT being reported in this instance.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 26: Was the HCT performed at a different institution?

Indicate if the prior HCT being reported in this instance was performed at another institution. If “yes” report the name and address of the institution in question 27. If “no” continue with question 28.

Question 27: Specify the institution that performed the prior HCT:

Report the name, city, state, and country of the institution where the recipient’s prior HCT being reported in this instance was performed. These data are used to identify and link the recipient’s existence in the database and, if necessary, obtain data from the previous transplant center.

Question 28: Specify the HSC source(s) for the prior HCT: (check all that apply)

Indicate the applicable cell source(s) for the prior HCT being reported in this instance.

An autologous product has cells collected from the recipient for his/her own use.
An **unrelated donor (allogeneic, unrelated)** is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or step-parents/children.

A **related donor (allogeneic, related)** is a blood-related relative. This includes monozygotic (identical twins), non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc.
Q29-46: Product Identification

Question 29: Specify the total number of products: (per protocol) (as part of this course of cellular therapy)

Report the number of products to be infused per protocol. This question is used to make the correct number of Cellular Therapy Product forms (Form 4003) come due. Each product must be part of the protocol and will be given regardless of disease response.

Example 1. A series of collections from the same donor that uses the same collection method and mobilization cycle, even if the collections are performed on different days, should be considered a single cellular therapy product if only one set of manufacturing steps are applied to the collected material.

Example 2. Products from the same donor but obtained using different manufacturing steps are considered different products and require multiple product forms.

Example 3. If the cells were manipulated or modified by different methods and at the end of the manufacturing process are combined for a single infusion or administration, it will be considered a single product and it will require a single Form 4003.

Question 30: Is the product genetically modified?

Genetically modified products include any product that was manipulated to alter its gene expression through the insertion of different genes, or editing of genes. An example of a genetically modified product is the manipulation of T-lymphocytes to express Chimeric Antigen Receptors (CAR T-cells) directed towards specific tumor targets (antigens). If more than one product is being infused, indicate if any of the products are genetically modified.

Questions 31-43 Reporting donor information
FormsNet3SM application: Complete questions 31-43 to report all donors, per protocol, used for the products reported in question 29 by adding an additional instance in the FormsNet application.
Paper form submission: Copy questions 31-43 and complete for all donors, per protocol, used for the products reported in question 29.

Question 31: Specify the cell source:

Select the cell source for the donor being reported in this instance. If the product is “off the shelf” or a “third party donor” product obtained from pharmaceutical companies or other corporate entities, donor type should
still be identified.

An autologous product has cells collected from the recipient for his/her own use. Continue with question 34.

An unrelated donor (allogeneic, unrelated) is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or step-parents/children. Continue with question 33.

A related donor (allogeneic, related) is a blood-related relative. This includes monozygotic (identical twins), non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc. Continue with question 32.

**Question 32: Specify the related donor type:**

Indicate the relationship and match between the recipient and the related donor being reported in this instance.

**Syngeneic:**
Includes: Monozygotic (identical) twins. Occurs when a single egg is fertilized to form one zygote, which then divides into two separate embryos.
Does not include: Other types of twins or HLA-identical siblings (see below).

**HLA-identical sibling:**
Includes: Non-monozygotic (dizygotic, fraternal, non-identical) twins. Occurs when two eggs are fertilized by two different sperm cells at the same time. This category also includes siblings who aren’t twins, but have identical HLA types.
Does not include: Half-siblings should be reported as “HLA matched other relatives” if their HLA typing is a match, or “mismatched relative” if it does not match.

**HLA-matched other relative:**
Includes: All blood-related relatives, other than siblings, who are HLA matched (e.g., parents, aunts, uncles, children, cousins, half-siblings).
Does not include: Adoptive parents/children or step-parents/children who are HLA matched.

**HLA-mismatched relative:**
Includes: Siblings who are not HLA-identical and all other blood-related relatives who have at least one HLA mismatch (mismatch can be at the antigen or allele level) (e.g., parents, aunts, uncles, children, cousins, half-siblings).
Does not include: Adoptive parents/children or stepparents/children.
Question 33: Was this donor used for any prior cellular therapies or HCT? (for this recipient)

Indicate if the allogeneic unrelated or related donor being reported in this instance was used for prior cellular therapies or HCT for this recipient. Do not answer this question for autologous donors.

Questions 34-37 allow for the selection of multiple tissue sources and cell types for a product. For example, if the product consists of two different types of lymphocytes, the source of cells will be peripheral blood and the cell types will be CD4+ and CD8+ lymphocytes. Also, in the case of a tumor vaccine, the sources will be tumor and peripheral blood and the cell type will be dendritic cells/tumor cell hybridomas.

Question 34-35: What is the tissue source of the cellular product? (check all that apply)

Select from the list the tissue source(s) of the cellular product being reported in this instance. If the source is selected as ‘Other tissue source’, specify the other source in question 35 and continue with question 36.

Question 36-37: What is the cell type? (check all that apply)

Select from the list the cell type(s) of the cellular product being reported in this instance. This should be the type of cell(s) in the product infused. If the cell type is selected as ‘Other cell type’, specify the other cell type in question 37 and continue with question 38. All cell types selected here must also be reported on the Cellular Therapy Infusion Form 4006. Please refer to the 4006 Manual, Q17-45, for description of cell types.

Question 38-43: Where was the cellular therapy product manufactured / processed?

If the product was manufactured by a pharmaceutical or biotech company, continue with question 40 and select the pharmaceutical or biotech company from the list. If the company is not in the dropdown list, select ‘other pharmaceutical company’ and report the name and location of the company in question 41.

If the company has a commercialized product, select the product name in question 42. If the product name is not in the list, select ‘other product’ and report the name in question 43.

If the product was manufactured by a cell processing laboratory off site that is not a pharmaceutical / biotech company, continue with question 41 and report the name and location of the laboratory. Continue with question 44.

If the product was manufactured by a cell processing laboratory at the same center as the product is being infused, continue with question 44. If the product is from an NMDP donor used for a prior HCT, please select this option.

If the product was manufactured by another site not listed above, continue with question 39 to specify the
other site and report the name and location in question 41.

**Question 44: Is a subsequent HCT part of the overall treatment protocol?**

This question intends to capture instances where the cellular therapy is administered in association with a HCT, either planned or dependent upon the response to the cellular therapy. If a subsequent HCT is part of the overall treatment plan, indicate “yes”, continue with question 45. If “no”, continue with question 47.

**Question 45: Specify the HCT type:**

Specify the type of the subsequent HCT that is planned as part of the overall treatment protocol.

An **autologous product** has cells collected from the recipient for his/her own use.

An **allogeneic product** is from a donor who is not the recipient, either related or unrelated to the recipient.

**Question 46: Specify the circumstances which the subsequent HCT will be performed:**

Specify the reason for which the subsequent HCT will be performed as “regardless of response to cellular therapy”, “only if the patient responds to cellular therapy” or “only if the patient fails to respond or has an incomplete response”.
Q47-60: Indication for Cellular Therapy

Question 47-48: Is the cellular therapy being given for prevention?

Reasons for prevention include:

- GVHD prophylaxis (with HCT)
- Prevent disease relapse (post-HCT)
- Infection prophylaxis

If the indication is any in the list above and the cell therapy is being given with HCT or post-HCT, no additional consent is required from the patient:

Question 49: What was the indication for performing treatment with cellular therapy?

From the list provided, select the indication for which the recipient is receiving the cellular therapy.

If the indication is any in the list below and the cell therapy is being given with HCT or post-HCT, no additional consent is required from the patient:

- Suboptimal donor chimerism (post-HCT)
- Immune reconstitution (post-HCT)
- GVHD treatment (post-HCT)

The Disease Classification Form 2402 will come due if the indication is reported as “malignant hematologic disorder”, “non-malignant disorder”, or “solid tumor”. This allows CIBMTR to capture disease specific information for cellular therapy utilizing an existing form to maintain consistency in data collection.

If the recipient is receiving post-HCT cellular therapy (e.g. DCI/DLI) for relapsed, persistent, or progressive disease, the indication should be recorded as “malignant hematologic disorders” and complete a new F2402 for the disease that has relapsed/persisted/progressed.

*Disease Classification Questions*

The newest versions of the TED forms use the World Health Organization (WHO) disease classifications. The disease classification questions contain all of the established WHO disease types and subtypes. The “other indication” category should be used only if the recipient’s disease is not one of the listed options. For more information regarding disease classification, consult a transplant physician, contact your center’s CIBMTR CRC, or visit CIBMTR.org.

*Forms Instruction Manual - 1*
**Malignant vs. Non-Malignant**

Malignant disease involve cells dividing without control that can spread to other parts of the body through blood and lymph systems. These diseases are usually characterized by unlimited, aggressive growth, invasion of surrounding tissues, and metastasis. Non-malignant tumors involve cell overgrowth, but lack the malignant properties of cancer. Non-malignant diseases include severe aplastic anemia, disorders of the immune system, inherited disorders of metabolism, etc. The CIBMTR database disease codes are represented in parentheses after the disease subtype on the Disease Classification questions and can be helpful in mapping diagnosis [e.g Myeloid Sarcoma (295)], and determining if the disease is malignant or non-malignant. Disease codes (10-299) indicate a malignant disease, with the exception of Paroxysmal Nocturnal Hemoglobinuria (PNH) (56). A disease code of (300) or above indicates a non-malignant disease, with the exception of disease code (900), which could indicate either a malignant or non-malignant disease.

### Question 50: Date of diagnosis:

This question is answered if the indication for cellular therapy is cardiovascular disease, musculoskeletal disease, neurologic disease, ocular disease, pulmonary disease, infection treatment or other indication. The diagnosis date for malignant hematologic disorder, non-malignant disorder or solid tumor will be captured on the Disease Classification Form (Form 2402).

Report the date (YYYY-MM-DD) of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease for which the patient is receiving cellular therapy. Enter the date the sample was collected for examination. If the indication is infection, report the date of diagnosis as the collection date for the first positive microbiology culture. If the diagnosis was determined at an outside center, and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.

If the recipient was diagnosed prenatally (in utero) or if the indication is a congenital disorder, report the date of birth as the date of diagnosis.

If the exact pathological diagnosis date is not known, use the process described in General Instructions, General Guidelines for Completing Forms.

### Question 51-53: Specify cardiovascular disease:

If cardiovascular disease is the indication for cellular therapy, indicate the specific disease in question 51. If “other cardiovascular disease” is selected, specify in question 52. If “other peripheral vascular disease” is
selected, specify in question 53. Continue with question 94.

**Question 54-55: Specify musculoskeletal disorder:**

If musculoskeletal disorder is the indication for cellular therapy, indicate the specific disorder in question 54. If “other musculoskeletal disorder”, specify in question 55. Continue with question 94.

**Question 56-57: Specify neurologic disease:**

If neurologic disease is the indication for cellular therapy, indicate the specific disease in question 56. If “other neurologic disease”, specify in question 57. Continue with question 94.

**Question 58: Specify ocular disease**

If ocular disease is the indication for which the recipient is receiving the cellular therapy, specify in question 58. Examples include treatment of glaucoma or photoreceptor degeneration. Continue with question 94.

**Question 59: Specify pulmonary disease**

If pulmonary disease is the indication for which the recipient is receiving the cellular therapy, specify in question 59. Examples include Chronic Obstructive Pulmonary Disease (COPD) or pulmonary fibrosis. Continue with question 94.

**Question 60: Specify other indication**

If the indication for which the recipient is receiving the cellular therapy is “other indication” because it does not fit into a category listed above, specify the indication in question 60. An example is treatment of autism by cellular therapy. Contact your CIBMTR CRC if there is a question on the indication. Continue with question 94.
Q61-67: Infection

This section to be completed when infection is the indication for the cellular therapy.

Question 61-67: Organism:

If treatment of infection is the indication for the cellular therapy, report the fungal or viral organism(s) for which the recipient is receiving the cellular therapy.

Organism:
From Table 1 entitled “Codes for Commonly Reported Organisms”, select the code corresponding to the identified organism as indicated on the microbiology report, laboratory report, or other physician documentation. Report the code in the boxes provided on the form.

Fungal infections: Note the inclusion of Pneumocystis (formerly found under parasites). The most commonly found fungal infections are Candida (C. albicans), Aspergillus (A. fumigatus), and Fusarium sp.

Viral infections: Caused by exposure to a new virus or reactivation of a dormant virus already present in the body. The most common viral infections are due to HSV (Herpes Simplex Virus), and CMV (Cytomegalovirus). If the site of CMV is the lung, confirm whether the patient had interstitial pneumonitis rather than CMV pneumonia.

Table 1: Codes for Commonly Reported Organisms

<table>
<thead>
<tr>
<th>Code</th>
<th>Organism</th>
<th>Code</th>
<th>Organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>201</td>
<td>Candida albicans</td>
<td>301</td>
<td>Herpes Simplex Virus (HSV)</td>
</tr>
<tr>
<td>208</td>
<td>Candida non-albicans</td>
<td>302</td>
<td>Varicella Virus</td>
</tr>
<tr>
<td>210</td>
<td>Aspergillus, NOS</td>
<td>303</td>
<td>Cytomegalovirus (CMV)</td>
</tr>
<tr>
<td>211</td>
<td>Aspergillus flavus</td>
<td>304</td>
<td>Adenovirus</td>
</tr>
<tr>
<td>212</td>
<td>Aspergillus fumigatus</td>
<td>306</td>
<td>Hepatitis A Virus</td>
</tr>
<tr>
<td>213</td>
<td>Aspergillus niger</td>
<td>307</td>
<td>Hepatitis B Virus</td>
</tr>
<tr>
<td>214</td>
<td>Aspergillus ustus</td>
<td>308</td>
<td>Hepatitis C Virus</td>
</tr>
<tr>
<td>215</td>
<td>Aspergillus terreus</td>
<td>309</td>
<td>Human Immunodeficiency Virus 1 or 2</td>
</tr>
<tr>
<td>221</td>
<td>Cryptococcus</td>
<td>310</td>
<td>Influenza, NOS</td>
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<tr>
<td></td>
<td></td>
<td>323</td>
<td>Influenza A Virus</td>
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<td></td>
<td></td>
<td>324</td>
<td>Influenza B Virus</td>
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<td></td>
<td></td>
<td>325</td>
<td>Enterovirus (ECHO, Coxsackie)</td>
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<td></td>
<td>326</td>
<td>Enterovirus (polio)</td>
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<td></td>
<td></td>
<td>327</td>
<td>Enterovirus D68 (EV-D68)</td>
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<td></td>
<td></td>
<td>328</td>
<td>Enterovirus NOS</td>
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<td></td>
<td></td>
<td>329</td>
<td>Hepatitis A Virus</td>
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<td></td>
<td></td>
<td>330</td>
<td>BK Virus</td>
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<tr>
<td></td>
<td></td>
<td>331</td>
<td>JC Virus (Progressive Multifocal)</td>
</tr>
<tr>
<td>Organism</td>
<td>Disease</td>
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<tr>
<td><strong>neoformans</strong></td>
<td>Leukoencephalopathy (PML))</td>
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</tr>
<tr>
<td><strong>222 Cryptococcus gattii</strong></td>
<td>311 Measles Virus (Rubeola)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>343 Human metapneumovirus</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>230 Fusarium (all species)</strong></td>
<td>312 Mumps Virus</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>344 Coronavirus</td>
<td></td>
<td></td>
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<tr>
<td><strong>240 Zygomyces, NOS</strong></td>
<td>314 Respiratory Syncytial Virus (RSV)</td>
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<tr>
<td></td>
<td>345 Norovirus</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>241 Mucorales (all species)</strong></td>
<td>315 Rubella Virus</td>
<td></td>
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<tr>
<td></td>
<td>346 Dengue Virus</td>
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<td></td>
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<tr>
<td><strong>242 Rhizopus (all species)</strong></td>
<td>316 Human Parainfluenza Virus (all species)</td>
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<tr>
<td></td>
<td>347 Chikaugunya virus</td>
<td></td>
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<tr>
<td><strong>260 Pneumocystis (PCP / PJP)</strong></td>
<td>317 Human herpesvirus 6 (HHV-6)</td>
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<tr>
<td></td>
<td>348 West Nile Virus (WNV)</td>
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<tr>
<td><strong>261 Histoplasma (capsulatum)</strong></td>
<td>318 Epstein-Barr Virus (EBV)</td>
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<tr>
<td></td>
<td>349 Human T-lymphotropic Virus 1 or 2</td>
<td></td>
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<tr>
<td><strong>270 Blastomyces (dermatitidis)</strong></td>
<td>320 Rotavirus (all species)</td>
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<tr>
<td></td>
<td>503 Suspected fungal infection</td>
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<tr>
<td><strong>271 Coccidioides (all species)</strong></td>
<td>321 Rhinovirus (all species)</td>
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<td></td>
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<tr>
<td></td>
<td>777 Other organism</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>272 Scedosporium (all species)</strong></td>
<td>322 Human Papillomavirus (HPV)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Q68-93: Disease Assessment at Last Evaluation Prior to Cellular Therapy

Question 68: Was the disease assessed prior to the cellular therapy?

Indicate if the disease status was assessed prior to the cellular therapy. If “yes”, continue with question 69. If “no”, continue with question 94.

Question 69: Was the disease status assessed by molecular testing (e.g. PCR)?

Molecular assessment involves testing blood, bone marrow, tumor or other source for the presence of known molecular markers. Molecular assessments are the most sensitive test for genetic abnormalities and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control. RFLP testing (with PCR amplification) is an example of a molecular test method used to detect BCR/ABL.

Select “yes” if a molecular method was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 70. If a molecular method was not used to determine disease status, check “no” and continue with question 73.

If a molecular method was used to evaluate the disease status, but has never been positive, check “not
applicable” and continue with question 73.

**Question 70: Date sample collected:**

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by molecular method. The sample collection date should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 95).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

**Question 71: Was disease detected?**

If molecular markers for disease were found, check “yes” and continue with question 72. If molecular markers for disease were not found, check “no” and continue with question 73.

**Question 72: Was the status considered a disease relapse or progression?**

If the physician believes the test results indicate disease relapse or progression, check “yes.” If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression (e.g., a recipient transplanted for CML exhibits such a low level of BCR-ABL positivity post-cellular therapy that the physician does not believe is disease), check “no”.

**Question 73: Was the disease status assessed via flow cytometry (immunophenotyping)?**

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material.

Select “yes” if flow cytometry was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 74. If flow cytometry was not performed or could not be used to determine disease status, check “no” and continue with question 77.

If flow cytometry was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 77.

**Question 74: Date sample collected:**

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by flow cytometry. The sample collection date should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 95).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for
more information on reporting partial and unknown dates.

**Question 75: Was disease detected?**

If flow cytometry detected disease, check “yes” and continue with question 76.

If flow cytometry did not detect disease, check “no” and continue with question 77.

**Question 76: Was the status considered a disease relapse or progression?**

If the physician believes the test results indicate disease relapse or progression, check “yes.” If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression, check “no.”

**Question 77: Was the disease status assessed by cytogenetic testing (karyotyping or FISH)?**

Cytogenetic studies involve the study of chromosomes, typically through one of two methods: karyotyping or fluorescence in situ hybridization (FISH). Blood, bone marrow, or tissue preparations may be tested by either of these two methods. Karyotyping is both less sensitive and less specific than FISH testing; FISH studies identify only abnormalities detectable by the employed probe set, and cannot provide information about the presence or absence of chromosomal abnormalities or markers outside the specific probe set utilized. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same. For more information of cytogenetic assessments, see [Appendix C](#).

Select “yes” if cytogenetic testing was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 78. If cytogenetic testing was not performed or was not used to determine disease status, check “no” and continue with question 86.

If cytogenetic testing was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 86.

**Question 78: Was the disease status assessed by karyotyping?**

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

Select “yes” if karyotyping was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 79. If karyotyping was not performed or used to determine disease
status, check “no” and continue with question 82.

If karyotyping was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 82.

**Question 79: Date sample collected:**

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by karyotyping. The sample collection date should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 95).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

**Question 80: Was disease detected?**

If disease was detected by karyotyping, check “yes” and continue with question 81. If disease was not detected by karyotyping, check “no” and continue with question 82.

**Question 81: Was the status considered a disease relapse or progression?**

If the physician believes the test results indicate disease relapse or progression, check “yes”. If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression, check “no.”

**Question 82: Was the disease status assessed by FISH?**

Fluorescence in situ hybridization (FISH) studies identify only abnormalities detectable by the employed probe set, and cannot provide information about the presence or absence of chromosomal abnormalities or markers outside the specific probe set utilized.

Select “yes” if FISH was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 83. If FISH was not performed or used to determine disease status, check “no” and continue with question 86.

If FISH was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 86.

**Question 83: Date sample collected:**

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by FISH. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular
therapy (date reported in question 95).

If the exact date is unknown, please view General Instructions, [General Guidelines for Completing Forms](#) for more information on reporting partial and unknown dates.

**Question 84: Was disease detected?**

If FISH markers for disease were found, check “yes” and continue with question 85. If FISH markers for disease were not found, check “no” and continue with question 86.

**Question 85: Was the status considered a disease relapse or progression?**

If the physician believes the test results indicate disease relapse or progression, check “yes”. If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression, check “no”.

**Question 86: Was the disease status assessed by radiological assessment? (e.g., PET, MRI, CT)**

Radiologic assessments are imaging techniques used to assess disease response to transplant, typically for lymphomas or solid tumors, though valuable in some less common presentations of disease, such as leukemia cutis. Imaging techniques used to evaluate disease response typically include PET, CT, or MIBG, but may include x-ray, skeletal survey, or ultrasound in some cases.

Select “yes” if a radiologic assessment was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 87. If a radiologic assessment was not performed or used to determine disease status, check “no” and continue with question 89.

If radiological assessment was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 89.

**Question 87: Date assessed:**

Indicate the date (YYYY-MM-DD) the disease was assessed by radiological assessment. The sample collection date should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 95).

If the exact date is unknown, please view General Instructions, [General Guidelines for Completing Forms](#) for more information on reporting partial and unknown dates.

**Question 88: Was disease detected?**

If radiologic evidence of disease was found, check “yes”. If radiologic evidence of disease was not found,
check “no”.

**Question 89: Was the disease status assessed by clinical / hematologic assessment?**

Clinical/hematologic assessment is the least sensitive method of disease detection. Examples include circulating blasts in the bloodstream for AML or enlargement of a malignant mass for lymphoma/solid tumor as determined by physical exam. Every recipient who has an evaluation by a physician has a “clinical” assessment.

Select “yes” if a clinical/hematologic assessment was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 90. If a clinical/hematologic assessment was not performed or used to determine disease status, check “no” and continue with question 92.

**Question 90: Date assessed:**

Indicate the date (YYYY-MM-DD) the disease was assessed by clinical/hematologic assessment. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy (date reported in question 95).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

**Question 91: Was disease detected?**

If clinical/hematologic evidence of disease was found, check “yes”. If clinical/hematologic evidence of disease was not found, check “no”.

**Question 92: What was the recipient’s disease status immediately prior to the cellular therapy?**

Indicate the disease status of the primary transplant disease immediately prior to the cellular therapy. Disease response criteria vary by disease, and are outlined in the CIBMTR Forms Instructions Manual.

**Question 93: Date assessed:**

Indicate the date (YYYY-MM-DD) of the disease status reported in question 92. The date assessed should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 95).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.
Q94-249: Systemic Therapy Prior to Cellular Therapy

Question 94: Was systemic therapy given immediately prior to cellular therapy as part of the cellular therapy protocol?

Systemic therapy may include intravenous or oral chemotherapy with the intent to deplete circulating lymphocytes, reduce tumor burden or other reasons. If “yes”, continue with question 95. If “no”, continue with question 250.

If the recipient is receiving a cellular therapy after an HCT, do not report any therapy that was already reported on a Pre-TED F2400. The intent of this question is to capture therapy specific to the cellular therapy infusion.

Question 95: Date started:

Indicate the date (YYYY-MM-DD) the systemic therapy started. This should be the earliest start date of the first drug given.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 96-97: Specify the reason for which the systemic therapy was given per protocol:

Lympho-depleting therapy: Used to “prime” the patient for optimal CAR T-cell in vivo expansion and antitumor activity. Examples of lympho-depleting therapy include, but not limited to, ATG, Alemtuzumab (Campath) and Cyclophosphamide plus fludarabine.

Reduction of tumor burden: Refers to the reduction of the number of the cancer cells, the size of the tumor or the amount of cancer in the body.

If systemic therapy was given as “Lympho-depleting therapy” or for “Reduction of tumor burden”, continue with question 98. If systemic therapy was given for another reason, select “other reason” and specify in question 97.
Question 98-249: Specify preparative regimen drugs:

The form lists each drug by the generic name. The form also lists some drugs by broad categories, with specific drugs listed individually. For example, anthracycline is listed as the broad drug category, followed by the specific drugs of daunorubicin, doxorubicin, and idarubicin.

For each drug listed, indicate whether or not it was given as part of the systemic therapy used prior to the cellular therapy infusion. Report the total dose of each drug that was actually given. Do not report the prescribed dose or the daily dose. The pharmacy record or Medication Administration Record (MAR) should be used for determining the exact total dose given.

Some drugs used as part of the systemic therapy regimen are administered with guidance of serum pharmacokinetic testing to determine the recipient’s metabolism of the drug. This allows for individual “customization” of the drug dosing to optimize the desired effect and minimize the toxicity.

A common example of this situation occurs in the use of busulfan. In some cases, a “test dose” of the drug is given before the actual systemic therapy regimen is started, and this dose is used for acquiring drug levels that are used to adjust the dose that will be used in the systemic therapy regimen. In other situations, the first dose of the drug is given in the usual fashion as part of the systemic therapy regimen. After this first dose, serum drug levels are drawn and sent to a reference lab. The drug is continued at the starting dose until the lab results are reported and adjustment is made to later doses.

When a drug is used for the systemic therapy regimen where pharmacokinetics will be tested, it is important to distinguish whether the testing will be done with a “test dose” before beginning the preparative regimen or using the first dose of the systemic therapy regimen. The reporting of the dosing for the CIBMTR forms depends upon this distinction. This helps distinguish whether the dose is part of the therapeutic regimen, or not.

A test dose was given > 24 hours prior to the intended therapeutic dosing.

Example: A patient with AML underwent a cellular therapy; busulfan and cyclophosphamide were used as the systemic therapy regimen. The patient presented to clinic 9 days before the cellular therapy infusion, where a dose of busulfan at 0.5 mg/kg was given intravenously. Blood samples were drawn for the next 6 hours, after which the patient left the clinic. His samples were sent to a lab, results were returned the next day, and an adjusted dose of busulfan was calculated. He returned to the hospital 6 days before the cellular therapy infusion, and began to receive busulfan at the adjusted dose intravenously for 4 days, followed by cyclophosphamide, and proceeded to receive his cells. Since he received 0.5 mg/kg as a “test dose,” this would not be reported in his total systemic therapy regimen dose.
If a test dose was given, where the dose was distinct from the therapeutic dosing systemic therapy regimen (often 1-2 or more days prior to the initiation of regular dosing), the start date of the chemotherapy agent should be reported as the date the first therapeutic dose was administered. The actual dose received would NOT include the test dose.

The first dose of therapeutic dosing is used for monitoring.

**Example:** A patient with ALL underwent a cellular therapy infusion; busulfan and fludarabine were used as the systemic therapy regimen. She was admitted to the hospital 7 days before her cellular therapy infusion, and received a dose of busulfan at 0.8 mg/kg IV at 6:00 AM. Serum samples were drawn every 30 minutes until the next dose of Busulfan at 0.8 mg/kg IV was given at 12:00 noon. Her blood was sent to a reference lab, and she continued to receive busulfan every 6 hours. On day -6, the lab called with her drug levels, and it was determined that the current dose was correct. No adjustment was made, and she completed all 16 doses of busulfan. Since the dose of busulfan (0.8 mg/kg) that was used for drug testing was ALSO her first dose of the preparative regimen, it should be included in the amount of drug that was given for systemic therapy regimen.

If the first dose of the systemic therapy regimen was used to determine pharmacokinetics, the start date of the chemotherapy agent should be reported as the date the first dose was administered. The actual dose received would include the dose used for monitoring.

Test doses must be reported consistently at your center. Since most centers follow a consistent approach to pharmacokinetic testing, it should be straightforward for the center to adopt a consistent approach to the reporting of test doses.

For each drug indicated as “yes”:

- Drug doses must be reported in whole numbers. If the total dose includes a decimal, round to the nearest whole number (round up if 0.5 or greater). For paper submission, do not modify the number of boxes or include decimal values.
- Report the date (YYYY-MM-DD) the drug was administered. If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

If monoclonal antibody (mAb) is indicated as “yes”, examples of “other mAb” include Inotuzumab, Daratumomab, and Immune Checkpoint Inhibitors (Pembrolizumab, Nivolumab, Durvalinomab).

The “other drug” category should only be used if the drug is not one of the listed options. If more than one “other” drug is prescribed, list the generic name of the drugs in the space provided and attach a copy of the
source document using the attachment feature in FormsNet3SM.
Q250-252: Functional Status

**Question 250: What scale was used to determine the recipient’s functional status prior to the cellular therapy?**

The CIBMTR uses the Karnofsky/Lansky scale to determine the functional status of the recipient immediately prior to the start of the cellular therapy. The Karnofsky Scale is designed for recipients aged 16 years and older, and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. For recipients less than one year old, questions 250-252 should be left blank.

Select the appropriate performance scale, Karnofsky or Lansky, based on the recipient’s age.

**Question 251-252: Performance score prior to the cellular therapy:**

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. The CIBMTR uses the Karnofsky/Lansky scale to determine the functional status of the recipient immediately prior to the start of the cellular therapy. For the purposes of this manual, the term “immediately prior” represents approximately one month prior to the cellular therapy infusion.

Using the appropriate scale as selected in question 250, select the score (10-100) that best represents the recipient’s activity status immediately prior to the start of the preparative regimen. For an example of the Karnofsky / Lansky scale, see Appendix L.

If a Karnofsky / Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician’s clinic note), data management professionals should not assign a performance score based on analysis of available documents. Rather, a physician should provide documentation of the performance score.

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The CIBMTR recognizes that some transplant centers prefer to collect and use the ECOG performance score as opposed to the Karnofsky / Lansky score. Although the ECOG and Karnofsky / Lansky performance score systems are based on similar principles, the scales are not the same. For example, the Karnofsky / Lansky scale is described in 11 categories, whereas the ECOG performance status is reported in six categories. Due to the overlap between the two systems, an ECOG score of “one” can represent either “80” or “90” on the Karnofsky / Lansky scale.
Karnofsky / Lansky scale. For centers that collect only an ECOG performance score, CIBMTR will make the following accommodations when auditing the source data: Centers collecting ECOG scores should do so using standard practices to ensure accuracy. For the purposes of CIBMTR reporting, conversion of ECOG to Karnofsky / Lansky should follow a standard and consistent practice. This practice should be clear and reproducible. For more information regarding converting an ECOG score to a Karnofsky / Lansky score, see Appendix L.
Q253-311: Comorbid Conditions

This section will be answered for malignant hematologic disorders and solid tumor indications only

Question 253: Were there clinically significant co-existing disease or organ impairment at the time of patient assessment prior to preparative regimen?

* Hepatic and Renal Comorbidities

In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities

**Hepatic Comorbidity**: The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the systemic therapy regimen. If no systemic therapy was given, then it would be day -24 and the cellular therapy infusion date. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

**Renal (Moderate/Severe) Comorbidity**: Serum creatinine > 2 mg/dL or > 177 μmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the systemic therapy regimen. If no systemic therapy was given, then it would be day -24 and the cellular therapy infusion date. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

Report “yes” to question 253 if the recipient has a documented history and/or current diagnosis of any of the following:

<table>
<thead>
<tr>
<th>Documented Medical History</th>
<th>Question Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmia</td>
<td>254</td>
</tr>
<tr>
<td>Cardiac&lt;sup&gt;2&lt;/sup&gt;</td>
<td>255</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>256</td>
</tr>
<tr>
<td>Heart valve disease&lt;sup&gt;3&lt;/sup&gt;</td>
<td>258</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>262</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>264</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current Diagnosis at the Time of Pre-HCT Evaluation</th>
<th>Question Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatologic</td>
<td>269</td>
</tr>
<tr>
<td>Condition</td>
<td>Page</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Solid tumor, prior</td>
<td>270</td>
</tr>
<tr>
<td>Diabetes</td>
<td>257</td>
</tr>
<tr>
<td>Hepatic, mild</td>
<td>259</td>
</tr>
<tr>
<td>Hepatic, moderate/severe</td>
<td>260</td>
</tr>
<tr>
<td>Infection</td>
<td>261</td>
</tr>
<tr>
<td>Obesity</td>
<td>263</td>
</tr>
<tr>
<td>Psychiatric disturbance</td>
<td>265</td>
</tr>
<tr>
<td>Pulmonary, moderate</td>
<td>266</td>
</tr>
<tr>
<td>Pulmonary, severe</td>
<td>267</td>
</tr>
<tr>
<td>Renal, moderate/severe</td>
<td>268</td>
</tr>
<tr>
<td>Other (specify)</td>
<td>289 and 290</td>
</tr>
</tbody>
</table>

2 Ejection fraction (EF) ≤ 50% should be reported only if present on most recent test

3 Excluding asymptomatic mitral valve prolapse

4 Excluding non-melanoma skin cancer, leukemia, lymphoma, or multiple myeloma

5 Including any history of hepatitis B or hepatitis C infection

6 Including renal transplantation at any time in the patient’s history

The intent of this question is to identify serious pre-existing conditions that may have an effect on the outcome of the cellular therapy. For the purposes of this manual, the term “clinically significant” refers to conditions that are being treated at the time of pre-infusion evaluation, or are in the recipient’s medical history and could cause complications post-infusion. Conditions listed in the recipient’s medical history that have been resolved (e.g., appendectomy), and/or that would not pose a concern during or after the infusion should not be reported.

Additionally, for the purposes of this manual, the term “at the time of patient assessment” is defined as the pre-infusion evaluation period prior to the start of the preparative regimen. If the recipient does not have a documented history of clinically significant disease(s) or organ impairment(s), check “no” and continue with question 291.

For information regarding reporting clinically significant co-existing disease or organ impairment, see Appendix J.
Questions 254-290: Co-existing diseases or organ impairments

For each listed co-existing disease or organ impairment, check "yes," "no," or "unknown."

**Arrhythmia:** Any history of atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias requiring treatment.

**Cardiac:** Any history of coronary artery disease (one or more vessel coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, or ejection fraction < 50% on the most recent test.

**Cerebrovascular disease:** Any history of transient ischemic attack, subarachnoid hemorrhage, or cerebrovascular accident.

**Diabetes:** Requiring treatment with insulin or oral hypoglycemics in the last 4 weeks but not diet alone

**Heart valve disease:** Except asymptomatic mitral prolapse.

**Hepatic (mild):** Chronic hepatitis, bilirubin > upper limit of normal to 1.5x upper limit of normal, or AST/ALT > upper limit of normal to 2.5x upper limit of normal, or any history of hepatitis B or hepatitis C infection. See note in question 97.

**Hepatic (moderate/severe):** Liver cirrhosis, bilirubin > 1.5x upper limit of normal, or AST/ALT > 2.5x upper limit of normal. See note in question 97.

**Infection:** Documented infection, fever of unknown origin, or pulmonary nodules requiring continuation of antimicrobial treatment after day 0.

**Inflammatory bowel disease:** Any history of Crohn’s disease or ulcerative colitis requiring treatment.

**Obesity:** Patients with a body mass index > 35 kg/m^2 or BMI-for-age ≥ 95% (pediatric recipients only) during pre-transplant work-up period.

**Peptic ulcer:** Any history of peptic ulcer confirmed by endoscopy and requiring treatment.

**Psychiatric disturbance:** Depression, anxiety, bipolar disorder, or schizophrenia requiring psychiatric consult or treatment in the last 4 weeks.

**Pulmonary (moderate):** Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 66-80% or dyspnea on slight activity at transplant.
**Pulmonary (severe):** Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 ≤ 65% or dyspnea at rest or requiring oxygen at transplant.

**Renal (moderate/severe):** Serum creatinine > 2 mg/dL or > 177 μmol/L, or on dialysis at transplant, or prior renal transplantation. *See note in question 97.*

**Rheumatologic:** Any history of systemic lupus erythematosus, rheumatoid arthritis, polymyositis, mixed connective tissue disease, or polymyalgia rheumatica requiring treatment (do NOT include degenerative joint disease, osteoarthritis)

**Solid tumor (prior):** Treated at any time point in the patient's past history, excluding non-melanoma skin cancer, leukemia, lymphoma, or multiple myeloma. For each listed prior solid tumor, check “yes” or “no.” If “yes,” enter the year of diagnosis of the corresponding solid tumor.

**Other co-morbid condition:** The “other, specify” category should be used to report co-morbid conditions that are of similar clinical concern as the other listed options. Chromosomal abnormalities, impairments and/or disorders associated with the primary disease should not be reported in this section, (e.g., Ph+ for CML/ALL recipients).

**Question 291:** Was there a history of malignancy (hematologic or non-melanoma skin cancer) other than the primary disease for which this cellular therapy is being performed?

The intent of this question is to identify other malignancies that may have an effect on the outcome of the cellular therapy. A history of any benign tumor(s) should not be reported in this section. Malignancies reported in the previous solid tumor options should not be reported again here.

If the recipient receives an infusion for a disease that has transformed from one disease to another, the original malignancy should not be reported in this section. Details regarding disease transformation will be captured on the Disease Classification form (Form 2402). For more information regarding disease combinations and transformations, refer to the Common Disease Combinations and Common Disease Transformations tables in the Primary Disease for HCT / Cellular Therapy section of the Disease Classification Form (Form 2402).

Indicate if there was a history of hematologic malignancy or non-melanoma skin cancer other than the disease for which this infusion is being performed.

**Question 292-311:** Specify which malignancy(ies) occurred:

For each listed prior malignancy, check “yes” or “no.” If “yes,” enter the year of diagnosis of the corresponding malignancy.

Use questions 292-311 to report any prior hematologic malignancies or non-melanoma skin cancer that were not listed in questions 254-290. Solid tumors (except for non-melanoma skin cancers) should be...
reported in questions 270-288, not in questions 309-311.

4003: Cellular Therapy Product

This form must be completed for all products for recipients of non-HCT cellular therapy (including post-HCT “DCI/DLI” infusions). For recipients of hematopoietic cellular transplants (HCT), complete the appropriate HCT infusion form (Form 2006).

The Form 4003 is designed to capture product specific information for all products/infusions given to a recipient as part of a course of cellular therapy. In addition to use in research, this information is used for quality assurance measures, both by the NMDP and the Cord Blood Banks.

A series of collections from the same donor that uses the same collection method and mobilization cycle, even if the collections are performed on different days, should be considered a single cellular therapy product if only one set of manufacturing steps are applied to the collected material.

If more than one type of cellular therapy product is infused, each product type must be analyzed and reported on a separate form 4003. Products from the same donor but obtained using different manufacturing steps are considered different products and require multiple 4003 forms, one for each product.

Additionally, if the cells were manipulated or modified by different methods and at the end of the manufacturing process are combined for a single infusion or administration, it will be considered a single product and it will require a single Form 4003.

For more information see Appendix D–How to Distinguish Infusion Types and Appendix E–Definition of a Product.

Links to sections of form:
Q1-19: Cellular Therapy Product Identification
Q20-21: Cell Product Source
Q22-27: Collection Procedure
Q28-59: Cell Product Manipulation
Q60-68: Cell Product Analysis
Q69: Product Infusion

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text. If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals.
<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
</table>
Q1-19: Cellular Therapy Product Identification

Question 1: Name of product:

The name of the product reported here must match what was reported on Form 4000 question 42. This question is limited to commercialized products and is used to disable questions related to manufacturing. If the name of the product is not an option or if the product has no commercialized name (e.g. DCI/DLI product), select ‘other product’ from the list.

Question 2: Specify donor:

Indicate the donor type for this product. If the product is “off the shelf” or a “third party” donor product obtained from pharmaceutical companies or other corporate entities, donor type should still be identified.

An autologous product has cells collected from the recipient for his/her own use. Continue with question 4.

A related donor (allogeneic, related) is a blood-related relative. This includes syngeneic, monozygotic (identical) twins, non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc. Do not include adoptive parents/children or stepparents/children. Continue with question 4.

An unrelated donor (allogeneic, unrelated) is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or stepparents/children. Continue with question 3.

Question 3: Did NMDP/Be the Match facilitate the procurement, collection, or transportation of the product?

Distinguish if the product is an NMDP product or a non-NMDP product. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank, Anthony Nolan, and StemCyte International Cord Blood Center. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation.
**Question 4: Was the product a cord blood unit?**

Indicate "yes" if the product was a cord blood unit.

- If the product was an **autologous** cord blood unit, continue with question 8 to report the non-NMDP CBU ID.
- If the product was a **related** cord blood unit, continue with question 8 to report the non-NMDP CBU ID.
- If the product was an **NMDP unrelated** cord blood unit, continue with question 5 to report the NMDP CBU ID.
- If the product was a **non-NMDP unrelated** cord blood unit, continue with question 8 to report the non-NMDP CBU ID.

Indicate "no" if the product was not a cord blood unit.

- If the **autologous** product was not a CBU, continue with question 19.
- If the product was related but not a CBU, continue with question 14 to report donor DOB.
- If the unrelated donor was **NMDP** but not a CBU, report the NMDP donor ID in question 6
- If the unrelated donor was **non-NMDP** but not a CBU, report the non-NMDP unrelated donor ID in question 7

**Question 5: NMDP Cord Blood Unit:**

Report the NMDP Cord Blood Unit ID. This information is included on the product label, the product insert accompanying the product, and within the NMDP search/product documentation. The ID is always numeric and begins with "9" (e.g., 9000-0000-0). If the product ID does not begin with a “9,” the product may not be an NMDP cord blood unit and the source of the product should be double-checked. Continue with question 19.

**Question 6: NMDP Donor ID:**

Report the NMDP Donor ID. This information is included on the product label, the product insert accompanying the product, and within the NMDP search/product documentation. The ID is always numeric (e.g., 0000-0000-0) and is unique for each donor, assigned by the NMDP. Continue with question 19.

**Question 7: Non-NMDP unrelated donor ID: (not applicable for related donors)**

Do not complete this field if the recipient has an NMDP donor, a related donor, or a cord blood donor. This ID is often located on the product label, the product insert accompanying the product, and the registry-specific search/product documentation. Continue with question 9.
Question 8: Non-NMDP cord blood unit ID: (include related and autologous CBUs)

Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank and StemCyte International Cord Blood Center. This ID is often located on the product label, the paperwork accompanying the product, and registry specific search/product documentation. Enter the non-NMDP cord blood ID. Note that some cord blood banks can ship their units either through the NMDP or directly to the center. Carefully review the accompanying documentation to determine which is appropriate for your unit. You may wish to consult with your center’s Transplant Coordinator, as they will have insight as to how the product was acquired. Continue with question 9.

Question 9: Global Registration Identifier for Donors (GRID):

The Global Registration Identifier for Donors (GRID) was developed by the WMDA to ensure secure, reliable and unambiguous assignment of donors. The GRID standard is a 19-character donor identifier composed of three elements: Issuing Organization Number (ION), Registration Donor Identifier, and Checksum (shown below). This standard will ensure each donor ID is globally unique and will reduce the risk of misidentification of donors or their donations.


Question 10: Is there an ISBT DIN number associated with the product?

Report “yes” if there is an International Society of Blood Transfusion (ISBT) Donation Identification Number (DIN) associated with the product. If the product is a cord blood unit, continue with question 11, all other products continue with question 13. If the product has an ISBT label on it, the ISBT DIN number is in the upper left-hand corner and consists of a letter followed by 12 numbers, two numbers on the end, and a letter in a box. Example below:
Please find additional information regarding the ISBT DIN numbers and traceability at ISBT 128 Basics. For example, you may see a barcode with an alphanumeric string below it.

Report “no” if there isn’t an ISBT DIN associated with the product. If the donor is auto, continue with question 20. If the donor is related continue with question 15. If the donor is unrelated, non-NMDP continue with question 13.

**Question 11: Is the CBU ID also the ISBT DIN number?**

Answered only for cord blood units. Report “yes” if the non-NMDP CBU ID is the same as the International Society of Blood Transfusion (ISBT) Donation Identification Number (DIN) and continue with question 13.

If the CBU ID is not the same as the ISBT DIN number, select “no” and continue with question 12.

**Question 12: Specify the ISBT DIN number:**

Report the ISBT DIN number using the letter, 12 digits, 2 numbers on end, and the letter in the box. See question 10 for an explanation on ISBT DIN.

**Question 13-14: Registry or UCB Bank ID:**

Specify the registry used to obtain the adult donor or umbilical cord blood unit. The Bone Marrow Donors Worldwide codes have been adopted to avoid submitting the entire name and address of the donor registry.

For example, the registry code for Belgium donors is (B) but Belgium cord blood units the registry code is (BCB).

Some common banks that do not list with BMDW have been added to the Form 2006 revision 4 list, including St Louis Cord Blood Bank (SLCBB) and Viacord (VIAC).

If the donor was found through DKMS, report the registry that facilitated the cellular therapy product. Some registries may be listed more than once with BMDW (once for marrow/PBSC products and differently for cord blood products). Ensure that the appropriate code for the product was selected, because distribution of data is dependent on the code.
If there is no match code for the adult donor registry or cord blood bank, provide the registry’s official name in the “Specify other registry” field.

Please ensure that the registry you are entering under “other” is not already listed in the pull-down list for question 13. Entries such as NMDP adult donors, NMDP cords, and New York Cord Bank each have their own entries above.

**Question 15-16: Date of birth (donor / infant):**

For related or non-NMDP donors only, report if the donor’s/infant’s date of birth is “known” or “unknown” for question 15. If the donor’s/infant’s date of birth is known, report the date of birth (YYYY-MM-DD) in question 16. If the donor’s/infant’s date of birth is unknown, continue with question 17.

**Question 17-18: Age (donor / infant):**

For related or non-NMDP donors only, if the DOB is unknown, report if the donor’s/infant’s age is “known” or “unknown” for question 17. If the donor’s/infant’s age is known, report the donor’s/infant’s age at the time of product collection in question 18. Report the age in months if the recipient is less than 1 year old, otherwise report the age in years. If the donor’s/infant’s age at collection is unknown, continue with question 19.

**Question 19: Sex (donor / infant):**

For related or NMDP donors only, indicate the donor’s biological sex as “male” or “female.” For cord blood units, report the infant donor’s sex.
Q20-21: Cell Product Source

**Question 20-21: Date of cell product collection**

Report if the date of cell product collection is "known" or "unknown" for question 20. If the date of cell product collection is known, report the date (YYYY-MM-DD) in question 21. If the date of cell product collection is unknown, continue with question 22.

If the exact date is not known, General Instructions, [General Guidelines for Completing Forms](#) for more information regarding reporting partial or unknown dates.
**Q22-27: Collection Procedure**

* This section applies to Autologous infusions only. If this was an allogeneic infusion, continue to question 28.

**Question 22: Did the recipient have more than one mobilization event to acquire cells?**

Stem cells do not typically circulate in the bloodstream. Therefore, in order to increase the quantity of cells for collection, an agent is frequently given to the autologous recipient. The purpose of the agent is to move the stem cells from the bone marrow into the peripheral blood. This practice is often referred to as mobilization or priming. Occasionally, a bone marrow product may be primed using a growth factor.

For the purposes of this manual, the CIBMTR defines a mobilization event as the planned administration of growth factors or systemic therapy designed to enhance stem cell collection. If the donor requires an additional mobilization at a later date to collect an additional product, this should be considered an additional mobilization event. If the mobilization methods change (e.g., plerixafor is added starting on Day 3 of collection) this would be considered an additional mobilization event.

**Example 1:** An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. Since the collection and mobilization methods remained the same over the duration of the collection, this is considered one mobilization event.

**Example 2:** An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection, but the cell count was poor. GM-CSF was administered and the autologous recipient was re-collected. This is considered two mobilization events due to the change in mobilization drugs administered.

**Example 3:** An autologous recipient was mobilized with G-CSF and underwent a one-day PBSC collection, but the cell count was poor. The recipient then received plerixafor to enhance the mobilization. This is considered two mobilization events due to the change in mobilization drugs administered.

If more than one mobilization event occurred, report the number of events in question 23, else continue with question 24.

**Question 23: Specify the total number of mobilization events performed for this cellular therapy: (regardless of the number of collections or which collections were used)**

Report the total number of mobilization events performed for this cellular therapy. Include all mobilization events, even if a product from the mobilization event for this cellular therapy was not used during the
infusion. See examples in question 22 for more details.

**Question 24: Number of collections:**

Report the number of collections that occurred after the mobilization event(s) reported in questions 22 and 23. It is possible to have more than one collection per mobilization or a failed mobilization with no collection.

**Example 1:** (from above) An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. The mobilization methods remained the same but the number of collections reported will be two.

**Example 2:** (from above) An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection, but the cell count was poor. GM-CSF was administered and the autologous recipient underwent another collection. This is considered two mobilization events, but three collections.

**Question 25-26: Specify the method of product collection:**

Specify how the product was collected:

- **Bone marrow aspirate:** a small sample of liquid bone marrow is removed, usually from the hip bone, breastbone, or thigh bone.
- **Leukapheresis:** removal of blood to collect specific blood cells
- **Byoptic sample:** sample taken from a biopsy, typically a tumor biopsy.
- **Other method:** not fitting in a category listed above.

If the method of product collection is selected as 'Other method', specify the other product collection method in question 26 and continue with question 27.

**Question 27: Specify agent(s) used in the mobilization events: (check all that apply)**

Report if any of the following agents were used in the mobilization event(s) reported in questions 22-23.

- **G-CSF:** granulocyte colony-stimulating factor, filgrastim, Neupogen®
- **GM-CSF:** granulocyte macrophage colony-stimulating factor, sargramostim, Leukine®
- **Peglygated G-CSF:** pegfilgrastim, Neulasta
- **Plerixafor:** Mozobil
- **Other CXCR4 inhibitor:** examples include POL6326 and AMD3465. Report experimental and other CXCR4 inhibitors used to mobilize the donor here.
Q28-59: Cell Product Manipulation

This section specifies any manipulation that was done to manufacture the final cellular therapy product.

**Question 28:** Were the cells in the infused product selected / modified / engineered prior to infusion?

Indicate “yes” if the cells contained in the product were selected (i.e. selective retention of a population of desired cells through recognition of specified characteristics), modified or genetically engineered and continue with question 29. Indicate “no” if the cells contained in the product were not selected, modified or genetically engineered in any way prior to infusion and continue with question 53.

**Question 29: Specify the portion manipulated:**

If the product being infused as a cellular therapy (e.g. DLI/DCI) is a portion from a prior HCT, the portion becomes the “entire” product for the purposes of this form. The product can then be further divided.

Indicate the portion of the product that was manipulated. If the entire product was manipulated, select “entire product” and continue with question 31.

If a portion of the product was removed and manipulated, select “portion of product” and continue with question 30.

**Question 30: Was the unmanipulated portion of the product also infused?**

Indicate “yes” if the unmanipulated portion of the product was also infused. Indicate “no” if the unmanipulated portion of the product was not infused.

**Question 31: Was the same manipulation method used on the entire product / all portions of the product?**

If the same manipulation was used on the entire product or all portions of the product, indicate “yes”. If different manipulation methods were used indicate “no”. All of the manipulations for each portion of the product should be reported in questions 32-59.

**Question 32-33: Specify method(s) used to manipulate the product: (check all that apply)**

Indicate the method(s) of manipulation.
**Steps in Manipulation**
If the manipulation consists of several steps, individual steps do not need to be reported as separate manipulations. For example, T-cell depletion that is part of expansion does not need to be reported. However, if T-cell depletion and/or washing are done as standalone manipulations, they should be reported.

**Cryopreservation as a Manipulation**
Do not report cryopreservation (including plasma removal as part of cryopreservation) as a method of manipulation

**Cultured (ex-vivo expansion):** cells were placed in culture to increase in number (i.e. to expand) allowing for sufficient cells for infusion. Continue with question 53.

**Induced cell differentiation:** cells were placed in culture to give rise to cellular elements with biological characteristics other than those of the cells being cultured (i.e. mesenchymal stromal cells cultured to make osteoblasts; pluripotent stem cells cultured to make neural cell precursors). Usually, the description of the process would include the term “differentiation of cells X into cells Y”. This scenario can be seen in regenerative medicine indications. Continue with question 53.

**Cell selection – positive:** the manipulation of a cellular therapy product that a specific cell population(s) is enriched. This may be achieved by using an antibody that binds to a specific population of cells (e.g., CD3+ selection). Continue with question 53.

**Cell selection – negative:** the manipulation of a cellular therapy product such that a specific cell population(s) is reduced. Continue with question 53.

**Cell selection based on affinity to a specific antigen:** the cellular product undergoes selection to isolate the target population based on the ability of the target population to bind or recognize a specific antigen (e.g. a T cell population recognizing viral proteins or a protein associated with a cancer). Continue with question 53.

**Genetic manipulation (gene transfer / transduction):** cells are manipulated via gene transfer, a process by which copies of a gene are inserted into living cells in order to induce synthesis of the gene’s product; or transduction, a process by which foreign DNA is introduced into a cell by a virus or viral vector. These techniques deliberately alter the genetic material of an organism in order to make them capable of making new substances or performing new or different functions. Continue with question 34 to report the types of genetic manipulation.
Other cell manipulation: not fitting an above category. Specify manipulation in question 32 and continue with question 53.

Questions 34-52: Specify the type of genetic manipulation.
This section only applies if “genetic manipulation” was selected in question 31

Question 34-42: Transfection:

Transfection is a process of deliberately introducing naked or purified nucleic acids by viral or non-viral methods into eukaryotic cells. Continue with question 35 if the product underwent transfection or continue with question 43 if it did not.

Viral transduction: Viral transduction occurs when there is gene transfer by infection of a cell with nucleic acid by a virus, followed by viral replication in the affected cell. If “yes”, indicate the virus used in the viral transduction in questions 36 and 37. Indicate “no” if the product did not undergo viral transduction and continue with question 38.

Lentivirus: Lentiviruses are members of the genus of retroviruses that have long incubation periods and cause chronic, progressive, usually fatal disease in humans and other animals. Indicate “no” if a Lentivirus was not used for the viral transfection.

Retrovirus: Retroviruses are any group of RNA viruses that insert a DNA copy of their genome into the host cell to replicate. HIV is an example of a Retrovirus. Indicate “no” if a Retrovirus was not used for the viral transfection.

Non-Viral transfection: Non-viral transfection is the process of deliberately introducing naked or purified nucleic acids into eukaryotic cells. If “yes”, indicate the method of non-viral transfection in question 39-42. Indicate “no” if the product did not undergo non-viral transfection and continue with question 43.

Transposon: Transposons are discrete mobile sequences in the genome that can transport themselves directly from one part of the genome to another without the use of a vehicle such as phage or plasmid DNA. They are able to move by making DNA copies of their RNA transcripts which are then incorporated into the genome at a new site. Indicate “no” if Transposons were not used for the non-viral transfection.

Electroporation: Electroporation is a process of introducing DNA or chromosomes into cells using a pulse of electricity to briefly open the pores in the cell membranes. Indicate “no” if Electroporation was not used for the non-viral transfection.

Other non-viral transfection: Indicate “yes” if a different non-viral transfection method not previously listed
was utilized. Specify the other non-viral transfection method in question 42.

**Question 43-45: Gene editing:**

Gene editing is a type of genetic engineering in which DNA is inserted or removed from a genome using artificially engineered nucleases. If “yes”, specify which gene was edited in the manipulation in question 57.

If “other gene” is answered for question 44, specify the gene in question 45. Indicate “no” for question 43 if the cells did not undergo gene editing.

**Question 46: Were cells engineered to express a non-native antigen receptor?**

Indicate “yes” if the cells underwent a type of genetic engineering in which a gene is transferred codes for an antigen receptor other than one that may already be naturally present in the cell (e.g. T-cells have natural T-cell receptors [TCRs]; a transgenic TCR or a Chimeric Antigen Receptor [CAR] are non-native antigen receptors). Indicate “no” if the cells did not undergo transfer of such a gene and continue with question 63.

**Question 47-50: Specify the protein inserted into the cellular product:**

Specify which construct was utilized as part of the genetic manipulation process:

**T-cell receptor:** Heterodimeric antigen receptors present on the surface of T-cells1. Continue with question 51.

**Chimeric Antigen Receptor (CAR):** A cell-surface receptor that has been engineered to combine novel features and specificities from various sources in order to enhance its antigen specificity. Engineered T-cells or B-cells will produce the specialized receptor that will be capable of binding to an epitope on its target cell1.

The CAR construct consists of several genes that can exert different functions, such as augment the immune response by co-stimulation, increase affinity, and increase the time it persists in the circulation without being cleared. The CAR construct information is usually unique and may influence its effect against the disease or the severity of side effects. Specify which construct(s) was used in the making of the Chimeric Antigen Receptor (CAR) in question 47. If a construct was utilized that is not in the list, check “other construct” and specify in question 49.

For more information related to the different constructs and their functions, see this article: [https://www.jci.org/articles/view/80010](https://www.jci.org/articles/view/80010).

**Suicide gene:** cells underwent manipulation to have cell suicide inducing transgenes inserted into the
product. Specify the suicide gene in question 50.

**Question 51-52: Other genetic manipulation:**

Indicate "yes" for other genetic manipulation that does not fit into a category listed above and specify in question 52.

**Question 53-54: Was the product manipulated to recognize a specific target/antigen?**

Indicate "yes" if the cells were cultured or engineered so that the majority of cells in the end product are able to recognize or bind to a chosen target (e.g. proteins from a virus or a protein from a tumor) and specify the target in question 54. This manipulation can be done outside of the context of 'genetic manipulation'. If "no", continue with question 60.

If the target is viral, continue with question 55.

If the target is tumor/cancer antigen, continue with question 57.

If the target is something other than viral or tumor/cancer antigen, continue with question 59.

**Question 55-56: Specify viral target(s): (check all that apply):**

Select all viral target(s) that apply to the product. If the target is “other virus”, specify in question 56. Continue with question 60.

**Question 57-58: Specify the target antigen:**

Select all target antigen(s) that apply to the product. If the target is “other target antigen”, specify in question 58. Continue with question 60.

**Question 59: Specify other target:**

If the product was manipulated to recognize a specific target/antigen that does fit in a category above, specify the other target. Continue with question 60.

¹ NCIthesaurus: https://ncit.nci.nih.gov/ncitbrowser/
Q60-68: Cell Product Analysis

Question 60: Was transfection efficiency done? (genetically engineered cells)

Answered for genetically engineered cells only. Transfection efficiency is calculated as a percentage of transfected cells from all cells in the sample. There are a number of methods used to determine transfection efficiency including flow cytometry, fluorometry, microscopy, real-time quantitative PCR, etc.

Question 61: Date:

Specify the date (YYYY-MM-DD) when sample was taken for the transfection efficiency testing.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 62: Transfection efficiency:

Report the percent transfection efficiency. Round to the nearest whole number.

Question 63: Was transfection efficiency target achieved?

Transfection efficiency target will be defined by the protocol. Indicate “yes” or “no” if the target defined by the protocol was met.

Question 64: Was viability of cells done?

If the viability of the cells was quantified, select “yes” and report the date the sample was collected to determine viability in question 65 and the percentage of viable cells in question 66. Methods of testing cell viability are listed in question 67.

Question 65: Date:

Specify the date (YYYY-MM-DD) when the sample was collected to determine viability.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 66: Viability of cells:

Report the percent viability. Round to the nearest whole number.
Question 67-68: Method of testing cell viability:

Indicate the method of testing viability.

7-AAD (7-aminoactinomycinD) and Propidium iodide are compounds that can stain dead cells but will not cross the membrane of living cells. Cytometric techniques are used to calculate the percentage of viable cells in a sample.

Trypan Blue is a technique where the dead cells become stained when in contact with the compound, but living cells remain impermeable to the dye. Cells are counted under a microscope to determine the percentage of viable cells in a sample.

If both methods of viability testing are performed, report 7-AAD results. If the cell viability was tested using a different method, select “other method” and specify the method in question 68.
Q69: Product Infusion

Question 69: Specify the total number of planned infusions: (of this product) (as part of the course of cellular therapy)

Report the number of infusions specified per protocol. This question is used to make the correct number of Cellular Therapy Infusion forms (Form 4006) come due. Each infusion must be part of the protocol and will be given regardless of disease assessment.

Example 1. The protocol specifies three infusions are to be given as part of the course of cellular therapy. Report the total number of planned infusions as “3”.

Example 2. The protocol specifies five infusions are to be given as part of the course of cellular therapy. The recipient will be assessed after the first three infusions to see if additional infusions will be tolerated (not based on disease status) and two more infusions may be given. Report the total number of planned infusions as “5”. If the last two infusions do not occur, contact your CIBMTR CRC.
4006: Cellular Therapy Infusion

This form must be completed for all infusions for recipients of non-HCT cellular therapy (including post-HCT “DCI/DLI” infusions). For recipients of hematopoietic cellular transplants (HCT), complete the appropriate HCT infusion form (Form 2006).

The Form 4006 is designed to capture infusion-specific information for all infusions given to a recipient as part of a course of cellular therapy. In addition to use in research, this information is used for quality assurance measures, both by the NMDP and the Cord Blood Banks.

Product specific information is collected on Cellular Therapy Product Form 4003. A Form 4003 is required for each product and a Form 4006 is required for each infusion of that product. For example, a single product may be infused three times per course of cellular therapy.

If more than one infusion occurs, as defined by event date, each infusion must be analyzed and reported on a separate form 4006. This is true even if it’s the same product being infused on a later date.

For more information see Appendix D–How to Distinguish Infusion Types and Appendix E–Definition of a Product.

Links to sections of form:
Q1-45: Product Infusion
Q46-49: Concomitant Therapy

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<td>Add</td>
<td>Added in additional clarification regarding total cell counts administered, what constitutes unselected lymphocytes, and T-helper cells (Q17-24).</td>
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<td>Version 3 of the 4006: Cell Therapy Infusion section of the Forms Instructions Manual released. Version 3 corresponds to revision 3 of the Form 4006.</td>
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Q1-45: Product Identification

Questions 1-6: Not all of these identifiers are applicable to all products. The ID/number should be found with the product bag or shipping manifest. Choose the identifier that is most appropriate. Please do not override a field, but rather select yes or no.

Question 1-2: Cell product ID:

Report if the product has a Cell product ID in question 1 and specify the ID in question 2. Product IDs can be numeric or alphanumeric.

Question 3-4: Batch number:

Report if the product has a Batch number in question 3 and specify the Batch number in question 4. Batch numbers can be numeric or alphanumeric.

Question 5-6: Lot number:

Report if the product has a Lot number in question 5 and specify the Lot number in question 6. Lot numbers can be numeric or alphanumeric.

Question 7: Date of this product infusion:

Report the date (YYYY-MM-DD) this product was infused. If the product was infused over multiple days, report the first date of infusion.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 8-10: Was the entire volume of product infused?

If the product being infused as a cellular therapy (e.g. DLI/DCI) is a portion from a prior HCT, the portion becomes the "entire" product for the purposes of this form. The intent is to capture if the product being infused was given in its entirety or not.

If the entire volume of the product was not infused, specify what happened to the reserved portion in question 9 and 10.
**Question 11-12: Specify the route of product infusion:**

Report the route by which the product was infused.

**Intravenous** refers to an infusion into the veins – examples include infusion via central line or via catheter. Intramedullary refers to an infusion into the marrow cavity within a bone, such as directly into the proximal tibia or anterior aspect of the femur. **Intraperitoneal** refers to an infusion within the peritoneal cavity. **Intra-arterial** refers to an infusion within an artery or arteries. **Intramuscular** refers to an infusion within a muscle. **Intrathecal** refers to an infusion within the cerebrospinal fluid at any level of the cerebrospinal axis, including injection into the cerebral ventricles. **Intraorgan** refers to an infusion within an organ such as the heart, liver, lungs, etc. Specify the site in question 13. **Locally in the tissue** refers to an infusion in a restricted area of the body or in a tumor that cannot be classified as intraorgan.

If the route of infusion is not one of the above options, select “other route of infusion” and specify the infusion route in question 12.

**Question 13-14: Specify the site of intraorgan administration of cells:**

If the route of product infusion was intraorgan, specify the site of intraorgan administration. If the site of infusion is not in the option list, select “other site” and specify the site in question 14.

**Question 15: Recipient weight used for this infusion:**

Report the recipient’s actual body weight used to calculate the cell dose for this infusion. This weight is usually documented on infusion orders or admitting orders. Report weight to the nearest whole kilogram or pound (round up if 0.5 or greater). Do not report adjusted body weight, lean body weight, or ideal body weight.

**Question 16: Recipient height used for this infusion:**

Report the recipient’s height at infusion. Report the recipient’s height to the nearest whole centimeter or inch (round up if 0.5 or greater).

**Question 17-45: Reporting total number of cells**

Report the total number of cells (not cells per kilogram) contained in the product administered, not corrected for viability.
This section collects the total number of cells that were infused in a specific product. All of the cells that were listed on the F4000 Pre-CTED in question 36 are included here. Only respond to the cells that are applicable to this infusion. Note, CD3 is present on all T-cells whether they are CD4+ or CD8+ T-cells.

**Question 17-18: Total number of cells administered:**

Report the total cell count contained in the product administered, not corrected for viability. If the type of cells are not specified, report the total number of cells present at time of the infusion. If multiple bags were infused together, report the sum of each bag.

**Question 19-20: Lymphocytes (unselected) administered:**

Unselected means a specific lymphocyte sub-population (e.g. CD4+) was not targeted. This includes all types of lymphocytes, those that have not been selected via flow cytometry or other method. If yes, report the total number of unselected lymphocytes (e.g., CD3+ cells) administered in the product in question 20.

**Question 21-22: CD4+ lymphocytes administered:**

The lab report may display this value as CD3+CD4+. These cells are also known as T-helper cells. If yes, report the total number of CD4+ cells administered in the product in question 22.

**Question 23-24: CD8+ lymphocytes administered:**

The lab report may display this value as CD3+CD8+. These cells are also known as T-helper cells. If yes, report the total number of CD8+ cells administered in the product in question 24.

**Question 25-26: Natural killer cells (NK cells) administered:**

NK cells are a type of cytotoxic lymphocyte critical to the innate immune system. They usually express CD56 / CD16 on their cell surface. If yes, report the total number of natural killer cells (NK cells) administered in the product in question 26.

**Question 27-28: Dendritic cells / tumor cell hybridomas administered:**

Dendritic cells are antigen-presenting cells (also known as accessory cells) of the immune system. Their main function is to process antigen material and present it on the cell surface to the T-cells of the immune system. If yes, report the total number of dendritic cells or tumor cell hybridomas administered in the product in question 28.

**Question 29-30: Mesenchymal stromal stem cells (MSCs) administered:**

MSCs are multipotent stromal cells that can differentiate into a variety of cell types, including: osteoblasts
(bone cells), chondrocytes (cartilage cells), myocytes (muscle cells) and adipocytes (fat cells). If yes, report the total number of MSCs administered in the product in question 30.

**Question 31-32: Unspecified mononuclear cells administered:**

A mononuclear cell is defined as any blood cell with a round nucleus (i.e., a lymphocyte, a monocyte, or a macrophage). These blood cells are a critical component of the immune system’s ability to fight infection and adapt to intruders. If yes, report the total number of unspecified mononuclear cells administered in the product in question 32.

**Question 33-34: Endothelial progenitor cells (EPC) administered:**

EPC is a term that is applied to multiple different cell types that play roles in the regeneration of the endothelial lining of blood vessels. If yes, report the total number of endothelial progenitor cells (EPCs) in the product in question 34.

**Question 35-36: Human umbilical cord perivascular (HUCPV) cells administered:**

HUCPV cell is a term that is applied to mesenchymal, non-hematopoietic, non-endothelial cells that are isolated from the umbilical cord. If yes, report the total number of human umbilical cord perivascular (HUCPV) cells in the product in question 36

**Question 37-38: Cardiac progenitor cells administered:**

Cardiac progenitor cells are tissue-specific stem progenitor cells within the heart. If yes, report the total number of cardiac progenitor cells administered in the product in question 38.

**Question 39-40: Islet cells administered:**

Islet cells are found in the pancreas. The pancreas contains clusters of cells that produce hormones and these clusters are known as islets. If yes, report the total number of islet cells administered in the product in question 40.

**Question 41-42: Oligodendrocytes administered:**

Oligodendrocytes are glial cells similar to an astrocyte but with fewer protuberances. These cells produce myelin in the central nervous system. If yes, report the total number of oligodendrocytes administered in the product in question 42.

**Question 43–45: Other cell type administered:**

If a different cell type not previously mentioned was infused, specify the other cell type in question 44 and
report the total number administered in the infusion in question 45.
**Q46-49: Concomitant Therapy**

**Question 46: Did the recipient receive concomitant therapy?**

Concomitant therapy is therapy given to enhance the function of the cellular therapy. In cases where a recipient has both HCT and cell therapy, this question applies to the cell therapy infusion, not the HCT. If the recipient had a prior HCT and the therapy was already captured on the HCT form as being HCT prep regimen, it is not reported again. See question 47 for a list of drugs that can be given as concomitant therapy.

**Question 47-48: Specify drugs: (check all that apply)**

Select the drug(s) given as concomitant therapy. If the drug given is not in the list, check “other” and specify the other drug in question 48.

**Question 49: Specify time point:**

This question applies to the therapy as a whole, not to each individual drug. Concomitant therapy can be given simultaneously with the cellular therapy infusion or up to 24 hours after infusion (post cell therapy).
4100: Cellular Therapy Essential Data Follow-Up

A form must be completed for all recipients of cellular therapy (non-HCT), including post-HCT “DCI/DLI” infusions. For recipients of hematopoietic cellular transplants, complete the appropriate HCT follow-up form.

The Post-Cellular Therapy Essential Data (Post-CTED) follow-up form focuses on key follow-up information, including the survival status of the recipient, causes of death if the recipient died in the period since the last report, additional cellular infusions performed for the same indication, response to the cellular therapy, relapse, current hematologic findings, development of second or new malignancies, persistence of the cellular product depending on the product, development and severity of toxicities (e.g. cytokine release syndrome, neurotoxicity) and fertility information.

The Post-CTED form must be completed at the following time points: 100 days, six months, and annually post-cellular therapy. The follow-up reporting schedule is determined by the product, being genetically modified or not. The structure of the Post-CTED is such that each form should fit on a timeline with distinct start and stop dates that do not overlap any other forms, except in the case where an HCT is also received.

In scenarios where both HCT and cellular therapy forms are being completed, completion of this form should be based on the time period after cellular therapy infusion date (i.e. 100 days after the cellular therapy infusion date). Duplicate questions between HCT and cellular therapy forms may be disabled on the Post-CTED.

Links to sections of form:

Q1-3: Survival
Q4-8: Subsequent Cellular Infusions
Q9-11: Best Response to Cellular Therapy
Q12-13: Disease Relapse or Progression
Q14-17: Peripheral Blood Count Recovery
Q18-32: Current Hematologic Findings
Q33: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder
Q34-55: Persistence of Cells
Q56-75: Graft vs. Host Disease
Q76-187: Toxicities
Q188-192: Infection
Q193-194: Functional Status
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
</table>
| 1/24/2019  | 4100: Cellular Therapy Essential Data Follow-up | Modify | Added examples (in red below) in question 33 on when to use “previously reported” option: If a new malignancy is reported, please complete the Subsequent Neoplasms Form 3500 to answer questions specific to the new malignancy. The option of ‘Previously reported’ should only be used if the same new malignancy instance has already been reported on a F3500. See examples below. If there is a question regarding use of this option, please contact your CIBMTR CRC.
Example 1. Recipient develops a new malignancy at day +68. It is reported at the time the 100-day form 4100 is completed. Question 33 should be answered as ‘yes’ and the form 3500 should be completed to report all new malignancy information.
Example 2. Recipient develops a new malignancy at day +68 and had received a commercial CAR-T product. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The form 3500 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. No other new malignancy develops during the 100-day reporting period. When the 100-day form 4100 is completed, question 33 should be answered as ‘previously reported’.
Example 3. Recipient develops a new malignancy at day +68 and had received a commercial CAR-T product. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The form 3500 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. Another new malignancy develops at day +100. It is decided to report the 2nd new malignancy on the 100-day form 4100 since it is due. Question 33 should be answered as ‘yes’ to create another form 3500.                                                                 |
| 1/17/2019  | 4100: Cellular Therapy Essential Data Follow-Up | Modify | Added (in red below) clarification on how hypogammaglobulinemia is documented: Report the date (YYYY-MM-DD) in question 126 when the hypogammaglobulinemia was documented by either a physician/health care provider or determined by lab results. If the hypogammaglobulinemia continues from a prior reporting period, report the original diagnosis date as the onset date and override the error.
Example 1. The recipient developed hypogammaglobulinemia at day +22 which was reported on the 4100 day 100 form. The lab results continue to show IgG levels < 600 mg/dl during the 6 month reporting period. Report the original diagnosis date on the 4100 6 month form and override the error.                                                                                                                                 |
<p>| 12/13/2018 | “Toxicities”                          | Modify | Added clarification on how hypogammaglobulinemia is documented: Report the date (YYYY-MM-DD) in question 126 when the hypogammaglobulinemia was documented by either a physician/health care provider or determined by lab results.                                                                                                                                                                                                                                                   |</p>
<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/20/2018</td>
<td>4100: Cellular Therapy Essential Data Follow-Up</td>
<td>Modify</td>
<td>Added further clarification for various portions of this manual to provide better instruction on new sections of revision 4 of the Form 4100.</td>
</tr>
<tr>
<td>11/19/2018</td>
<td>4100: Cellular Therapy Essential Data Follow-Up</td>
<td>Modify</td>
<td>Added the following reporting instruction for question 76: This rapid cytokine release into the circulation results in fever (must be ≥100.4F or ≥38C), nausea, chills, hypotension, tachycardia, asthenia, headache, rash, sore throat, respiratory failure or death.</td>
</tr>
<tr>
<td>11/19/2018</td>
<td>4100: Cellular Therapy Essential Data Follow-Up</td>
<td>Modify</td>
<td>Added the following reporting instruction for questions 81-96: Symptoms of CRS: Fevers (≥100.4F or ≥38C): A disorder characterized by elevation of the body’s temperature above the upper limit of normal. Do not report fever less if than 100.4F or 38C in this field. Fever less than 100.4F or 38C does not qualify as a symptom of CRS.</td>
</tr>
</tbody>
</table>
Q1-3: Survival

Question 1: Name of Product: (for most recent cell therapy infusion)

The name of the product reported here must match what was reported on Form 4000 R5 question 42. This question is limited to commercialized products and is used to enable/disable questions related to toxicities. If the name of the product is not an option or if the product does not have a commercialized name (e.g. DCI/DLI product), select ‘other product’ from the list.

Question 2: Date of actual contact with the recipient to determine medical status for this follow-up report:

Enter the date of actual contact with the recipient to evaluate medical status for this follow up report. For cases where both cellular therapy and HCT forms are being completed, the contact date on the F4100 should be in relation to the cellular therapy event date.

In general, the date of contact closest to the designated time point indicated on the form (e.g. Day+100, 6 months, or annual follow-up visit) should be reported. Report the date of actual contact with the recipient to evaluate medical status for the reporting period. Preferred evaluations include those from the cellular therapy physician, referring physician, or other physician currently assuming responsibility for the recipient’s care. In the absence of contact with a physician, other types of contact may include a documented phone call with the recipient, a laboratory evaluation, or any other documented recipient interaction on the date reported. If there was no contact on the exact time point, choose the date of contact closest to the actual time point.

Below, the guidelines show an ideal approximate range for reporting each post-cellular therapy time point:

<table>
<thead>
<tr>
<th>Form</th>
<th>Time Point</th>
<th>Approximate Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>F4100</td>
<td>100 days</td>
<td>+/- 15 days</td>
</tr>
<tr>
<td>F4100</td>
<td>6 months</td>
<td>+/- 30 days</td>
</tr>
<tr>
<td>F4100</td>
<td>Yearly</td>
<td>+/- 30 days</td>
</tr>
</tbody>
</table>

Recipients are not always seen within the approximate ranges and some discretion is required when determining the date of contact to report. In that case, report the date closest to the date of contact within reason. The examples below assume that efforts were undertaken to retrieve outside medical records from the primary care provider, but source documentation was not available.

Example 1. The 100 day date of contact doesn’t fall within the ideal approximate range.
The recipient had an infusion on 1/1/18 and is seen regularly until 3/1/18. After that, the recipient was referred home and not seen again until 7/1/18 for a restaging exam and 7/5/18 for a meeting to discuss the results.

What to report:
100 Day Date of Contact: 3/1/18 (Since there was no contact closer to the ideal date of 4/11/18, this date is acceptable)
6 Month Date of Contact: 7/5/18 (note the latest disease assessment would likely be reported as 7/1/18)

**Example 2.** The 100 day date of contact doesn't fall within the ideal approximate range and the recipient wasn't seen again until 1 year post-HCT.
The recipient had an infusion on 1/1/18 and is seen regularly until 3/1/18. After that, the recipient was referred home and not seen again until 1/1/19 for a restaging exam and 1/4/18 for a meeting to discuss the results.

What to report:
100 Day Date of Contact: 3/1/18 (Since there was no contact closer to the ideal date of 4/11/18, this date is acceptable)
6 Month Form: Indicate the recipient is lost to follow-up in FormsNet3
1 Year Date of Contact: 1/4/19 (note the latest disease assessment would likely be reported as 1/1/19)

**Additional information:**

A date of contact should never be used multiple times for the same recipient’s forms.
*For example, 6/1/18 should not be reported for both the 6 month and 1 year. Instead, determine the best possible date of contact for each reporting period; if there is not a suitable date of contact for a reporting period, this may indicate that the recipient was lost to follow-up.

If the recipient has a disease evaluation just after the ideal date of contact, capturing that data on the form may be beneficial.

- For example, if the recipient’s 90 day restaging exam was delayed until day 115 and the physician had contact with the recipient on day 117, the restaging exams can be reported as the latest disease assessment and day 117 would be the ideal date of contact, even though it is just slightly after the ideal approximate range for the date of contact.

**Date of Contact & Subsequent Infusion**
The date of contact reported depends on the regulatory requirements of the product and whether follow-up is required.
**Example 3.** The recipient receives a subsequent HCT or cellular therapy.
The recipient had a cellular therapy on 1/1/18 and was seen regularly through the first 100 days. During the 6 month reporting period, the recipient goes on to receive an HCT or subsequent cellular therapy.

**What to report**

**Regulatory requirements specify at least 15 years of follow-up data be collected on recipients of genetically modified cellular therapy products:** The date of contact reported should be appropriate to the time frame of the form being completed (e.g. 6 months)

**Cellular therapy products where regulatory requirements do not specify follow-up reporting:** The date of contact reported will be the date prior to the start of the preparative regimen for the subsequent infusion (in cases where no prep is given, it is the day prior to the infusion).

**Date of Contact & Death**

In the case of recipient death, the date of death should be reported as the date of contact regardless of the time until the ideal date of contact. The date of death should be reported no matter where the death took place (inpatient at the transplant facility, at an outside hospital, in a hospice setting, or within the recipient’s home).

**Example 4.** The recipient has died before their six month reporting period.
The recipient had an infusion on 1/1/18 and was seen regularly through the first 100 days. They had restaging exams on 4/4/18 and were seen on 4/8/18, and then died on 5/13/18 in the hospital emergency room.

**What to report:**

100 Day Date of Contact: 4/8/18 (note the latest disease assessment would likely be reported as 4/4/18)
6 Month Date of Contact: 5/13/18 (though the death does not occur within the ideal approximate range for 6 months)

**Example 5.** The recipient has died after their six month time point.
The recipient had an infusion on 1/1/18 and was seen regularly through the first 100 days. The recipient had restaging exams on 4/22/18 and was seen on 4/23/18. Based on findings in the restaging exam, the recipient was admitted for additional treatment. The disease was found to be refractory on a 6/25/18 restaging exam, and the recipient was discharged to hospice on 7/8/18. The hospital was notified via telephone that the recipient died on 7/16/18.

**What to report:**

100 Day Date of Contact: 4/23/18 (note the latest disease assessment would likely be reported as 4/22/18)
6 Month Date of Contact: 7/16/18 (note the latest disease assessment would likely be reported as 6/25/18)
If the exact date is unknown, please view General Instructions, [General Guidelines for Completing Forms](#) for more information on reporting partial and unknown dates.

**Survival status**
For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2100 and F4100. To reduce the reporting burden, duplicated questions on the Cellular Therapy forms are disabled. This includes Survival Status reported on F4100.

**Question 3: Specify the recipient’s survival status at the date of last contact:**

Indicate the clinical status of the recipient on the date of actual contact for follow-up evaluation. If the recipient has died, answers to subsequent questions should reflect the recipient’s clinical status between the date of last report and their death. The center must also complete a Recipient Death Data Form (Form 2900).
**Q4-8: Subsequent Cellular Infusions**

All additional cellular therapy infusions given for the same indication per protocol require a separate infusion form (Form 4006) and should be reported on the Form 4003 for this course of cellular therapy. If a cellular therapy was administered for treatment of a different indication, or in response to disease progression / no response, a new Form 4000 (Pre-CTED) must be completed.

**Question 4: Has the recipient received a new course of cellular therapy (unplanned) since the date of the last report?**

If the recipient started a new course of cellular therapy (unplanned) that is different than the course reported on the form 4000, answer “yes” and continue with question 5.

In cases where the course of cellular therapy is being given post-HCT and HCT follow-up forms are also being completed, and where the cellular therapy course overlaps two HCT reporting periods, the new course only needs to be reported once on the HCT follow-up forms.

Example 1. The new course of cellular therapy consisted of multiple infusions that happened at the end of the 6 month HCT reporting period into the beginning of the 1 year HCT reporting period. The new course of cellular therapy should be reported only on the 6 month HCT form.

If the recipient has not received a new course of cellular therapy (unplanned) since the date of last report, continue with question 7.

**Question 5: Specify the reason for which cellular therapy was given:**

If additional infusions were given for the same indication per protocol, do not report those here. Please update form 4003 for the applicable product with the correct number of infusions given per protocol. Each infusion requires a separate form 4006.

If the reason for the new course of cellular therapy was failure to respond or in response to disease assessment, or for a new indication, report the event date in question 6.

**Question 6: Date of cellular therapy:**

Report the date (YYYY-MM-DD) of the new course of cellular therapy (unplanned). If the new course of cellular therapy includes multiple infusions, the date of the first infusion should be reported here. This will
require completion of a new form 4000.

**Subsequent HCT**
For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2100 and F4100. To reduce the reporting burden, duplicated questions on the Cell Therapy forms are disabled. This includes a subsequent HCT reported on F4100.

**Question 7 & 8: Did the recipient receive an HCT since the date of last report?**

If the recipient received an HCT since the date of the last report, report the date (YYYY-MM-DD) of HCT in question 11 and also complete CIBMTR HCT form 2400 (Pre-Transplant Essential Data).

If the recipient did not receive an HCT since the date of the last report, continue with question 9.
Q9-11: Best Response to Cellular Therapy

This section may not fit perfectly to all possible indications for cellular therapy. Please select the response that is most applicable to the indication for treatment.

Question 9: What was the best response to the cellular therapy?

This section collects the data known as “best response to cellular therapy”. The purpose of this section is to report the recipient’s best response to the planned course of cellular therapy. This section applies to both malignant and non-malignant diseases and disorders. If the recipient received a prior HCT, do not report the response to the HCT, a separate evaluation after the cellular therapy is required.

For malignant diseases, appropriate responses would be:

- complete response
- partial response
- no response
- disease progression
- unknown

For recipients with continued complete response (CCR) (those in CR at the time of infusion), please report CR for best response.

For non-malignant disorders, appropriate responses would be:

- normalization of organ function
- partial normalization of organ function
- no response
- worsening of organ function
- unknown

If the indication is infection, the appropriate responses would be:

- complete response
- partial response
- no response
- unknown
<table>
<thead>
<tr>
<th>Indication</th>
<th>Partial Response</th>
<th>Complete Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promote stem cell engraftment</td>
<td>- Neutrophil engraftment without platelet engraftment</td>
<td>Engraftment occurs</td>
</tr>
<tr>
<td></td>
<td>- Platelet engraftment without neutrophil engraftment</td>
<td></td>
</tr>
<tr>
<td>Suboptimal donor chimerism (post-HCT)</td>
<td>Increase in chimerism but not 100% donor</td>
<td>100% donor chimerism</td>
</tr>
<tr>
<td>Immune Reconstitution (post-HCT)</td>
<td>N/A</td>
<td>CD3 &gt;200/mm³</td>
</tr>
<tr>
<td>GVHD prophylaxis (with HCT)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>GVHD treatment (post-HCT)</td>
<td>- Improvement but not resolution of symptoms</td>
<td>- Resolution of symptoms</td>
</tr>
<tr>
<td></td>
<td>- Remains on immune suppression</td>
<td>- Able to wean immune suppression</td>
</tr>
<tr>
<td>Prevent disease relapse</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Relapsed, persistent or progressive disease</td>
<td>Improvement in disease burden, but with persistent disease</td>
<td>No evidence of disease</td>
</tr>
<tr>
<td>(post-HCT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection treatment</td>
<td>Decrease in infectious burden without resolution</td>
<td>Undetectable infection</td>
</tr>
<tr>
<td>Infection prophylaxis</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>B-cell lymphoproliferative disorder</td>
<td>Improvement in disease burden, but with persistent disease</td>
<td>No evidence of disease</td>
</tr>
<tr>
<td>(PTLD, EBV lymphoma)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoimmune Disease</td>
<td>Improvement in organ function but with residual organ dysfunction</td>
<td>Normalization of organ function</td>
</tr>
<tr>
<td>Cardiovascular Disease</td>
<td>Improvement in organ function but with residual organ dysfunction</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal Disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurologic Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ocular Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid Tumor</td>
<td>Improvement in disease burden, but with persistent disease</td>
<td>No evidence of disease</td>
</tr>
<tr>
<td>Malignant Hematologic Disorder</td>
<td>Improvement in disease burden, but with persistent disease</td>
<td>Hematologic Remission or MRD negative</td>
</tr>
<tr>
<td>Non-Malignant Disorder</td>
<td>Persistent Disease</td>
<td>Resolution of Disease Process</td>
</tr>
</tbody>
</table>

If the recipient relapses/progresses and receives therapy for the disease relapse/progression, the response
to that additional therapy should not be reported in this section. The best response prior to the relapse/progression should be reported.

**Question 10-11: Was the date of best response previously reported?**

If the date of best response was previously reported, select “yes” and continue with question 12. **This option is not available on the 100 day report.**

If the date of best response has not been reported, select “no” and report the date (YYYY-MM-DD) in question 11.

If the exact date is unknown, please view General Instructions, [General Guidelines for Completing Forms](#) for more information on reporting partial and unknown dates.
Question 12-13: Was a disease relapse or progression detected since the date of last report?

Disease relapse or progression can be documented by a variety of methods including molecular, flow cytometry, cytogenetic/fluorescent in situ hybridization (FISH), radiographic or hematological/clinical. Answer “yes” if disease relapse or progression was documented by any one of the methods and report the date (YYYY-MM-DD) of the relapse or progression detected since the date of the last report in question 13.

If a disease relapse or progression was not documented, answer “no” and continue to question 14.
Q14-17: Peripheral Blood Count Recovery

Questions 14-17 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.

Question 14: Was there evidence of initial recovery?

Absolute neutrophil recovery (ANC) recovery is defined as an ANC of $\geq 500/mm^3$ (or $\geq 0.5 \times 10^9/L$) for three consecutive laboratory values obtained on different days. Date of ANC recovery is the date of the first of three consecutive laboratory values where the ANC is $\geq 500/mm^3$. At some institutions, the laboratory reports display the ANC value once there are sufficient white blood cells to perform a differential count. At other institutions, the laboratory reports do not display the ANC, and it must be calculated from the white blood cell count (WBC) and the percent of segmented and band neutrophils (if the differential was performed on a machine, the percent neutrophils will include both segmented and band neutrophils). If the laboratory report displays an automated ANC value of exactly $500/mm^3$, the actual ANC value should be calculated from the manual differential if available. The calculated value from the manual differential will determine ANC recovery. If your institution’s laboratory reports do not display the ANC value, use the following calculation to determine the ANC:

**Example 1: Calculating Absolute Neutrophil Count (ANC)**

\[
\frac{\% \text{ segmented neutrophils}}{+} \frac{\% \text{ band neutrophils}}{=} \% \text{ neutrophils} \\
\times \text{ white blood cell count/mm}^3 = \text{ absolute neutrophil count/mm}^3
\]

**Example:**

(Divide percentage by 100 to convert to decimal)

\[
0.45 \text{ segmented neutrophils} \\
+ 0.05 \text{ band neutrophils} \\
= 0.50 \text{ neutrophils} \\
\times 1000/mm^3 \text{ white blood cell count} \\
= 500/mm^3 \text{ absolute neutrophil count}
\]

\[
\text{ANC} = 500/mm^3 = 0.5 \times 10^9/L = 0.5 \times 10^9/mL = 0.5 \times 10^3/mm^3
\]

Traditionally, the definition of ANC recovery required the selection of the first date of three consecutive days
in which the recipient's ANC was ≥ 0.5×10^9/L (500/mm^3). For various reasons it may not be possible to obtain daily laboratory values. Under those circumstances, report ANC recovery based upon three consecutive laboratory values (drawn more than a day apart) as long as the ANC remains ≥ 0.5×10^9/L (500/mm^3).

Tracking the date of ANC recovery may not always be straightforward. In some cases the ANC may fluctuate for a period of time before the recipient fully recovers. In other cases the ANC may remain above ≥ 500/mm^3 for several days immediately post-HCT and then fall below ≥ 500/mm^3. Do not begin counting ANC values of ≥ 500/mm^3 towards recovery until the ANC has dropped to the lowest level (nadir) post-infusion. See the following example for more information regarding tracking the date of ANC recovery.

To report dates in this question, use the first of 3 consecutive laboratory values obtained on different days.

**Example 2: Tracking ANC Recovery**

*Infusion Date = May 6
Contact Date = August 15*

<table>
<thead>
<tr>
<th>Date</th>
<th>WBC</th>
<th>%Neutrophils</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 7</td>
<td>900</td>
<td>0.6</td>
<td>540</td>
</tr>
<tr>
<td>May 8</td>
<td>850</td>
<td>0.59</td>
<td>502</td>
</tr>
<tr>
<td>May 9</td>
<td>720</td>
<td>0.7</td>
<td>504</td>
</tr>
<tr>
<td>May 10</td>
<td>300</td>
<td>0.45</td>
<td>135</td>
</tr>
<tr>
<td>May 11</td>
<td>15</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 12</td>
<td>30</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 13</td>
<td>50</td>
<td>No differential</td>
<td>—</td>
</tr>
<tr>
<td>May 14</td>
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<td>0.4</td>
<td>100</td>
</tr>
<tr>
<td>May 15</td>
<td>800</td>
<td>0.7</td>
<td>560</td>
</tr>
<tr>
<td>May 16</td>
<td>840</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May 17</td>
<td>1000</td>
<td>0.7</td>
<td>700</td>
</tr>
<tr>
<td>May 18</td>
<td>1080</td>
<td>0.6</td>
<td>1080</td>
</tr>
<tr>
<td>May 19</td>
<td>1100</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>May 20</td>
<td>1325</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Date of initial recovery: ANC ≥ 500/mm^3 (report this date in question 15)
| May 21-August 14 | — | — | — | ANC ≥ 500/mm³ for timeframe |
| — | — | — | August 15 (contact date) | 2250 | 0.43 | 968 |

**Question 15: Date ANC >500/mm³ (first of 3 lab values):**

Enter the first date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm³ (or ≥ 0.5 × 10⁹/L). For an example of tracking ANC, see Example 2 above. For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 16: Was an initial platelet count > 20 × 10⁹/L achieved?**

This question is not applicable to all cellular therapies. Some cellular therapies require a course of chemotherapy prior to the infusion, such as in the case of chimeric antigen receptor (CAR) T-cells. One of the described toxicities is the inability for hematologic recovery, either by an added cycle of chemotherapy in a recipient who received many prior lines of chemotherapy or by a direct toxicity from the cellular therapy. If the patient never dropped the platelet count, there is no need to answer further.

The following questions refer to initial platelet recovery following the cellular therapy infusion for which this form is being completed. All dates should reflect no platelet transfusions administered for seven consecutive days. Report the date of the first of three consecutive laboratory (≥ 20 × 10⁹/L) obtained on different days, as shown in Example 1 below. Note that platelet recovery may take place well after the recipient has returned to the referring physician for care. It is essential that information and laboratory values be obtained from the referring physician.

Transfusions temporarily increase platelet counts. When the data is later used for analysis, it is important to be able to distinguish between a recipient whose body was creating the platelets on its own and a recipient who required transfusions to support the counts.

The following example illustrates the procedure to follow for reporting platelet recovery.

**Example 1. Reporting Platelet Recovery**
This question relates to initial platelet recovery. Dates should not reflect transfusions that took place 7 days prior to the date that it listed. To report dates in this question, use the first of 3 consecutive laboratory values obtained on different days.

Indicate whether or not there was evidence of initial platelet recovery following this cellular therapy infusion.

Check only one response:

- If “yes,” continue with question 17.
- If “no,” continue with question 18.
- Check “not applicable,” if the recipient’s platelets never dropped below $20 \times 10^9$/L at any time post-cellular therapy infusion and a platelet transfusion was never required. If the recipient’s platelet count drops below $20 \times 10^9$/L and/or the recipient received a platelet transfusion even once, do not use this option. This option is only applicable in the 100 day reporting period. Continue with question 18.
- Check “previously reported” if this is the 6 month or annual follow-up, and initial platelet recovery has already been reported on a previous form. Continue with question 18.

**Question 20: Date platelets > 20 × 10^9/L:**

Enter the first date of three consecutive laboratory values obtained on different days where the platelet count was $\geq 20 \times 10^9$/L. Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in Example 1 above, when determining the recovery date.

If three laboratory values were not obtained on consecutive days, but a sequential rise of $\geq 20 \times 10^9$/L is demonstrated, follow the examples below when determining an estimated date.

**Reporting Scenarios:**

A. The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is $22 \times 10^9$/L on January 2, $24 \times 10^9$/L on January 3, and $28 \times 10^9$/L on January 4. The
recipient does not come into the clinic for evaluation until one month later. The recipient has not received any more platelet transfusions and the platelet count is well above $20 \times 10^9$/L. Report January 8 (day seven post-platelet transfusion) for the date of platelet recovery.

B. The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is $\geq 20 \times 10^9$/L on January 2, January 3, and January 4. The recipient is then discharged back to their primary care physician. The transplant center receives a follow-up note from the primary care physician that states “recipient recovered their platelets in January of 2011.” Report an estimated date of recovery using the guidelines available in General Instructions, General Guidelines for Completing Forms.
Questions 18-32: Provide the most recent laboratory values recorded

These questions are intended to determine the hematological status of the recipient after the infusion. Testing may be performed multiple times within the reporting period; however, report only the most recent (closest to the contact date) laboratory values.

Report the laboratory value and unit (if applicable) for each hematologic finding. If a value is not known, select “unknown” and continue with the next laboratory value.

For hematocrit, check the box if red blood cells were transfused within 30 days prior to the testing. For platelets, check the box if platelets were transfused within seven days prior to the testing.
**Q33: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder**

**New Malignancies**

Report new malignancies that are different than the disease / disorder for which cellular therapy was performed. Do not include relapse, progression or transformation of the same disease subtype. New malignancy related questions will now be asked on the Subsequent Neoplasms Form 3500. The form will come due when question 33 is answered as ‘yes’.

**Question 33:** Did a new malignancy, myelodysplastic, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the cellular therapy was performed? (Include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders):

Indicate whether a new or second primary malignancy, including lymphoproliferative disorder, or myeloproliferative disorder, has developed. Do not report recurrence, progression, or transformation of the recipient’s primary disease (disease for which the cellular therapy was performed) or relapse of a prior malignancy.

New malignancies, lymphoproliferative disorders, and myeloproliferative disorders include but are not limited to:

- Skin cancers (basal, squamous, melanoma)
- New leukemia
- New myelodysplasia
- Solid tumors
- PTLD (post-transplant lymphoproliferative disorder) report as lymphoma or lymphoproliferative disease

The following should not be reported as new malignancy:

- Recurrence of primary disease (report as relapse or disease progression)
- Relapse of malignancy from recipient’s pre-cellular therapy medical history
- Breast cancer found in other (i.e., opposite) breast (report as relapse)
- Post-cellular therapy cytogenetic abnormalities associated with the pre-cellular therapy diagnosis (report as relapse)

If a new malignancy is reported, please complete the Subsequent Neoplasms Form 3500 to answer
questions specific to the new malignancy. The option of ‘Previously reported’ should only be used if the same new malignancy instance has already been reported on a F3500. See examples below. If there is a question regarding use of this option, please contact your CIBMTR CRC.

**Example 1.** Recipient develops a new malignancy at day +68. It is reported at the time the 100-day form 4100 is completed. Question 33 should be answered as ‘yes’ and the form 3500 should be completed to report all new malignancy information.

**Example 2.** Recipient develops a new malignancy at day +68 and had received a commercial CAR-T product. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The form 3500 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. No other new malignancy develops during the 100-day reporting period. When the 100-day form 4100 is completed, question 33 should be answered as ‘previously reported’.

**Example 3.** Recipient develops a new malignancy at day +68 and had received a commercial CAR-T product. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The form 3500 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. Another new malignancy develops at day +100. It is decided to report the 2nd new malignancy on the 100-day form 4100 since it is due. Question 33 should be answered as ‘yes’ to create another form 3500.
Q34-55: Persistence of Cells

This section pertains to the evaluation of persistence of a cellular product in the recipient. It only applies to genetically-modified cellular products.

Question 34: Were tests performed to detect persistence of the cellular product since the date of last report?

Methods such as PCR assays, flow cytometry (immunophenotyping) or immunohistochemistry can be used to detect persistence of the cellular product in the recipient.

If tests were performed to detect persistence of the cellular product since the date of the last report, select “yes” and continue with question 35.

If tests were not performed to detect persistence of the cellular product since the date of the last report, select “no” and continue with question 56.

Question 35: Was persistence evaluated by molecular assay (PCR)?

Molecular assessment involves testing blood, bone marrow, tumor or other source for the presence of known molecular markers. Molecular assessments are the most sensitive test and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control.

Indicate whether molecular assay testing was performed to detect the persistence of the genetically-modified cellular product within the reporting period. If “yes”, continue with question 36. If “no”, continue with question 40.

Question 36: Date Sample collected:

Report the date (YYYY-MM-DD) the sample was collected for molecular assay. If multiple tests were performed in the reporting period and

- all tests were negative: report the first negative test result
- there were positive and negative results: report the date of the last positive test.
If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

**Question 37-38: Specify the cell source:**

Select bone marrow, peripheral blood, tumor, or other source as the cell source of the sample collected for evaluation by molecular assay. If the source is “other”, specify in question 38.

**Question 39: Were the infused cells detected?**

Select “yes” if the infused cells were detected by molecular assay. Select no” if the infused cells were not detected by molecular assay.

**Question 40: Was persistence evaluated by flow cytometry testing (immunophenotyping)?**

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. The nature of flow cytometry is to detect cells based on a specific probe. To report flow cytometry results, the test must have been performed to specifically detect the genetically-modified cellular product.

Indicate whether flow cytometry testing was performed to detect the persistence of the genetically-modified cellular product within the reporting period. If “yes”, continue with question 41. If “no”, continue with question 45.

**Question 41: Date sample collected:**

Report the date (YYYY-MM-DD) the sample was collected for flow cytometry testing (immunophenotyping). If multiple tests were performed in the reporting period and

- all tests were negative: report the first negative test result
- there were positive and negative results: report the date of the last positive test

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

**Question 42-43: Specify the cell source:**

Select bone marrow, peripheral blood, tumor, or other source as the cell source of the sample collected for evaluation by flow cytometry. If other, specify in question 43.
Question 44: Were the infused cells detected?

Select "yes" if the infused cells were detected by flow cytometry testing (immunophenotyping). Select "no" if the infused cells were not detected by flow cytometry testing (immunophenotyping).

Question 45: Was persistence evaluated by immunohistochemistry?

Immunohistochemistry is a process that uses antibodies to test for certain antigens (markers) in a sample. When the antibodies bind to the antigen in the tissue sample, the enzyme or dye is activated, and the antigen can then be seen under a microscope.

Indicate whether immunohistochemistry testing was performed to detect the persistence of the genetically-modified cellular product within the reporting period. If “yes”, continue with question 46. If “no”, continue with question 50.

Question 46: Date sample collected:

Report the date (YYYY-MM-DD) the sample was collected for immunohistochemistry studies. If multiple tests were performed in the reporting period and

- all tests were negative: report the first negative test result
- there were positive and negative results: report the date of the last positive test

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 47-48: Specify the cell source:

Select bone marrow, peripheral blood, tumor, or other source as the cell source of the sample collected for evaluation by immunohistochemistry testing. If other, specify in question 48.

Question 49: Were the infused cells detected?

Select “yes” if the infused cells were detected by immunohistochemistry testing. Select “no” if the infused cells were not detected by immunohistochemistry testing.

Questions 50-51: Was persistence evaluated by other method?

If persistence of cells was tested by a method not listed above, select “yes” and continue with question 51. If “no”, continue with question 56.

Specify the other method used to evaluate persistence of cells in question 51.
**Question 52: Date sample collected:**

Report the date (YYYY-MM-DD) the sample was collected for the other method. If multiple tests were performed in the reporting period and

- all tests were negative: report the first negative test result
- there were positive and negative results: report the date of the last positive test

If the exact date is unknown, please view General Instructions, [General Guidelines for Completing Forms](#) for more information on reporting partial and unknown dates.

**Question 53-54: Specify the cell source:**

Select bone marrow, peripheral blood, tumor, or other source as the cell source of the sample collected for evaluation by other method. If other, specify in question 54.

**Question 55: Were the infused cells detected?**

Select “yes” if the infused cells were detected by other method. Select “no” if the infused cells were not detected by other method.
Q56-75 Graft vs. Host Disease

Autologous Infusions
Questions 56-75 should be completed for allogeneic infusions only. If this was an autologous infusion, continue to question 76.

GVHD
For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2100 and F4100. To reduce the reporting burden, duplicated questions on the Cellular Therapy forms are disabled. This includes GVHD reported on F4100.

Graft versus Host Disease (GVHD) is an immunological phenomenon resulting from the reaction of donor immune cells against major or minor histocompatibility antigens of the recipient. GVHD is primarily caused by donor-derived T-cells. Very rarely, GVHD may occur due to autologous reactivity (autologous GVHD), third party transfusions, or with identical twin transplantation.

Factors influencing the severity of GVHD are related to three main categories: 1) donor or graft, 2) recipient, and 3) treatment. The most influential donor/graft factor is the degree of genetic disparity between the donor and the recipient (HLA match), but other risk factors include female donor to male recipient, donor parity, older donors, and T-cell dose. The occurrence of acute GVHD becomes a risk factor for the development of chronic GVHD. Recipient age and prior infections are also factors.

In the past, GVHD was classified as acute or chronic based on its time to diagnosis following transplant, and other clinical and histological (biopsy or post-mortem) features. Today, there has been increased recognition that acute and chronic GVHD are not dependent upon time since infusion, so determination of acute or chronic should rest on clinical and histologic features. However, organ staging, and overall grade should only be calculated from the clinical picture, not histology. Acute GVHD usually begins between 10 and 40 days after HCT but can appear earlier or later. The organs most commonly affected by acute GVHD are the skin, gut, or liver. Other sites, such as the lung, may be involved.

Acute / Chronic GVHD
If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 56-67). Do not include
Question 56: Did acute GVHD develop since the date of last report?

Questions 56 and 58 on the Cellular Therapy Essential Data Follow-Up Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 56 or question 58 must be answered “yes” unless there has been a prior / concurrent diagnosis of chronic GVHD (see note above question 56). There will not be a situation where “yes” is reported for both question 56 and question 58. If question 56 is answered yes and a diagnosis date has been reported in question 57, question 58 will be disabled in FormsNet3SM. Centers should report “yes” for question 56 to indicate the recipient developed acute GVHD in the following scenarios:

- Acute GVHD is diagnosed for the first time during the reporting period.
- An acute GVHD flare is diagnosed during the current reporting period and all of the following conditions are met:
  - The recipient’s prior acute GVHD symptoms did not persist from the prior reporting period into the beginning of the current reporting period.
  - The flare is diagnosed after at least 30 days without any active acute GVHD symptoms.
  - The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 56).

If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report “no” for question 56 and “yes” for question 58. Question 58 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer questions 56 and 58.

Report “no” for questions 56 and 58 if the recipient had no active acute GVHD symptoms during the reporting period OR all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 56).
Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

**Acute GVHD Diagnosis Scenarios:**

**A.** A recipient receives a cellular therapy infusion of an allogeneic product on 1/1/2015 and develops acute GVHD which is clinically diagnosed on 2/1/2015. At least one of their symptoms, attributed to acute GVHD, persists beyond the 100 day date of contact which is 4/5/2015. Treatment continues and symptoms completely resolve on 5/1/2015. Immunosuppression is tapered until a flare of acute GVHD is diagnosed on 5/25/2015. Immunosuppression is given and symptoms quickly resolve with no active acute GVHD beginning 6/10/2015. The six month date of contact is 6/20/2015. Another flare of acute GVHD is clinically diagnosed on 8/15/2015.

**100 Day Post-TED Form:**
Question 56: Report “yes” to indicate a new clinical diagnosis of acute GVHD.
Question 57: Report the initial date of diagnosis (2/1/2015).
Question 58: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 57.
Questions 59-65: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

**Six Month Post-TED Form:**
Question 56: Report “no” to indicate acute GVHD persists from a previous report. Note, the flare of acute GVHD was < 30 days from symptoms resolution so it doesn’t count as a new reportable episode.
Question 57: Leave blank. This question will be skipped whenever question 56 is answered “no.”
Question 58: Report “yes” to indicate GVHD persists from a previous report.
Questions 59-65: Leave blank. Answering “yes” for question 58 prevents the center from re-reporting diagnosis information already captured on the 100 day form.

**One Year Post-Infusion Data Form:**
Question 56: Report “yes” to indicate a flare of acute GVHD occurred at least 30 days after resolving during a prior reporting period.
Question 57: Report the diagnosis date of the flare occurring during the reporting period (8/15/2015).
Question 58: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 57.
Questions 59-65: Answer these questions based on the assessments performed at the time of diagnosis of the flare of acute GVHD (8/15/2015).
B. A recipient receives a cellular therapy infusion of an allogeneic product on 1/1/2015 and develops acute skin GVHD on 2/1/2015 and then chronic eye GVHD on 3/1/2015. Both acute and chronic symptoms resolve by the 100 day date of contact (4/5/2015). While tapering their immunosuppression, the recipient has a flare of their acute skin GVHD on 5/30/2015. Treatment continues and symptoms completely resolve by the six month date of contact (6/20/2015).

100 Day Post-Infusion Data Form:
Question 56: Report “yes” to indicate a new clinical diagnosis of acute GVHD.
Question 57: Report the initial date of diagnosis (2/1/2015).
Question 58: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 57.
Questions 59-65: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

Six Month Post-Infusion Data Form:
Question 56: Report “no” to indicate acute GVHD did not develop during the reporting period.
Question 57: Leave blank. This question will be skipped whenever question 56 is answered “no.”
Question 58: Report “no” to indicate acute GVHD did not persist from a previous report.

If chronic GVHD has been diagnosed in a prior reporting period, report “no” for questions 56 and 58. Any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD must be reported in the chronic GVHD section of the form. Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section. This instruction has been provided in the note above question 56.

Question 57: Date of acute GVHD diagnosis:
Report the date of clinical diagnosis of acute GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed a rash one week prior to the physician clinically diagnosing acute skin GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of acute GVHD in the same reporting period, report the date of onset of the first episode of acute GVHD.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.
**Question 58: Did acute GVHD persist since the date of last report?**

Question 58 will only be enabled in FormsNet3 if the center has reported “no” for question 56 and, therefore, has not reported a date of diagnosis in question 57. If prompted to answer question 58, report “yes” if acute GVHD was diagnosed in a prior reporting period and any of the following conditions are met:

- The recipient's acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).
- The recipient's acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred within 30 days of symptom resolution / quiescence.
- The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 56).

Report “no” for questions 56 and 58 if the recipient had no active acute GVHD symptoms during the reporting period or all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 56).

Indicate “unknown” if there is no information about the recipient's GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

**Question 59: Overall grade of acute GVHD at diagnosis:**

Indicate the overall grade of acute GVHD at the time of diagnosis. The acute GVHD grading scale is based on clinical evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on clinical severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, overall grading remains clinical and is based on the criteria published by Przepiorka et al., Bone Marrow Transplant 1995; 15(6):825-8, see the GVHD Grading and Staging table below.

If acute GVHD was present, but the grade at diagnosis was not documented and it cannot be determined from the grading and staging table, report “not applicable.”

Examples may include:

- Only elevated liver function tests without increased bilirubin
- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description below)
Upper GI GVHD
If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

GVHD Grading and Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Skin</th>
<th>Liver</th>
<th>Gut</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rash on &lt;25% of skin</td>
<td>Bilirubin 2-3 mg/dl</td>
<td>Diarrhea &gt; 500 ml/day or persistent nausea&lt;br&gt;Note: For pediatric patients, the volume of diarrhea should be based on body surface area. Downgrade one stage if an additional cause of diarrhea has been documented.</td>
</tr>
<tr>
<td>2</td>
<td>Rash on 25-50% of skin</td>
<td>Bilirubin 3-6 mg/dl</td>
<td>Diarrhea &gt;1000 ml/day&lt;br&gt;Note: For pediatric patients, the volume of diarrhea should be based on body surface area. Downgrade one stage if an additional cause of diarrhea has been documented.</td>
</tr>
<tr>
<td>3</td>
<td>Rash on &gt;50% of skin</td>
<td>Bilirubin 6-15 mg/dl</td>
<td>Diarrhea &gt;1500 ml/day&lt;br&gt;Note: For pediatric patients, the volume of diarrhea should be based on body surface area. Downgrade one stage if an additional cause of diarrhea has been documented.</td>
</tr>
<tr>
<td>4</td>
<td>Generalized erythroderma with bullous formation</td>
<td>Bilirubin &gt;15 mg/dl</td>
<td>Severe abdominal pain with or without ileus</td>
</tr>
</tbody>
</table>

Grade

| I     | Stage 1-2 | None | None |
| II    | Stage 3   | Stage 1 | Stage 1 |
| III   | —         | Stage 2-3 | Stages 2-4 |
| IV    | Stage 4   | Stage 4 | — |

1. Use “Rule of Nines” ([Percent Body Surfaces table](#)) or burn chart to determine extent of rash.

2. Range given as total bilirubin. Downgrade one stage if an additional cause of elevated bilirubin has been documented.

3. Volume of diarrhea applies to adults. For pediatric patients, the volume of diarrhea should be based on body surface area. Downgrade one stage if an additional cause of diarrhea has been documented.

4. Persistent nausea with or without histologic evidence of GVHD in the stomach or duodenum.

5. Criteria for grading given as minimum degree of organ involvement required to confer that grade.
Grade IV may also include lesser organ involvement with an extreme decrease in performance status.

**Question 60-65: List the stage for each organ at diagnosis of acute GVHD:**

**Skin:** Select the stage that reflects the body surface area involved with a maculopapular rash attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. See the Percent Body Surfaces table below to determine the percent of body surface area involved with a rash. Do not report ongoing rash not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

**Percent Body Surfaces**

<table>
<thead>
<tr>
<th>Body Area</th>
<th>Percent</th>
<th>Total Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each Arm</td>
<td>9%</td>
<td>18%</td>
</tr>
<tr>
<td>Each Leg</td>
<td>18%</td>
<td>36%</td>
</tr>
<tr>
<td>Chest &amp; Abdomen</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Back</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Head</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Pubis</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Lower intestinal tract (use mL/day for adult recipients and mL/m²/day for pediatric recipients):** Select the stage that reflects the volume of diarrhea attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Use mL/day for adult recipients and mL/m²/day for pediatric recipients. Input and output records may be useful in determining the volume of diarrhea. Do not report ongoing diarrhea not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, report “stage 0” for lower intestinal tract involvement. In this case, report “not applicable” for the overall grade unless stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status was also documented at the time point being reported (at diagnosis or maximum grade during the reporting period). Report an overall grade of IV if stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status is documented at the time point being reported (see GVHD Staging and Grading Table). Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.

**Upper intestinal tract:** Select the stage that reflects the presence of persistent nausea or vomiting attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report ongoing nausea or vomiting not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.
Liver: Select the stage that reflects the bilirubin level attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report ongoing hyperbilirubinemia not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

For recipients who have a normal bilirubin level with elevated transaminase levels attributed to acute GVHD, report this in questions 64-65 “Other site(s) involved with acute GVHD”.

Other site(s) involved with acute GVHD: Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 65. If reporting transaminitis under “other site,” write in “transaminitis” rather than “liver” when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under “other site.”

Question 66: Maximum Overall Grade of Acute GVHD:

Indicate the overall maximum grade of acute GVHD since the date of the last report. Grading is based on clinical evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on clinical severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, overall grading remains clinical and is based on the criteria published by Przepiorka et al., Bone Marrow Transplant 1995; 15(6):825-8; see the GVHD Grading and Staging table above.

If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. See question 56 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.

Report the recipient’s maximum acute GVHD grade in the reporting period; this may differ from the grade at diagnosis or may be the same. If acute GVHD was present, but the maximum grade was not documented and it cannot be determined from the grading and staging table, report “not applicable.”

Examples may include:

- Only elevated liver function tests without increased bilirubin
- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description above)
Acute GVHD Grading Scenarios:

A. A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging / grading can be determined using the GVHD Grading and Staging table above.

B. A recipient developed acute liver GVHD with elevated LFTs (i.e., transaminases) with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in the GVHD Grading and Staging table above; “not applicable” would be the best option to report.

C. A recipient developed stage 2 skin involvement, which showed improvement in response to topical steroids. However, the recipient then developed hyperbilirubinemia attributed to stage 1 liver involvement; the skin involvement at that time was stage 1. In this case, grade II would be reported (assuming this was the extent of the recipient’s acute GVHD in the reporting period).

D. A recipient developed stage 2 skin involvement which resolved in response to topical steroids. Later in the reporting period, the recipient was diagnosed with mild chronic eye GVHD. Shortly thereafter, they were diagnosed with a stage 3 flare of acute skin GVHD. In this case, grade I would be reported. Do not consider any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD when completing the acute GVHD section of the form.

Question 67: Date maximum overall grade of acute GVHD

Report the date (YYYY-MM-DD) of maximum acute GVHD involvement, based on clinical grade. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date. If “not applicable” was reported for question 66, question 67 must be left blank.

Question 68: Did chronic GVHD develop since the date of last report?

Indicate whether a new clinical diagnosis of chronic GVHD was documented during the reporting period. If chronic GVHD was diagnosed during the reporting period, report “yes” and continue with question 69.

If the recipient had a flare of chronic GVHD occurring after at least a 30 day period of symptom quiescence,
report “yes” and continue with question 69. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent chronic GVHD which is captured in question 70.

Report “no” if chronic GVHD was not clinically diagnosed – initially or as a flare – in the reporting period; this includes instances where chronic GVHD persists from a prior reporting period without flare in the current reporting period.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

**Question 69: Date of chronic GVHD diagnosis:**

Report the date (YYYY-MM-DD) of clinical diagnosis of chronic GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed shortness of breath one month prior to the clinical diagnosis of pulmonary chronic GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of chronic GVHD in the same reporting period, report the date of onset of the first episode of chronic GVHD.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

**Question 70: Did chronic GVHD persist since the date of last report?**

Question 70 will only be enabled in FormsNet3 if the center has reported “no” for question 68 and, therefore, has not reported a date of diagnosis in question 69. Indicate whether chronic GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive chronic GVHD, or a prior history of GVHD. If “yes,” continue with question 71; See question 68 for instructions on reporting a chronic GVHD flare.

If the recipient has no active symptoms during the reporting period, report “no” and continue with question 74.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.
**Question 71: Maximum grade of Chronic GVHD (according to best clinical judgement):**

Report the maximum chronic GVHD involvement, based on clinical grade, as documented by the recipient’s primary care provider. The intent of this question is to capture the maximum grade based on the best clinical judgment. If the maximum clinical grade is not documented, request documentation from the recipient’s primary care provider.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

**Question 72: Specify if chronic GVHD was limited or extensive:**

The grading system for chronic GVHD is divided into two categories: limited and extensive. Definitions are based on Sullivan KM, Blood 1981; 57:267.

Report “limited” if chronic GVHD includes only localized skin involvement and/or liver dysfunction. Report “extensive” if any of the following symptoms are attributed to chronic GVHD:

- Generalized skin involvement and/or liver dysfunction
- Liver histology showing chronic aggressive hepatitis, bridging necrosis, or cirrhosis
- Involvement of the eye: Schirmer’s test with <5 mm wetting**, or
- Involvement of the salivary glands or oral mucosa, or
- Involvement of any other target organ

**Note:** Schimer’s test is required if eye involvement is the only symptom of chronic GVHD. If there are other symptoms of chronic GVHD such as lichen sclerosis of the mouth and skin involvement in addition to the eye symptoms, the Schirmer’s test is not required.

**Question 73: Date of maximum grade of chronic GVHD:**

Report the date (YYYY-MM-DD) of maximum chronic GVHD involvement, based on clinical grade. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.
Question 74: Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, ≤10 mg/day for adults, <0.1 mg/kg/day for children)

Corticosteroids
Corticosteroids are captured differently depending on whether they are used topically or systemically. Use the following guidelines when determining how to report corticosteroids used to treat GVHD:

Topical Creams for Skin: Do not report topical ointments or creams used to treat skin GVHD including corticosteroid creams such as Triamcinolone or Hydrocortisone.

Other Topical Treatments: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. Do not consider these medications when answering question 74.

Systemic Treatments: Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in question 74.

Indicate whether the recipient is still taking immunosuppressive agents to treat or prevent GVHD on the date of contact. Refer to the guidelines included in the question text if the recipient is taking low dose steroids or steroids for adrenal insufficiency.

Indicate “not applicable” in any of the following scenarios:

- The recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD.
- The recipient stopped taking systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD in a previous reporting period and did not restart systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) during the current reporting period.

Indicate “unknown” if there is no information to determine if the recipient is still taking systemic steroids. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD on the date of contact. If the recipient has died prior to the discontinuation of systemic steroids used to treat or prevent acute and / or chronic GVHD, select “yes.”

Question 75: Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for GVHD?

Indicate whether the recipient is still taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent acute and / or chronic GVHD on the date of contact. Descriptions of many immunosuppressive agents are included below.

If the recipient did not receive non-steroidal immunosuppressive agents to treat or prevent acute and / or
chronic GVHD during the reporting period, report “not applicable.”

Indicate “not applicable” in any of the following scenarios:

- The recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD.
- The recipient stopped taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD in a previous reporting period and did not restart non-steroidal immunosuppressive agents (including PUVA) during the current reporting period.

Indicate “unknown” if there is no information to determine if the recipient is still taking non-steroidal immunosuppressive agents. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD in the reporting period.

Examples of Immunosuppressive Agents:

Aldesleukin (Proleukin): Increases production of several white blood cells including regulatory T-cells. This drug is also known as interleukin-2.

ALG (Anti-Lymphocyte Globulin), ALS (Anti-Lymphocyte Serum), ATG (Anti-Thymocyte Globulin)

ATS (Anti-Thymocyte Serum): Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes. Also report the animal source. If “other” is selected, specify the source.

ATS (Anti-Thymocyte Serum): Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes. Also report the animal source. If “other” is selected, specify the source.

Azathioprine (Imuran): Azathioprine inhibits purine synthesis. Usually it is used at low doses in combination with other treatments.

Bortezomib (Velcade): A proteasome inhibitor.

Cyclosporine (CSA, Neoral, Sandimmune): Calcineurin inhibitor which decreases cytokine production by T-cells. Usually given for ≥ 3 months.

Cyclophosphamide (Cytoxan): Given in high doses near the date of infusion as single agent
prophylaxis.

Extra-corporeal photopheresis (ECP): The recipient’s blood is removed from the body, exposes to psoralen and ultraviolet light, and re-infused.

FK 506 (Tacrolimus, Prograf): Inhibits the production of interleukin-2 by T-cells.

Hydroxychloroquine (Plaquenil): Hydroxychloroquine inhibits transcription of DNA to RNA and is commonly used as an anti-malarial drug.

Interleukin Inhibitor: Interleukin inhibitors suppress production of white blood cells and are grouped according to their target. Examples of IL-2 inhibitors include daclizumab (Zynbryta) and basiliximab (Simulect). Examples of IL-6 inhibitors include tocilizumab (Actemra) and siltuximab (Sylvant).

In vivo monoclonal antibody: Antibody preparations that are infused in the recipient following HSCT. Specify the antibody used as: anti CD25 (Zenapax, Daclizumab, AntiTAC), alemtuzumab (Campath), entanercept (Enbrel), infliximab (Remicade), and / or rituximab (Rituxan).

In vivo immunotoxin: Antibody preparations linked to a toxin that is infused in the recipient following HCT. Specify the immunotoxin.

Janus Kinase 2 Inhibitors: Suppress function of T-effector cells. Examples: ruxolitinib (Jakafi, Jakavi) and tofacitinib (Xeljanz, Jakvinus).

Methotrexate (MTX) (Amethopterin): Inhibits the metabolism of folic acid. It is most often used with cyclosporine and is usually for a short duration of time.

Mycophenolate mofetil (MMF) (CellCept, Myfortic): Inhibits the de novo pathway used for lymphocyte proliferation and activation.

Pentostatin (Nipent): Inhibits adenosine deaminase, which blocks DNA (and some RNA) synthesis.

Sirolimus (Rapamycin, Rapamune): Inhibits the response to interleukin-2, blocking the activation of T-cells.

Tyrosine Kinase Inhibitor (TKI): Suppress function of tyrosine kinases thereby downregulating the function of many other cellular proteins / processes including fibrosis and inflammation. Examples: imatinib (Gleevec, Glivec), nilotinib (Tasigna), and dasatinib (Sprycel).

UV Therapy: UVA or UVB radiation administered to affected areas of the skin in order to suppress
proliferation of cells responsible for GVHD.

**PUVA (Psoralen and UVA):** Psoralen is applied or taken orally to sensitize the skin, and then the skin is exposed to UVA radiation.

**UVB:** Broadband- or Narrowband-UVB radiation is applied to the affected areas of the skin.
Q76-187: Toxicties

Question 76: Did the recipient develop Cytokine Release Syndrome (CRS) since the date of last report?

Cytokine Release Syndrome (CRS) is defined by development of a constellation of signs and symptoms that are seen after the infusion of monoclonal antibodies or cellular therapy products. It results from the rapid release of several inflammatory cytokines as a consequence of immune response triggered by a drug (i.e. monoclonal antibody) or cellular product. This rapid cytokine release into the circulation results in fever (must be ≥100.4F or ≥38C), nausea, chills, hypotension, tachycardia, asthenia, headache, rash, sore throat, respiratory failure or death. This section attempts to collect different clinical and laboratory information to understand the severity of this event.

If the recipient developed CRS since the date of last report, select “yes” and continue with question 77. If the recipient did not develop CRS, continue with question 99.

Question 77: Date of diagnosis:

Report the date (YYYY-MM-DD) when the first symptom of CRS was documented by a physician or other health care provider in the progress note or chart.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 78: Was therapy given? (for CRS)

Indicate “yes” if the recipient received therapy for CRS and continue with question 79. Indicate “no” if no therapy was given for CRS and continue with question 81.

Questions 79-80: Specify therapy given for CRS: (check all that apply)

Check all that apply from the list if given to treat the CRS. If “other therapy” is selected, specify the therapy in question 80.

Questions 81-96: Symptoms of CRS

Indicate which symptoms of CRS the recipient experienced. For each symptom reported, also report the date of onset. If there were multiple occurrences of a symptom (e.g. fever), report the first occurrence.

Fevers (≥100.4F or ≥38C): A disorder characterized by elevation of the body’s temperature above the upper limit of normal. Do not report fever less if than 100.4F or 38C in this field. Fever less than 100.4F or
38C does not qualify as a symptom of CRS.

**Hypotension requiring therapy:** Abnormally low blood pressure requiring treatment with volume resuscitation using intravenous isotonic fluids or vasopressors such as norepinephrine, dopamine, dobutamine, epinephrine, phenylephrine, or vasopressin. The use of vasopressors to control blood pressure is an indirect assessment of severity of CRS.

Options for number of vasopressors include 1 or >2 and can be used to determine the grade. One important consideration here is the use of vasopressin, which can be used with fluids or other vasopressors to stabilize the blood pressure. In order to assess severity, only patients who received two or more vasopressor agents *excluding vasopressin*, should be marked as >2 vasopressors. Addition of vasopressin to other vasopressor agents does not reflect the same level of acuity compared to a patient requiring 2 or more vasopressors without vasopressin. Only use the option of number of vasopressors as >2 for patients who are receiving multiple vasopressors excluding vasopressin. Also specify therapy given for hypotension (intravenous fluids vasopressors, other) and if hypotension was controlled with therapy (meaning not worsening clinically).

**Hypoxia requiring minimal supplemental oxygen (FiO2<40%):** A lower than normal concentration of oxygen in arterial blood requiring supplemental oxygen of <40% FiO2. One example here is the delivery of supplemental oxygen with a low-flow nasal cannula or blow-by device.

**Hypoxia requiring more than minimal supplemental oxygen (FiO2>40%):** A lower than normal concentration of oxygen in arterial blood requiring supplemental oxygen of >40% FiO2. Also specify if positive pressure ventilatory support is required, such as CPAP, BiPAP, intubation or mechanical ventilation. Do not report use of CPAP for sleep apnea. Examples here include the requirement of supplemental oxygen delivered through a high-flow nasal cannula, facemask, opti-flow, non-rebreather mask or Venturi mask.

**Was positive pressure ventilatory support required (CPAP, BiPAP, intubation, and mechanical ventilation):** This option outlines the need of devices considered as positive pressure ventilation which could be non-invasive like continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP or BPAP), or invasive, which requires endotracheal intubation with mechanical ventilation. Patients who use BiPAP or CPAP for obstructive sleep apnea are not considered the same here and should not be reported in this question. The intent of this question is the treatment of respiratory insufficiency or failure.

Source: Common Terminology Criteria for Adverse Events (CTCAE) v5.0

**Questions 97-98: Did cytokine release syndrome resolve?**

If the cytokine release syndrome resolved, select “yes” and report the date (YYYY-MM-DD) in question 98.
Questions 99-100: Neurotoxicity:

Neurotoxicity is the development of different neurologic signs and symptoms reported after the infusion of genetically modified lymphocytes. This was initially thought to be part of CRS, but it was also observed in the absence of any other signs of CRS. Neurotoxicity also appears to be a spectrum of signs and symptoms that vary from fine tremors and word finding difficulties to seizure and loss of conscience. This section collects different neurologic signs that have been described after cellular therapy infusions.

Indicate “yes” if neurotoxicity occurred and continue with question 100. Indicate “no” if neurotoxicity did not occur or “unknown” if unsure whether neurotoxicity occurred and continue with question 125.

Report the date (YYYY-MM-DD) in question 100 when the first symptom of neurotoxicity was documented by a physician or other health care provider in the progress note or chart.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Specify symptoms of neurotoxicity. Report the highest grade observed in this reporting period:

Question 101: Was a CARTOX-10 neurological assessment performed? (Or similar, Immune Effector Encephalopathy – ICE Assessment)

The CAR Toxicity (CARTOX) 10-point neurologic assessment assigns one point for each task performed correctly. A score of 10 is normal. These scales assess cognition and the level of encephalopathy more precisely. They include assessments of orientation, naming, writing, and attention with a score associated with each positive answer. Lower scores are associated with a higher level of encephalopathy. Unresponsive patients score 0 for all scales. Some centers performed these evaluations multiple times a day. These questions attempt to capture the worst score.

<table>
<thead>
<tr>
<th>Assessment</th>
<th>CARTOX-10 (12)</th>
<th>ICE SCORE (IMMUNE EFFECTOR ENCEPHALOPATHY) ASSESSMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation</td>
<td>Orientation to year, month city, hospital, or President/Prime Minister of country of residence: 5 points</td>
<td>Orientation to year, month, city, or hospital: 4 points</td>
</tr>
<tr>
<td>Naming</td>
<td>Name 3 objects (e.g., point to clock, pen, button): 3 points</td>
<td>Name 3 objects (e.g., point to clock, pen, button): 3 points</td>
</tr>
</tbody>
</table>
Writing

Ability to write a standard sentence (e.g., Our national bird is the bald eagle): 1 point

Attention

Count backwards from 100 by 10: 1 point

Following Commands

“Show me two fingers,” or, “Close your eyes and stick out your tongue.”: 1 point

10: No impairment
7-9: Grade 1 Neurotoxicity
3-6: Grade 2 Neurotoxicity
0-2: Grade 3 Neurotoxicity

- Orientation to year, month, city, hospital, President: 5 points
- Name 3 objects (e.g. point to a clock, pen, button): 3 points
- Ability to write a standard sentence (e.g., Our national bird is the bald eagle.): 1 point
- Count backwards from 100 by ten: 1 point

Question 102: What was the lowest CARTOX score?

<table>
<thead>
<tr>
<th>Neurological assessment score</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (7-9)</td>
<td>Moderate (3-6)</td>
<td>Severe (0-2)</td>
<td>Critical/ obtunded</td>
<td></td>
</tr>
</tbody>
</table>

Questions 103-120: Specify symptoms of neurotoxicity.

Indicate which symptoms of neurotoxicity the recipient experienced.

**Depressed level of consciousness:** A disruption in how the brain works that causes a change in behavior. This change can happen suddenly or over days and ranges from slight confusion to total disorientation and increased sleepiness to coma.

**Dysphasia / aphasia:** The loss of ability to understand or express speech, caused by brain damage. Also report the grade – note grade 3 dysphasia is defined as aphasia.

**Seizure:** Uncontrolled electrical activity in the brain, which may produce a physical convulsion, minor physical signs, thought disturbances or a combination of symptoms. Also specify the type of seizure and severity (grade).

**Hemiparesis / paraparesis / other motor deficit:** Weakness on one side of the body (hemiplegic, partial paralysis of the lower limbs (legs), or other sudden loss of connectivity between the CNS and muscles.
**Cerebral edema:** A swelling in the brain caused by the presence of excessive fluid. Also report the grade of cerebral edema.

**Hallucinations:** A disorder characterized by a false sensory perception in the absence of an external stimulus (visual or other type).

**Tremors:** A disorder caused by the rapid alternating contraction and relaxation of muscles (involuntary) and is a common symptom of diseases of the nervous system.

**Cerebral vascular accident (stroke):** A disorder characterized by a decrease or absence of blood supply to the brain caused by obstruction (thrombosis or embolism) of an artery resulting in neurological damage. Also report the date of onset and the type of stroke. Hemorrhagic stroke occurs when a weakened blood vessel ruptures. Two types of weakened blood vessels usually cause hemorrhagic stroke: aneurysms and arteriovenous malformations (AVMs). Ischemic strokes occur when the arteries to your brain become narrowed or blocked, causing severely reduced blood flow (ischemia).

**Leukoencephalopathy:** A disorder characterized by diffuse reactive astrocytosis with multiple areas of necrotic foci without inflammation.

**Other symptom:** If the recipient experienced a symptom of neurotoxicity not listed above, report here and specify the symptom in question 120.

Source: Common Terminology Criteria for Adverse Events (CTCAE) v5.0

**Questions 121-122: Did neurotoxicity resolve?**

If the cellular therapy associated neurotoxicity resolved, select “yes” and report the date (YYYY-MM-DD) in question 122. Resolution means complete normalization of neurologic function. It is possible that patients might remain with residual neurologic dysfunction which would not qualify as complete resolution of this complication.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

**Questions 123-124: Specify all therapy given for neurotoxicity: (check all that apply)**

Report all agents given to the recipient to treat the neurotoxicity.
Other toxicities

Questions 125-126 Hypogammaglobulinemia:

Hypogammaglobulinemia refers to low levels of circulating gammaglobulins, or immunoglobulins, in the blood and often determined by quantitative levels of immunoglobulins G (Ig G), A (IgA) and M (IgM); or most commonly IgG only. Levels lower than 600mg/dL of circulating IgG are considered to be hypogammaglobulinemia. Normal limits of IgG concentration in the blood vary with age. Children ages 4 to 10, levels lower than 500mg/dL are considered hypogammaglobulinemia. Children younger than 4 years, as levels of IgG can be much lower and still be within normal ranges for the age, the diagnosis of hypogammaglobulinemia needs to be confirmed with the treating physician.

Hypogammaglobulinemia is common after CAR-T infusions that target CD19+ cells, which produce immunoglobulins. The degree of hypogammaglobulinemia is associated with a higher risk of infection.

Report the date (YYYY-MM-DD) in question 126 when the hypogammaglobulinemia was documented by either a physician/health care provider or determined by lab results. If the hypogammaglobulinemia continues from a prior reporting period, report the original diagnosis date as the onset date and override the error.

Example 1. The recipient developed hypogammaglobulinemia at day +22 which was reported on the 4100 day 100 form. The lab results continue to show IgG levels < 600 mg/dl during the 6 month reporting period. Report the original diagnosis date on the 4100 6 month form and override the error.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Questions 127-128: Did hypogammaglobulinemia resolve?

If the hypogammaglobulinemia resolved, select “yes” in question 127 and report the date (YYYY-MM-DD) in question 128 as documented by a physician or other health care provider in the progress note or chart.

Questions 129-130: Did recipient require immunoglobulin replacement therapy?

Replacement therapy is given to prevent infections. If the recipient required immunoglobulin replacement therapy as a result of hypogammaglobulinemia, select “yes” in question 129, and indicate if the recipient is still requiring the therapy at the time of this report in question 130.

Questions 131-133: Tumor lysis syndrome

Tumor lysis syndrome (TLS) is a disorder characterized by metabolic abnormalities that result from a
spontaneous or therapy-related cytolysis of tumor cells.

Report the date (YYYY-MM-DD) in question 132 when the tumor lysis syndrome was documented by a physician or other health care provider in the progress note or chart. Report the grade of tumor lysis syndrome in question 133

- Grade 3: Present
- Grade 4: life-threatening consequences: urgent intervention indicated
- Grade 5: death

Questions 134-136: Other toxicity:

If the recipient experienced a toxicity that does not fit in a category above, select “yes” in question 134 and specify the other toxicity in question 135.

Report the date (YYYY-MM-DD) in question 136 when the other toxicity was documented by a physician or other health care provider in the progress note or chart.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Questions 137-154: Grade 3 organ toxicity

This question will enable only if the commercialized product ‘Kymriah’ is selected in question 1.

As defined by the CTCAE criteria, grade 3 toxicity represents severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care Activities of Daily Living (ADL), which refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

If “yes” is reported for an organ, report the date of onset (YYYY-MM-DD) as documented by a physician or other health care provider in the progress note or chart.

Questions 155-172: Grade 4 organ toxicity

As defined by the CTCAE criteria, grade 4 toxicity represents life-threatening consequences and urgent intervention is indicated.

If “yes” is reported for an organ, report the date of onset (YYYY-MM-DD) of each organ toxicity as documented by a physician or other health care provider in the progress note or chart.
Specify the maximum lab results since the date of last report

Questions 173-175: Interleukin-6:

Interleukin-6 is a pro-inflammatory cytokine derived from macrophages and endothelial cells that increases synthesis and secretion of immunoglobulins by B lymphocytes.

Indicate if the lab value is “known” or “unknown” in question 173. If known, report the value in question 174 and the date (YYYY-MM-DD) the sample was collected in question 175.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Questions 176-178: Interferon gamma IFN-γ:

Interferon gamma is a pro-inflammatory cytokine produced by macrophages and T-cells that is involved in the regulation of the immune system and activation of phagocytes.

Indicate if the lab value is “known” or “unknown” in question 176. If known, report the value in question 177 and the date (YYYY-MM-DD) the sample was collected in question 178.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Questions 179-181: Soluble interleukin-2 receptor α (sIL2RA or soluble CD25):

Interleukin-2 receptor alpha or CD25 can shed from the surface of cells during inflammatory conditions. This test detects soluble or circulating sIL2RA.

Indicate if the lab value is “known” or “unknown” in question 179. If known, report the value in question 180 and the date (YYYY-MM-DD) the sample was collected in question 181.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Questions 182-184: Total serum ferritin:

Ferritin is an acute phase reactant and is often found in high concentration in highly inflammatory conditions.

Indicate if the lab value is “known” or “unknown” in question 182. If known, report the value in question 183
and the date (YYYY-MM-DD) the sample was collected in question 184.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Questions 185-187: C-reactive protein:

C-reactive protein (CRP) is a protein produced by the liver and found in the blood. CRP levels increase with tissue injury or trauma, infection or inflammation. CRP is also highly associated with IL-6 levels.

Indicate if the lab value is “known” or “unknown” in question 185. If known, report the value in question 186 and the date (YYYY-MM-DD) the sample was collected in question 187.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.
Infections occur frequently in recipients of cellular therapy or transplant. Questions 188-192 are intended to capture detailed information on *clinically significant* infections diagnosed during the reporting period. A single infection may be found on multiple cultures or at multiple sites. Infections may recur following resolution of symptoms and negative testing. Use the instructions provided in this section to determine when an infection should be considered clinically significant, and therefore reported, as well as when to report new and/or recurrent infections.

**Question 188-192: Did the recipient develop a clinically significant infection since the date of the last report?**

Indicate whether the recipient developed a clinically significant bacterial, viral, or fungal infection during the reporting period. For the purpose of this manual, the term “clinically significant” refers to any infection requiring treatment. Surveillance cultures in which normal flora is present and the recipient is asymptomatic do not need to be reported. If no clinically significant infections occurred during the reporting period, report “no” for question 188 and skip to question 193.

Do **not** report the following scenarios:

- Culture-negative neutropenic fever without clear source;
- Suspected (unconfirmed) viral or bacterial infections;
- Upper respiratory infections which are presumed viral, but no virus has been identified;
- Candida detected in oral or stool samples (includes oral thrush);
- Toenail fungus;
- Yeast infection in the groin, vagina, or under the breasts;
- Surveillance cultures in which normal flora is present and the recipient is asymptomatic;
- Infections persisting from a prior reporting period (including infections which have progressed to new sites since the last report); or
- Infections recurring within the time frames specified in the Definitions for Same Infection table below.

If an organism is identified by molecular report, laboratory report, or other physician documentation, the infection should be reported in questions 189-192. If no organism is identified, the center should use the following guidelines to determine whether to report an infection:

- If a fungal infection is suspected (per radiology assessments), but no organism is isolated during the reporting period, report the suspected infection in questions 188-192.
• If a bacterial or viral infection is suspected, but not confirmed, do **not** report an infection in questions 188-192.
• If no particular organism group is identified or suspected, do **not** report an infection in questions 188-192.

For each infection, report the organism, site, and date of diagnosis.

**Definitions for Same Infection**

**Organism:**
Select the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. If the specific organism is not listed, use the code “777 – Other organism” and report the name of the organism in the space provided. If a fungal infection is suspected, but not identified, report using code “503 – Suspected fungal infection.” As noted above, only report infections which are **clinically significant**.

**Site:**
Infections can occur virtually anywhere. In order to capture sufficient detail without excess burden, there is a list for the potential sites. An infection may occur in more than one site at the same or at different times.

• If the infection is identified at multiple sites with the same organism and within the recurrence interval to be considered the same infection (Definitions for Same Infection table), please report all sites the organism was identified.
• If the infection is identified at multiple sites with an organism already reported but is outside of the recurrence interval to be considered the same infection, please report as a new infection.

Select the site(s) of the infection from the options provided on the form. Report all sites of infection which were confirmed by microbiology, laboratory report, or other physician documentation during the reporting period. This includes any new sites identified after the date of diagnosis as well as after treatment has been initiated.

For clarification, the following site definitions are provided:

- **Blood:** includes blood or serum obtained from a central IV line, catheter tip, or from a direct needle stick (Peripheral draw). Blood should be the reported site for infections identified in the **bone marrow**.

- **Bone:** an infection in the bone itself (Osteomyelitis)
CNS: includes CSF (cerebrospinal fluid) specimens as well as abscesses and/or inflammation noted on brain imaging (encephalitis, meningitis)

Eyes: includes infection in any part of the eye (i.e. retinitis)

Genital: includes vagina, penis, perineum, ovaries, scrotum, testes, uterus

GI tract, lower: includes jejunum, ileum, colon, rectum, and stool

GI tract, upper: includes mouth, dentition, esophagus, stomach, and duodenum

Joints: includes fibrous connective tissue and cartilage at any site of bone articulation, typically isolated to a single area (i.e., not a diffuse infection) such as the knee, elbow, or shoulder

Liver/Spleen: includes the gallbladder and biliary tract

Lung: also known as the lower respiratory tract

Skin, cellulitis: a spreading bacterial or viral infection of the skin and tissues beneath the skin

Skin, necrotizing fasciitis: a severe bacterial infection of the fascia, the tissues that line and separate muscles, that causes extensive tissue death including damage to skin and overlying tissues

Sinus and/or upper respiratory tract: all areas from the nose to the throat and sinuses, does not include lungs (report as “Lung”), mouth, or dental infections (report mouth and dental as “GI tract, upper”).

Urinary tract, lower: includes urinary tract infections and cystitis (bladder inflammation)

Urinary tract, upper: includes the kidneys and ureters

Date of Diagnosis:
Report the date of diagnosis of the infection as the collection date for the positive microbiology culture or laboratory report. For suspected fungal infections, enter the date of a radiological test or the date treatment was started as the date of diagnosis. If multiple sites of infection are identified during the reporting period, report the collection date of the first positive microbiology culture or laboratory report.

Copy and complete questions 189-192 to report more than one infection during this reporting period.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.
If a pregnancy is reported, please complete the Pregnancy Form 3501 to answer questions specific to the pregnancy. The option of 'Previously reported' should only be used if the same pregnancy instance has already been reported on a F3501. If there is a question regarding use of this option, please contact your CIBMTR CRC.

**Question 193: Was the recipient pregnant at any time in this reporting period? (Female Only)**

Indicate “yes” if the female recipient was pregnant at any time during the reporting period and complete a form 3501. Indicate “no” if the female recipient was not pregnant at any time during the reporting period.

**Question 194: Was the recipient’s female partner pregnant at any time in this reporting period? (Male only)**

Indicate “yes” if the male recipient’s female partner was pregnant at any time during the reporting period and complete a form 3501. Indicate “no” if the male recipient’s female partner was not pregnant at any time during the reporting period.
Infection & Miscellaneous Manuals

These manuals provide explanatory information for forms that are less routinely completed.

2047/2147: Hepatitis Serology
2553: VOD / SOS
2046 / 2146 Fungal Infection

Fungal infections are significant opportunistic infections affecting transplant recipients. Because these infections are quite serious, it is important to collect additional information on them. Fungal infection specific forms (Form 2046 and 2146) collect more detailed information about infections reported on the comprehensive report forms and cellular therapy forms.

2046: Fungal Infection Pre-Infusion Data
2146: Fungal Infection Post-Infusion Data
2046: Fungal Infection Pre-Infusion Data

Fungal infections are significant opportunistic infections affecting transplant patients. Because these infections are quite serious, it is important to collect additional information on them. The Fungal Infection Pre-Infusion Data Form (Form 2046) captures information regarding the diagnosis, treatment, and response to treatment of any proven or suspected fungal infections diagnosed prior to receiving a HCT or cellular therapy. This form must be completed when one of the fungal infections listed below has been reported on the Baseline Form (Form 2000). One form will be completed for each applicable infection reported.

The following infections will cause a Fungal Infection Pre-Infusion Data Form (Form 2046) to come due when reported on the Baseline Form (Form 2000):

- Aspergillus flavus
- Aspergillus fumigatus
- Aspergillus niger
- Aspergillus, NOS
- Aspergillus terreus
- Aspergillus ustus
- Blastomyces (dermatitidis)
- Candida albicans
- Candida non-albicans
- Cryptococcus gattii
- Cryptococcus neoformans
- Fusarium (all species)
- Histoplasma (capsulatum)
- Mucorales (all species)
- Rhizopus (all species)
- Scedosporium (all species)
- Zygomycetes, NOS
- Suspected fungal infection

For reference, definitions of some common terms concerning fungal infections are provided below. These definitions are for clarification only and should not be considered to be reporting criteria or instructions.

Fungemia: the presence of fungus (mold or yeasts) in blood cultures.

Proven invasive fungal infections: based on EORTC published recommendations1 as follows:
A. Histopathologic, cytopathologic, or direct microscopic examination of a specimen obtained by needle aspiration or biopsy in which hyphae or melanized yeast-like forms are seen accompanied by evidence of associated tissue damage (molds) or showing encapsulated budding yeasts or Candida species showing pseudohyphae or true hyphae (yeasts); or

B. Cultures of specimens obtained by a sterile procedure from a normally sterile site (excludes bronchial lavage, sinus specimen, and urine) with clinical or radiologic evidence of abnormality growing mold, ‘black yeast’, or yeast.

Probable invasive fungal infections: based on EORTC published recommendations\(^1\) requires presence of one each of host factors, clinical features, and mycological features:

A. Host Factors

1. Receipt of allogeneic HCT.
2. Treatment with steroids of at least 0.3mg/kg/day prednisone equivalent for 3 weeks of longer.
3. Treatment with T-cell immunosuppressents (cyclosporine, tacrolimus), monoclonal antibodies (alemptuzumab), or nucleoside analogues (fludarabine) in the past 90 days.

B. Clinical Features

1. Lower respiratory tract disease includes CT findings of one of the following:
   a. dense, well-circumscribed lesions with or without a halo;
   b. air-crescent sign; or
   c. cavity.
2. Tracheobronchitis with evidence of ulceration, nodule, pseudomembrane, plaque, or eschar on bronchoscopy.
3. Sinonasal infection with; CT documenting acute sinusitis and at least one of the following:
   a. acute localized pain (including radiation to the eye);
   b. nasal ulceration with black eschar; or
   c. bone destruction of the sinuses.

C. Mycological Features

1. Direct: Fungal elements of mold or culture of specific mold from sputum, bronchoalveolar lavage, bronchial brushings, or sinus aspirate.
2. Indirect: Galactomannan antigen detected in serum, plasma, bronchial lavage fluid, or cerebrospinal fluid or Beta-D-glucan detected in serum.
Disseminated infections with Histoplasmosis, Blastomycosis, or Coccidiomycosis:

A. Culture of any of these organisms from an affected site or from the blood.
B. Histopathology or direct microscopic demonstration of the appearance characteristic of these dimorphic (can exist in both a yeast and mold [hyphae] form based on external conditions) fungi;
C. Demonstration of coccidioidal antibody in CSF or a 2-dilution rise in 2 consecutive blood samples in the appropriate setting; or
D. Presence of a host factor (see above) plus an appropriate clinical picture with mycological evidence such as a positive Histoplasma antigen test from urine, blood, or cerebrospinal fluid.

Disseminated Cryptococcus: cryptococcal antigen detected in the cerebrospinal fluid.

Links to Form Sections
Q1-25: Infection Episode
Q26-31: Treatment of Infection

1 Clin Infect Dis. 2008 June 15; 46(12): 1813–1821

Manual Updates
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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<th>Description</th>
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</thead>
</table>
Q1-25: Infection Episode

**Question 1: Organism**

This field is auto-populated to match the fungus reported on the Baseline Form (Form 2000). Review the value to ensure it is accurate. A Fungal Infection Pre-Infusion Data Form will come due for each applicable infection reported on the Baseline Form (Form 2000) so it is imperative to identify the fungal infection to which this form will correspond.

If multiple infections of the same fungus are reported during the same reporting period, the center must complete a Fungal Infection Pre-Infusion Data Form (Form 2046) for each infection instance, or episode, reported.

**Question 2: Date of Infection Diagnosis**

This field is auto-populated to match the date reported on the Baseline Form. Review the value to ensure it is accurate. See the Baseline section of the manual for further instructions on reporting the date of diagnosis.

If multiple infections of the same fungal organism are reported in the same reporting period, the diagnosis date in question two will clarify for which infection episode the form is being completed.

**Question 3-25: Diagnostic Testing**

Report all testing that had positive results and which indicated the fungal infection was present. Do not report negative or indeterminate / equivocal testing in this section. As indicated in the instructions for question one, if the recipient was diagnosed with multiple fungal infections prior to infusion, multiple Fungal Infection Pre-Infusion Data Forms must be completed (one for each organism). Ensure the testing reported in these questions only reflects the assessments used to identify the infection / organism being reported on this form. For reporting purposes, only report methods performed and samples collected (or sites assessed for radiological findings) within 14 days (+ / -) of the diagnosis date reported in question two.

Links to specific instructions

- [Methods of Assessment](#)
- [Site / Sample Source](#)

**Methods of Assessment:**

A fungal infection may be identified by multiple assessments near the time of diagnosis. A description of
each method of assessment is provided below. Report “Yes” for all assessments which were positive for signs of the fungal infection being reported on this form. Report “no” for assessments which were never performed or were never considered to be positive for the fungal infection being reported on this form. If the significance of the test result is not clear, obtain documentation from the recipient’s physician confirming whether the assessment was considered positive. Report “No” for assessments with results which are determined to be equivocal or indeterminate.

**Radiographic Findings**: includes all imaging assessments. Examples include x-ray, CT scan, PET scan, and MRI. These assessments are capable of identifying the presence of a fungal infection, but cannot identify specific organisms. Refer to the clinical interpretation of an imaging assessment to determine whether the test was considered positive for the infection being reported. If the provider’s notes do not specify whether the test was positive, obtain documentation from the physician clarifying how the assessment should be reported.

**Pathology**: samples obtained from the recipient via biopsy or fine needle aspirate are evaluated via microscopy without incubation. Presence and classification is assessed solely by microscopy. If a sample is grown in culture or stained, report these test methods under the more specific options below. Generally, the results / interpretation section of the pathology report will specify whether the assessment was positive or negative for signs of a fungal infection. If this is not the case, refer to the provider notes and obtain clarification from the recipient’s physician if both the pathology report and provider notes are not clear.

**Culture**: samples taken from the recipient are incubated in media supporting fungal growth. Presence of infection is assessed by colony formation / growth and classification is done via microscopy following incubation. Results are typically found in the microbiology / virology section of the medical record. The culture report will document whether growth is detected (positive) or not detected (negative). Staining may also be performed to classify the infection following incubation. Report the results of any staining techniques in the more specific methods below.

**KOH / Calcofluor / Giemsa stain**: samples taken from the recipient (usually fluids such as sputum or wash samples) are exposed to a stain which binds to structures specific to fungal cells. The sample is evaluated via microscopy to determine whether stained cells are present (positive result) or absent (negative result).

- **KOH**: potassium hydroxide also referred to a “fungal wet prep.”
- **Calcofluor**: white stain which binds to fungal cell walls causing them to appear bright green / blue.
- **Giemsa stain**: often used to identify *Histoplasma*.

**Galactomannan Assay**: a sample (i.e., serum, bronchial lavage, bronchial wash or CSF) taken from the...
recipient are exposed to galactomannan-specific antibodies followed by antibody-specific enzymes (ELISA method). Galactomannan is a molecule specific to *Aspergillus*. The enzyme activity is quantified and the test is considered positive if the activity is above the upper limit of normal (as indicated on the test report). If the report is unclear regarding whether the result is considered positive, negative, or equivocal, contact your center’s laboratory to confirm.

**1,3-Beta-D-glucan (Fungitell) assay**: a sample (i.e., serum, bronchial lavage, bronchial wash or CSF) taken from the recipient is exposed to beta-d-glucan-specific antibodies followed by antibody-specific enzymes (ELISA method). Beta-d-glucan is a molecule found on a multiple fungi including *Candida* and *Aspergillus*. The enzyme activity is quantified and the test is considered positive if the activity is above the upper limit of normal (as indicated on the test report). If the report is unclear regarding whether the result is considered positive, negative, or equivocal, contact your center’s laboratory to confirm.

**PCR Assay**: samples taken from the recipient are manipulated using polymerase chain reaction techniques. Presence and classification of fungi are assessed by identifying DNA sequences unique to specific fungi. Reports can generally be found in the microbiology / virology section or the molecular pathology section of the medical record. The lab report will document whether an infection is detected (positive) or not detected (negative). If the report is unclear, contact your center’s laboratory to confirm.

**Sites / Sample Source:**

For each method of assessment which showed evidence of the fungal infection being reported, indicate every site or sample source where the infection was detected. Do not report sites yielding negative or indeterminate / equivocal results. Note the time window provided in the initial instructions for questions 2-35.
Q26-31: Treatment of Infection

Question 26: Did the recipient receive any therapy between 7 days prior to the date of infection diagnosis and the date of infusion?

Report “Yes” if the recipient received any antifungal treatment from seven days prior to the date of diagnosis (refer to question two) through the day of infusion (Day 0 for HCT or cellular therapy). If the recipient did not receive any antifungal therapy during this time frame, report “No” and go to question 31.

Question 27-30: Antifungal Drugs

One instance of questions 27-30 must be completed for each drug administered during the time window indicated in the instructions for question 26. For each drug given, indicate the specific drug in questions 27-28 and then specify the start date in questions 29-30. If the exact start date is not known, but the year the drug was started is known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates. If an estimated date is reported, check the “Date Estimated” box next to question 30.

If an antifungal drug was started greater than seven days prior to the date of infection diagnosis and was continued to within seven days of the diagnosis date, report seven days prior to the diagnosis date as the date the medication was started and check the “Date estimated” box next to question 30.

Antifungal Drug Reporting Scenarios:

A. If a patient was diagnosed with Aspergillus fumigatus on 1/15/2016, go back to 1/8 to determine the medications the patient was receiving. If the patient is on drug “X” (e.g., fluconazole) on 1/8 but you also note the patient was receiving the drug on a prior visit on 1/3, please record the start date for drug “X” as 1/8 and mark “Date estimated”.

B. If the patient was diagnosed with Aspergillus fumigatus on 1/15/2016, and it is noted in a clinic note dated 1/19 that the patient was started on drug “Y” (e.g., posaconazole) “a few days ago” on the form, please record the start date for drug “Y” as 1/19 and mark “Date estimated”.

Question 31: What was the status of the infection?

Report the status of the fungal infection immediately prior to the start of the preparative regimen (or infusion if no preparative regimen was given) based on the primary care provider’s clinical judgement. If the status of the infection is not documented in the primary care provider’s note summarizing their last evaluation prior to the start of the preparative regimen, obtain documentation from the provider indicating which option to
report. For reporting purposes, centers should indicate “Ongoing” if the infection is still present, but cannot be considered improved or resolved.
The Fungal Infection Post-Infusion Data Form (Form 2146) captures information regarding the diagnosis, treatment, and response to treatment of fungal infections diagnosed after receiving a HCT or cellular therapy. This form must be completed when one of the fungal infections listed below has been reported on the Post-HCT Follow-Up Data Form (Form 2100). One form will be completed for each applicable infection reported.

The following infections will cause a Fungal Infection Post-Infusion Data Form (Form 2146) to come due when reported on the Post-HCT Follow-Up Data Form (Form 2100):

- Aspergillus flavus
- Aspergillus fumigatus
- Aspergillus niger
- Aspergillus, NOS
- Aspergillus terreus
- Aspergillus ustus
- Blastomyces (dermatitidis)
- Candida albicans
- Candida non-albicans
- Cryptococcus gattii
- Cryptococcus neoformans
- Fusarium (all species)
- Histoplasma (capsulatum)
- Mucorales (all species)
- Rhizopus (all species)
- Scedosporium (all species)
- Zygomycetes, NOS
- Suspected fungal infection

Refer to the 2046: Fungal Infection Pre-Infusion Data section of the Forms Instructions Manual for definitions of common terms concerning fungal infections.

Links to Form Sections
Q1-25: Infection Episode
Q26-42: Hematologic Findings at Diagnosis of Infection
Q43-49: Treatment of Infection
Manual Updates

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</table>
**Q1-25: Infection Episode**

**Question 1: Organism**

This field is auto-populated to match the fungus reported on the Post-HCT Follow-Up Form (Form 2100). Review the value to ensure it is accurate. A Fungal Infection Post-Infusion Data Form will come due for each applicable infection reported on the Post-HCT Follow-Up Form (Form 2100) so it is imperative to identify the fungal infection to which this form will correspond.

If multiple infections of the same fungus are reported during the same reporting period, the center must complete a Fungal Infection Post-Infusion Data Form (Form 2146) for each infection instance, or episode, reported.

**Question 2: Date of Infection Diagnosis**

This field is auto-populated to match the date reported on the Post-HCT Follow-Up Data Form (Form 2100). Review the value to ensure it is accurate. See the Post-HCT Follow-Up Data section of the manual for further instructions on reporting the date of diagnosis.

If multiple infections of the same virus are reported in the same reporting period, the diagnosis date in question two will clarify for which infection episode the form is being completed.

**Question 3-25: Diagnostic Testing**

Report all testing that had positive results and which indicated the fungal infection was present. Do not report negative or indeterminate / equivocal testing in this section. As indicated in the instructions for question one, if the recipient was diagnosed with multiple fungal infections during the reporting period, multiple Fungal Infection Post-Infusion Data Forms must be completed (one for each organism). Ensure the testing reported in these questions only reflects the assessments used to identify the infection / organism being reported on this form. For reporting purposes, only report methods performed and samples collected (or sites assessed for radiological findings) within 14 days (+/-) of the diagnosis date reported in question two.

**Links to specific instructions**

Methods of Assessment
Site / Sample Source
Methods of Assessment:

A fungal infection may be identified by multiple assessments near the time of diagnosis. A description of each method of assessment is provided below. Report “Yes” for all assessments which were positive for signs of the fungal infection being reported on this form. Report “no” for assessments which were never performed or were never considered to be positive for the fungal infection being reported on this form. Note, the time window provided in the initial instructions for questions 3-25. If the significance of the test result is not clear, obtain documentation from the recipient’s HCT / cellular therapy physician confirming whether the assessment was considered positive. Report “No” for assessments with results which are determined to be equivocal or indeterminate.

Radiographic Findings: includes all imaging assessments. Examples include x-ray, CT scan, PET scan, and MRI. These assessments are capable of identifying the presence of a fungal infection, but cannot identify specific organisms. Refer to the clinical interpretation of an imaging assessment to determine whether the test was considered positive for the infection being reported. If the provider’s notes do not specify whether the test was positive, obtain documentation from the HCT / cellular therapy physician clarifying how the assessment should be reported.

Pathology: samples taken from the recipient which are evaluated via microscopy without incubation. Presence and classification is assessed solely by microscopy. If a sample is grown in culture or stained, report these test methods under the more specific options below. Generally, the results / interpretation section of the pathology report will specify whether the assessment was positive or negative for signs of a fungal infection. If this is not the case, refer to the provider notes and obtain clarification from the recipient’s HCT / cellular therapy physician if both the pathology report and provider notes are not clear.

Culture: samples taken from the recipient which are incubated in media supporting fungal growth. Presence of infection is assessed by colony formation / growth and classification is done via microscopy following incubation. Results are typically found in the microbiology section of the medical record. The culture report will document whether growth is detected (positive) or not detected (negative). Staining may also be performed to classify the infection following incubation. Report the results of any staining techniques in the more specific methods below.

KOH / Calcofluor / Giemsa stain: samples taken from the recipient are exposed to a stain which binds to structures specific to fungal cells. The sample is evaluated via microscopy to determine whether stained cells are present (positive result) or absent (negative result).

KOH: potassium hydroxide also referred to a “fungal wet prep.”
Calcofluor: white stain which binds to fungal cell walls causing them to appear bright green / blue.
Giemsa stain: often used to identify Histoplasma.
**Galactomannan assay:** a sample (i.e., serum, bronchial lavage, bronchial wash or CSF) taken from the recipient are exposed to galactomannan-specific antibodies followed by antibody-specific enzymes (ELISA method). Galactomannan is a molecule specific to *Aspergillus*. The enzyme activity is quantified and the test is considered positive if the activity is above the upper limit of normal (as indicated on the test report). If the report is unclear regarding whether the result is considered positive, negative, or equivocal, contact your center’s laboratory to confirm.

**1,3-Beta-D-glucan (Fungitell) assay:** a sample (i.e., serum, bronchial lavage, bronchial wash or CSF) taken from the recipient is exposed to beta-d-glucan-specific antibodies followed by antibody-specific enzymes (ELISA method). Beta-d-glucan is a molecule found on a broad range of fungi. The enzyme activity is quantified and the test is considered positive if the activity is above the upper limit of normal (as indicated on the test report). If the report is unclear regarding whether the result is considered positive, negative, or equivocal, contact your center’s laboratory to confirm.

**PCR assay:** samples taken from the recipient are manipulated using polymerase chain reaction techniques. Presence and classification of fungi are assessed by identifying DNA sequences unique to specific fungi. Reports can generally be found in the microbiology section or the molecular pathology section of the medical record. The lab report will document whether an infection is detected (positive) or not detected (negative). If the report is unclear, contact your center’s laboratory to confirm.

**Sites / Sample Source:**

For each method of assessment which showed evidence of the fungal infection being reported, indicate every site or sample source where the infection was detected. Do not report sites yielding negative or indeterminate / equivocal results. Note the time window provided in the initial instructions for questions 3-25.
Q26-42: Hematologic Findings at Diagnosis of Infection

Question 26-36: Complete Blood Count

Report the date of the complete blood count (CBC) performed closest to the date of diagnosis of the fungal infection being reported on this form. The CBC must have been performed within seven days of the date of diagnosis. For each value listed in questions 27-36, indicate whether the value was known on the date reported in question 26. If known, report the value and corresponding units (when asked). If the value is not known on the date reported in question 26, report “Unknown” and go to the next value.

If a CBC was not performed within the indicated time window, or it is not known if a CBC was performed, leave question 26 blank and override the error in FormsNet3 using the code “Unknown.” If the exact date of the CBC is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

Question 37-39: Serum Creatinine

Report the result of the serum creatinine test performed closest to the date of diagnosis of the fungal infection being reported on this form. The test must have been performed within seven days of the date of diagnosis. If known, report the value and associated units. Also report the upper limit of normal and associated units for the test being reported.

If a serum creatinine test was not performed within the indicated time window, or it is not known if a serum creatinine test was performed, report “Unknown” for question 37 and go to question 40.

Question 40-42: ALT (SGPT)

Report the result of the alanine aminotransferase (ALT / SGPT) test performed closest to the date of diagnosis of the fungal infection being reported on this form. The test must have been performed within seven days of the date of diagnosis. If known, report the value and associated units. Also report the upper limit of normal and associated units for the test being reported.

If an ALT test was not performed within the indicated time window, or it is not known if a test was performed, report “Unknown” for question 40 and go to question 43.
**Q43-49: Treatment of Infection**

**Question 43:** Did the recipient receive any therapy between 7 days prior to the date of infection diagnosis and the date of contact for this reporting period?

Report “Yes” if the recipient received any antifungal treatment from seven days prior to the date of diagnosis (refer to question two) through the date of contact for the reporting period (refer to the date of contact reported on the corresponding follow-up form). If the recipient did not receive any antifungal therapy during this time frame, report “No” and go to question 49.

**Question 44-48: Antifungal Drugs**

One instance of questions 44-48 must be completed for each drug administered during the time window indicated in the instructions for question 43. For each drug given, indicate the specific drug in questions 43-44 and then specify the start date in questions 46-47. If the exact start date is not known, but the year the drug was started is known, refer to the refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates. If an estimated date is reported, check the “Date estimated” box next to question 47.

If an antifungal drug was started greater than seven days prior to the date of infection diagnosis and was continued to within seven days of the diagnosis date, report seven days prior to the diagnosis date as the date the medication was started and check the “Date estimated” box next to question 47.

For question 48, indicate whether the treatment being reported in this instance of questions 44-48 was still being given 30 days (+ / – three days) after the date of diagnosis. This includes treatment which may have been interrupted, but was still being given 30 days (+ / – three days) after diagnosis. If the fungal infection reported on this form was diagnosed within 30 days (+ / – three days) of the date of contact for this reporting period (refer to the corresponding follow-up form), indicate whether the drug was still being given on the date of contact.

If it is not known whether treatment was still being given within the time window indicate above, leave question 48 blank and override the error in FormsNet3 using the code “Unknown.”

**Question 49: What was the status of the infection?**

Report the status of the fungal infection on the date of contact for this reporting period (refer to the corresponding follow-up form) based on the primary care provider’s clinical judgement. If the status of the infection is not documented in the primary care provider’s note summarizing their last evaluation performed during the reporting period, obtain documentation from the provider indicating which option to report. For
reporting purposes, centers should indicate “Ongoing” if the infection is still present, but cannot be considered improved or resolved.
Hepatitis is a general term referring to non-specific inflammation of the liver, which can be caused by multiple conditions, including viral infection. This form is intended to capture information regarding two forms of viral hepatitis infections, Hepatitis B and Hepatitis C. Viral hepatitis is the leading cause of liver cancer and the most common reason for liver transplantation. Hepatitis B is caused by infection with the Hepatitis B virus (HBV); similarly, Hepatitis C is caused by infection with the Hepatitis C virus (HCV). Both Hepatitis B and C are spread through contact with infected blood or bodily fluids, though they are both more highly concentrated in blood than in other bodily fluids, such as semen or wound exudates. Acute HBV and HCV can present on a spectrum ranging from asymptomatic to moderate-severe symptoms, including abdominal pain, jaundice, fatigue, nausea, and vomiting. Chronic hepatitis infections can result from either HBV or HCV infections. Chronic HBV tends to be more severe and is associated with a higher incidence of liver cancer compared to HCV, whereas patients with HCV are more likely than HBV patients to develop liver cirrhosis and associated complications.


- **2047: Hepatitis Serology Pre-HCT**
- **2147: Hepatitis Serology Post-HCT**
2047: Hepatitis Serology Pre-HCT

The Hepatitis Serology Pre-HCT Data, Form 2047, will come due when any of the following IDM

s are reported as “positive” on the Form 2000, Recipient Baseline Data:

- Hepatitis B surface antigen
- Hepatitis B core antibody
- Hepatitis B DNA
- Hepatitis C antibody
- Hepatitis C NAT

Because viral hepatitis can be transmitted from the donor to the recipient via hematopoietic stem cell transplantation, this form will also be triggered when any of the following IDM
s are reported as “reactive” on the Form 2004, Infectious Disease Markers:

- Hepatitis B surface Antigen
- Hepatitis B core Antibody
- Hepatitis C Antibody

- Q1-6: Serological Evidence of Prior Hepatitis Exposure / Infection – Recipient
- Q7-26: History of Antiviral Therapy for Hepatitis – Recipient
- Q27-34: Serological Evidence of Prior Hepatitis Exposure / Infection – Donor
- Q35-54: History of Antiviral Therapy for Hepatitis – Donor

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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Q1-6: Serological Evidence of Prior Hepatitis Exposure / Infection – Recipient

Question 1: Specify and/or confirm previous Hepatitis B surface antigen (HBsAg) testing performed and reported on the Form 2000 – Recipient Baseline Data

The hepatitis B surface antigen is a protein expressed on the surface of the hepatitis B virus. Its presence in the blood serum indicates acute or active chronic infection. In acutely infected patients, blood will test HBsAg positive within one to nine weeks of exposure to the virus. Patients who do not go on to develop chronic infection will be surface antigen negative by 15 weeks after the onset of symptoms. Chemiluminescent immunoassay (CIA), electrochemiluminescent immunoassay (ECLIA), or enzyme-linked immunosorbent assay (ELISA) are used to test for the presence of hepatitis B surface antigens; research indicates CIA and ECLIA may be more sensitive for detecting low levels of HBsAg. Positive HBsAg results require confirmation with a neutralization procedure using human Anti-HBs (HBsAg Confirmation Assay). If the sample is neutralizable in the confirmatory test, the specimen is considered positive for HBsAg.

Report the laboratory result as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for recipient HBsAg testing. If HBsAg testing was not done, indicate “not tested.” Continue with question 2.


Hepatitis B viral load testing
Hepatitis B viral load testing is used to quantify hepatitis B viral DNA in the blood. The diagnosis of hepatitis B infection, either acute or chronic, is generally made by serologic testing, though DNA testing may be useful in the diagnosis of early acute HBV. Additionally, DNA testing is useful to determine whether the infection is active and to monitor response to anti-HBV therapies. Hepatitis B viral load testing is performed by PCR amplification of HBV DNA in the patient’s serum.

Report all instances of Hepatitis B viral load testing performed within three months prior to the start of the preparative regimen; create an instance for each test result. If no testing was performed within three months prior to the start of the preparative regimen, report the testing performed prior to this period; report only the latest instance.

Question 2: Pre-HCT Hepatitis B viral load – date

Specify the date recipient Hepatitis B viral load testing was performed and continue with question 3.
Question 3: Hepatitis B viral load level

Report the result for recipient viral load testing as indicated on the laboratory report. If necessary, convert values so they can be reported in the unit of measurement options available on the form.

Hepatitis C viral load testing

Hepatitis C viral load testing is primarily used to monitor response to anti-viral therapy and confirm activity of infection; additionally, it may be used to diagnosis early acute HCV infection and to detect active chronic infection. Hepatitis C viral load testing is performed by RT-PCR amplification of HCV RNA in the patient’s serum.

Report all instances of Hepatitis C viral load testing performed within three months prior to the start of the preparative regimen; create an instance for each test result. If no testing was performed within three months prior to the start of the preparative regimen, report the testing performed prior to this period; report only the latest instance.

Question 4: Pre-HCT Hepatitis C viral load – date

Specify the date recipient Hepatitis C viral load testing was performed and continue with question 5.

Question 5: Hepatitis C viral load level

Report the result for recipient viral load testing as indicated on the laboratory report. If necessary, convert values so they can be reported in the unit of measurement options available on the form.

Question 6: Were any liver biopsies performed for cytology and/or pathology prior to HCT?

Indicate if the recipient had a liver biopsy performed, either for cytologic or histopathologic evaluation, prior to the start of the preparative regimen. If “yes,” submit a copy of the biopsy report using a Log of Appended Documents, Form 2800. Proceed with question 7.
Q7-26: History of Antiviral Therapy for Hepatitis – Recipient

**Question 7: Did the recipient receive therapy for hepatitis prior to HCT?**

Hepatitis antiviral therapy is intended to prevent progression of the disease and minimize sequelae of infection. The National Institutes of Health (NIH) in the United States recommends antiviral therapy for Hepatitis B patients with acute liver failure, cirrhosis or advanced cirrhosis with positive viral load, and for reactivation of chronic HBV during or after chemotherapy and/or immunosuppression. ² Lamivudine, pegylated interferon alfa, entecavir, and tenofovir are medications currently used to treat Hepatitis B. Hepatitis C therapy has similar goals of sustaining a viral response and minimizing sequelae of infection. Therapy is generally recommended for patients with elevated liver enzymes and/or significant histologic damage on liver biopsy.

Indicate if the recipient received antiviral therapy for hepatitis at any time prior to the preparative regimen. If “yes,” continue with question 8. If “no,” continue with question 27 for allogeneic recipients and the signature section for autologous recipients.


For each therapeutic agent below, create an instance for each course. A course is defined as the period from therapy start to discontinuation of therapy, during which the patient is regularly scheduled to receive the medication; if the dose is changed, please continue the course and only report therapy stopped if the medication is discontinued for at least 14 consecutive days.

**Question 8: Lamivudine therapy – course given**

Indicate if the recipient received a course at any time prior to the start of the preparative regimen; create an instance for each course given. If “yes,” continue with question 9; if “no,” continue with question 14.

**Question 9: Date started**

Report the date therapy was initiated and continue with question 10.

**Question 10: Daily dose**

Report the daily prescribed dose at the start of the therapy
Question 11: Reason started

This is a free text data field. Concisely document the rationale for starting this course of therapy; suggested examples include “prophylaxis” and “treatment.” If the patient received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”

Question 12: Therapy stopped?

Indicate if therapy was stopped prior to the start of the preparative regimen. If “yes,” continue with question 13. If “no,” continue with question 14.

Question 13: Date stopped

Report the date therapy was stopped and continue with question 14.

Question 14: Interferon therapy – course given

Indicate if the recipient received a course at any time prior to the start of the preparative regimen; create an instance for each course given. If “yes,” continue with question 15; if “no,” continue with question 20.

Question 15: Date started

Report the date therapy was initiated and continue with question 16.

Question 16: Daily dose

Report the daily prescribed dose at the start of the therapy

Question 17: Reason started

This is a free text data field. Concisely document the rationale for starting this course of therapy; suggested examples include “prophylaxis” and “treatment.” If the patient received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”

Question 18: Therapy stopped?

Indicate if therapy was stopped prior to the start of the preparative regimen. If “yes,” continue with question 19. If “no,” continue with question 20.
**Question 19: Date stopped**

Report the date therapy was stopped and continue with question 20.

**Questions 20-21: Other antiviral therapy – course given**

Indicate if the recipient received a course of any other (not Lamivudine or interferon) antiviral therapy for hepatitis infection at any time prior to the start of the preparative regimen; create an instance for each course given. If “yes,” continue with question 21 and specify the other antiviral therapy given; if “no,” continue with question 27.

**Question 22: Date started**

Report the date therapy was initiated and continue with question 23.

**Question 23: Daily dose**

Report the daily prescribed dose at the start of therapy.

**Question 24: Reason started**

This is a free text data field. Concisely document the rationale for starting this course of therapy; suggested examples include “prophylaxis” and “treatment.” If the patient received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”

**Question 25: Therapy stopped?**

Indicate if therapy was stopped prior to the start of the preparative regimen. If “yes,” continue with question 26. If “no,” continue with question 27.

**Question 26: Date stopped**

Report the date therapy was stopped and continue with question 27.
Q27-34: Serological Evidence of Prior Hepatitis Exposure / Infection – Donor

Complete questions 27-34 for allogeneic transplants only; if donor information is unknown, leave the data field(s) blank. Complete all data fields for which relevant donor information is documented and available to the CIBMTR center completing the form.

Question 27: Hepatitis B core antibody (HBcAb)

The total hepatitis B core antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of the core antigen by liver cells. Since core antigen is present only in infected liver cells and cannot be detected in the blood of an infected individual, only core antibody is tested, since it circulates in the peripheral blood. After infection, total core antibodies will persist for life. Presence of core antibodies can indicate active and/or prior infection, but hepatitis core antibodies will not be present in individuals with no history of natural infection with HBV. This means that vaccinated individuals will not be anti-HBc positive because vaccination results in the body developing antibodies to the hepatitis B surface antigen. Chemiluminescent immunoassay (CIA), enzyme-linked immunosorbent assay (ELISA), or Elecsys anti-HBc is used to test for the presence of hepatitis B core antibodies. Currently, there is no licensed confirmatory test for anti-HBc in the United States; confirmation of antibody presence is done by performing a second anti-HBc test using a different manufacturer’s test kit.

Report the laboratory result of most recent donor testing prior to donation as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate). If testing was not done, indicate “not tested.” If the donor previously had test results reported on the Form 2004, Infectious Disease Markers, and results are unchanged or testing was not repeated, indicate “confirm prior result.”

Question 28: Hepatitis B surface antigen (HBsAg)

The hepatitis B surface antigen is a protein expressed on the surface of the hepatitis B virus. Its presence in the blood serum indicates acute or active chronic infection. In acutely infected patients, blood will test HBsAg positive within one to nine weeks of exposure to the virus. Donors who do not go on to develop chronic infection will be surface antigen negative by 15 weeks after the onset of symptoms. Chemiluminescent immunoassay (CIA), electrochemiluminescent immunoassay (ECLIA), or enzyme-linked immunosorbent assay (ELISA) are used to test for the presence of hepatitis B surface antigens; research indicates CIA and ECLIA may be more sensitive for detecting low levels of HBsAg. Positive HBsAg results require confirmation with a neutralization procedure using human Anti-HBs (HBsAg Confirmation Assay). If the sample is neutralizable in the confirmatory test, the specimen is considered positive for HBsAg.
Report the laboratory result of most recent donor testing prior to donation as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for donor testing. If testing was not done, indicate “not tested.” If the donor has previously had test results reported on the Form 2004, Infectious Disease Markers, and results are unchanged or testing was not repeated, indicate “confirm prior result.”


**Question 29: Hepatitis B e antigen (HBeAg)**

The hepatitis B e antigen is the extracellular form of the hepatitis B core antigen. Hepatitis B core antigen does not circulate and therefore cannot be detected in serum testing; as a result, hepatitis B e antigen may be used as a proxy measure. Its presence is associated with active viral replication and increased infectivity. The hepatitis B e antigen is present in the serum during the early phase of acute HBV infection, shortly after the hepatitis B surface antigen is first seen. Hepatitis B e antigen would only be seen during active infection; however, there are some variants of hepatitis B virus which are known to be hepatitis e negative, even during periods of high viral replication and increased infectivity.

Report the laboratory result of most recent donor testing prior to donation as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for donor testing. If testing was not done, indicate “not tested.”

**Question 30: Hepatitis C antibody (HCAb)**

The total hepatitis C antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of the hepatitis C virus. Antibodies can generally be detected as soon as four weeks after exposure and will persist for life. Enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA) is used to screen for hepatitis C antibodies; confirmatory testing is done by recombinant immunoblot assay (RIBA). A positive ELISA or CIA result without confirmation by RIBA is considered an indeterminate result, unless HCV RNA is detected in the blood by PCR.

Report the laboratory result of most recent donor testing prior to donation as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for donor testing. If testing was not done, indicate “not tested.” If the donor has previously had test results reported on the Form 2004, Infectious Disease Markers, and results are unchanged or testing was not repeated, indicate “confirm prior result.”

**Donor Hepatitis B viral load testing**

Hepatitis B viral load testing is used to quantify hepatitis B viral DNA in the blood. The diagnosis of hepatitis B infection, either acute or chronic, is generally made by serologic testing, though DNA testing may be
useful in the diagnosis of early acute HBV. Additionally, DNA testing is useful to determine whether the infection is active and to monitor response to anti-HBV therapies. Hepatitis B viral load testing is performed by PCR amplification of HBV DNA in the patient’s serum.

Report all instances of donor Hepatitis B viral load testing performed prior to donation; create an instance for each test result. If no testing was performed, proceed with question 33.

**Question 31: Donor Hepatitis B viral load – date**

Specify the date donor Hepatitis B viral load testing was performed and continue with question 32.

**Question 32: Hepatitis B viral load level**

Report the result for donor viral load testing as indicated on the laboratory report. If necessary, convert values so they can be reported in the unit of measurement options available on the form.

**Donor Hepatitis C viral load testing**

Hepatitis C viral load testing is primarily used to monitor response to anti-viral therapy and confirm activity of infection; additionally, it may be used to diagnosis early acute HCV infection and to detect active chronic infection. Hepatitis C viral load testing is performed by RT-PCR amplification of HCV RNA in the patient’s serum.

Report all instances of donor Hepatitis C viral load testing performed prior to donation; create an instance for each test result. If no testing was performed, proceed with question 35.

**Question 33: Donor Hepatitis C viral load – date**

Specify the date donor Hepatitis C viral load testing was performed and continue with question 34.

**Question 34: Hepatitis C viral load level**

Report the result for donor viral load testing as indicated on the laboratory report. If necessary, convert values so they can be reported in the unit of measurement options available on the form.
Q35-54: History of Antiviral Therapy for Hepatitis – Donor

Complete questions 35-54 for allogeneic transplants only; if donor information is unknown, leave the data field blank. Complete all data fields for which relevant donor information is documented and available to the CIBMTR center completing the form.

Question 35: Did the donor receive therapy for hepatitis prior to the stem cell harvest?

Hepatitis antiviral therapy is intended to prevent progression of the disease and minimize sequelae of infection. The National Institutes of Health (NIH) in the United States recommends antiviral therapy for Hepatitis B patients with acute liver failure, cirrhosis or advanced cirrhosis with positive viral load, and for reactivation of chronic HBV during or after chemotherapy and/or immunosuppression. Lamivudine, pegylated interferon alfa, entecavir, and tenofovir are medications currently used to treat Hepatitis B. Hepatitis C therapy has similar goals of sustaining a viral response and minimizing sequelae of infection. Therapy is recommended for patients with elevated liver enzymes and/or significant histologic damage on liver biopsy.

Indicate if the donor received antiviral therapy for hepatitis at any time prior to the stem cell harvest. If “yes,” continue with question 36. If “no,” continue with the signature section. If “unknown,” leave the data field blank and continue with the signature section.


For each therapeutic agent below, create an instance for each course. A course is defined as the period from therapy start to discontinuation of therapy, during which the donor is regularly scheduled to receive a certain dose of medication; if the daily dose is changed, report a new line of therapy starting with the date the changed dosage is administered. Complete all data fields for which information is available.

Question 36: Lamivudine therapy given?

Indicate if the donor received a course at any time prior to the stem cell harvest; create an instance for each course given. If “yes,” continue with question 37; if “no,” continue with question 42.
Question 37: Date started
Report the date therapy was initiated and continue with question 38.

Question 38: Currently receiving?
Indicate if the donor was receiving therapy at the time of stem cell donation. If they were continuing to receive Lamivudine, report “yes.”

Question 39: Therapy stopped?
Indicate if therapy was stopped prior to the stem cell harvest. If “yes,” continue with question 40. If “no,” continue with question 42.

Question 40: Date stopped
Report the date therapy was stopped and continue with question 41.

Question 41: Reason stopped
This is a free text data field. Concisely document the rationale for stopping this course of therapy; suggested examples include “planned stop” and “undesirable side effects.” If the donor received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”

Question 42: Interferon therapy given?
Indicate if the donor received a course at any time prior to the stem cell harvest; create an instance for each course given. If “yes,” continue with question 43; if “no,” continue with question 48.

Question 43: Date started
Report the date therapy was initiated and continue with question 44.

Question 44: Currently receiving?
Indicate if the donor was receiving therapy at the time of stem cell donation. If they were continuing to receive interferon therapy, report “yes.”

Question 45: Therapy stopped?
Indicate if therapy was stopped prior to the stem cell harvest. If “yes,” continue with question 46. If “no,” continue with question 48.
Question 46: Date stopped

Report the date therapy was stopped and continue with question 47.

Question 47: Reason stopped

This is a free text data field. Concisely document the rationale for stopping this course of therapy; suggested examples include “planned stop” and “undesirable side effects.” If the donor received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”

Questions 48-49: Other antiviral therapy given?

Indicate if the donor received a course of any other (not Lamivudine or interferon) antiviral therapy for hepatitis infection at any time prior to the stem cell harvest; create an instance for each course of each agent given. If “yes,” continue with question 49 and specify the other antiviral therapy given; if “no,” continue with continue with signature section of the form.

Question 50: Date started

Report the date therapy was initiated and continue with question 51.

Question 51: Currently receiving?

Indicate if the donor was receiving therapy at the time of stem cell donation. If they were continuing to receive another antiviral agent, report “yes.”

Question 52: Therapy stopped?

Indicate if therapy was stopped prior to the stem cell harvest. If “yes,” continue with question 53. If “no,” continue with the signature section.

Question 53: Date stopped

Report the date therapy was stopped and continue with question 54.

Question 54: Reason stopped

This is a free text data field. Concisely document the rationale for stopping this course of therapy; suggested examples include “planned stop” and “undesirable side effects.” If the donor received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”
2147: Hepatitis Serology Post-HCT

The Hepatitis Serology Post-HCT Data, Form 2147, will come due when the following IDMs are reported as "positive" on the Form 2000, Recipient Baseline Data:

- Hepatitis B surface antigen
- Hepatitis B core antibody
- Hepatitis B DNA
- Hepatitis C antibody
- Hepatitis C NAT

This form will also come due if a recipient received cells from a donor who was reported as “reactive” on the Form 2004, Infectious Disease Markers

- Hepatitis B surface Antigen
- Hepatitis B core Antibody
- Hepatitis C Antibody

This form will also come due when a recipient’s post-transplant Hepatitis B and/or Hepatitis C viral infection is reported on the post-transplant follow-up forms for recipients on the comprehensive report form (CRF) track.

- Q1-9: Serological Evidence of Hepatitis Exposure / Infection – Recipient
- Q10-17: Serological Evidence of Hepatitis Exposure / Infection – Donor
- Q18-37: Antiviral Therapy for Hepatitis

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Q1-9: Serological Evidence of Hepatitis Exposure / Infection – Recipient

Question 1: Hepatitis B core antibody (HBcAb)

The total hepatitis B core antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of the core antigen by liver cells. Since core antigen is present only in infected liver cells and cannot be detected in the blood of an infected individual, only core antibody is tested, since it circulates in the peripheral blood. After infection, total core antibodies will persist for life. Presence of core antibodies can indicate active and/or prior infection, but hepatitis core antibodies will not be present in individuals with no history of natural infection with HBV. This means that vaccinated individuals will not be anti-HBc positive because vaccination results in the body developing antibodies to the hepatitis B surface antigen.

Chemiluminescent immunoassay (CIA), enzyme-linked immunosorbent assay (ELISA), or Elecsys anti-HBc is used to test for the presence of hepatitis B core antibodies. Currently, there is no licensed confirmatory test for anti-HBc in the United States; confirmation of antibody presence is done by performing a second anti-HBc test using a different manufacturer's test kit.

Report the laboratory result as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for recipient HBcAb testing performed in the reporting period; if multiple tests were performed, report the most recent. If testing was performed and is the same as the result reported prior to transplant, report “confirm prior result.” If HBcAb testing was not done, indicate “not tested.”


Question 2: Hepatitis B surface antigen (HBsAg)

The hepatitis B surface antigen is a protein expressed on the surface of the hepatitis B virus. Its presence in the blood indicates acute or active chronic infection. In acutely infected patients, blood will test HBsAg positive within one to nine weeks of exposure to the virus. Patients who do not go on to develop chronic infection will be surface antigen negative by 15 weeks after the onset of symptoms. Chemiluminescent immunoassay (CIA), electrochemiluminescent immunoassay (ECLIA), or enzyme-linked immunosorbent assay (ELISA) are used to test for the presence of hepatitis B surface antigens; research indicates CIA and ECLIA may be more sensitive for detecting low levels of HBsAg. Positive HBsAg results require confirmation with a neutralization procedure using human Anti-HBs (HBsAg Confirmation Assay). If the sample is neutralizable in the confirmatory test, the specimen is considered positive for HBsAg.

Report the laboratory result as “positive” (reactive), “negative” (non-reactive), or “inconclusive”
(indeterminate) for recipient HBcAb testing performed in the reporting period; if multiple tests were performed, report the most recent. If testing was performed and is the same as the result reported prior to transplant, report “confirm prior result.” If HBcAb testing was not done, indicate “not tested.”


**Question 3: Hepatitis B e antigen (HBeAg)**

The hepatitis B e antigen is the extracellular form of the hepatitis B core antigen. Hepatitis B core antigen does not circulate and therefore cannot be detected in serum testing; as a result, hepatitis B e antigen may be used as a proxy measure. Its presence is associated with active viral replication and increased infectivity. The hepatitis B e antigen is present in the serum during the early phase of acute HBV infection, shortly after the hepatitis B surface antigen is first seen. Hepatitis B e antigen would only be seen during active infection; however, there are some variants of hepatitis B virus which are known to be hepatitis e negative, even during periods of high viral replication and increased infectivity.

Report the laboratory result as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for recipient HBeAg testing performed in the reporting period; if multiple tests were performed, report the most recent. If testing was performed and is the same as the result reported prior to transplant, report “confirm prior result.” If HBeAg testing was not done, indicate “not tested.”

**Question 4: Hepatitis C antibody (HCAb)**

The total hepatitis C antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of antigens by the hepatitis C virus. Antibodies can generally be detected as soon as four weeks after exposure and will persist for life. Enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA) is used to screen for hepatitis C antibodies; confirmatory testing is done by recombinant immunoblot assay (RIBA). A positive ELISA or CIA result without confirmation by RIBA is considered an indeterminate result, unless HCV RNA is detected in the blood by PCR.

Report the laboratory result as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for recipient HCAb testing performed in the reporting period; if multiple tests were performed, report the most recent. If testing was performed and is the same as the result reported prior to transplant, report “confirm prior result.” If HCAb testing was not done, indicate “not tested.”

**Hepatitis B viral load testing**

Hepatitis B viral load testing is used to quantify hepatitis B viral DNA in the blood. The diagnosis of hepatitis B infection, either acute or chronic, is generally made by serologic testing, though DNA testing may be useful in the diagnosis of early acute HBV. Additionally, DNA testing is useful to determine whether the
infection is active and to monitor response to anti-HBV therapies. Hepatitis B viral load testing is performed by PCR amplification of HBV DNA in the patient’s serum.

Report all instances of Hepatitis B viral load testing performed within the reporting period; create an instance for each test result. If no testing was performed during the reporting period, proceed with question 7.

**Question 5: Recipient Post-HCT Hepatitis B viral load – date**

Specify the date recipient Hepatitis B viral load testing was performed and continue with question 6.

**Question 6: Hepatitis B viral load level**

Report the result for recipient viral load testing as indicated on the laboratory report. If necessary, convert values so they can be reported in the unit of measurement options available on the form.

**Hepatitis C viral load testing**

Hepatitis C viral load testing is primarily used to monitor response to anti-viral therapy and confirm activity of infection; additionally, it may be used to diagnosis early acute HCV infection and to detect active chronic infection. Hepatitis C viral load testing is performed by RT-PCR amplification of HCV RNA in the patient’s serum.

Report all instances of Hepatitis C viral load testing performed within the reporting period; create an instance for each test result. If no testing was performed during the reporting period, proceed with question 9.

**Question 7: Recipient Post-HCT Hepatitis C viral load – date**

Specify the date recipient Hepatitis C viral load testing was performed and continue with question 8.

**Question 8: Hepatitis C viral load level**

Report the result for recipient viral load testing as indicated on the laboratory report. If necessary, convert values so they can be reported in the unit of measurement options available on the form.

**Question 9: Were any liver biopsies performed for cytology and/or pathology or liver samples taken from an autopsy, since the date of last report (or, if this is the first post-HSCT report, since diagnosis)?**

Indicate if the recipient had a liver biopsy performed, either for cytologic or histopathologic evaluation, during the reporting period for this form. If “yes,” submit a copy of the biopsy report using a Log of Appended Documents, Form 2800. Proceed with question 10 for allogeneic recipients or question 18 for autologous recipients.
Q10-17: Serological Evidence of Hepatitis Exposure / Infection – Donor

Complete questions 10-17 for allogeneic transplants only; if donor information is unknown, leave the data field blank. These data fields should be used to report new information available for donors that developed hepatitis post-transplant. If this is the first post-transplant report & the donor developed hepatitis, then report information from the date of the stem cell harvest; do not duplicate data reported on the Form 2047 prior to transplant. Complete all data fields for which relevant donor information is documented and available to the CIBMTR center completing the form.

Question 10: Hepatitis B core antibody (HBcAb)

The total hepatitis B core antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of the core antigen by liver cells. Since core antigen is present only in infected liver cells and cannot be detected in the blood of an infected individual, only core antibody is tested, since it circulates in the peripheral blood. After infection, total core antibodies will persist for life. Presence of core antibodies can indicate active and/or prior infection, but hepatitis core antibodies will not be present in individuals with no history of natural infection with HBV. This means that vaccinated individuals will not be anti-HBc positive because vaccination results in the body developing antibodies to the hepatitis B \textit{surface} antigen. Chemiluminescent immunoassay (CIA), enzyme-linked immunosorbent assay (ELISA), or Elecsys anti-HBc is used to test for the presence of hepatitis B core antibodies. Currently, there is no licensed confirmatory test for anti-HBc in the United States; confirmation of antibody presence is done by performing a second anti-HBc test using a different manufacturer’s test kit.

Report the laboratory result of most recent donor testing as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for donor testing. If testing was not done, indicate “not tested.”

Question 11: Hepatitis B surface antigen (HBsAg)

The hepatitis B surface antigen is a protein expressed on the surface of the hepatitis B virus. Its presence in the blood serum indicates acute or active chronic infection. In acutely infected patients, blood will test HBsAg positive within one to nine weeks of exposure to the virus. Patients who do not go on to develop chronic infection will be surface antigen negative by 15 weeks after the onset of symptoms. Chemiluminescent immunoassay (CIA), electrochemiluminescent immunoassay (ECLIA), or enzyme-linked immunosorbent assay (ELISA) are used to test for the presence of hepatitis B surface antigens; research indicates CIA and ECLIA may be more sensitive for detecting low levels of HBsAg.\textsuperscript{1} Positive HBsAg results require confirmation with a neutralization procedure using human Anti-HBs (HBsAg Confirmation Assay). If
the sample is neutralizable in the confirmatory test, the specimen is considered positive for HBsAg.

Report the laboratory result of most recent donor testing during the reporting period as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for donor testing. If testing was not done, indicate “not tested.”


**Question 12: Hepatitis B e antigen (HBeAg)**

The hepatitis B e antigen is the extracellular form of the hepatitis B core antigen. Hepatitis B core antigen does not circulate and therefore cannot be detected in serum testing; as a result, hepatitis B e antigen may be used as a proxy measure. Its presence is associated with active viral replication and increased infectivity. The hepatitis B e antigen is present in the serum during the early phase of acute HBV infection, shortly after the hepatitis B surface antigen is first seen. Hepatitis B e antigen would only be seen during active infection; however, there are some variants of hepatitis B virus which are known to be hepatitis e negative, even during periods of high viral replication and increased infectivity.

Report the laboratory result of most recent donor testing during the reporting period as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for donor testing. If testing was not done, indicate “not tested.”

**Question 13: Hepatitis C antibody (HCAb)**

The total hepatitis C antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of antigens by the hepatitis C virus. Antibodies can generally be detected as soon as four weeks after exposure and will persist for life. Enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA) is used to screen for hepatitis C antibodies; confirmatory testing is done by recombinant immunoblot assay (RIBA). A positive ELISA or CIA result without confirmation by RIBA is considered an indeterminate result, unless HCV RNA is detected in the blood by PCR.

Report the laboratory result of most recent donor testing during the reporting period as “positive” (reactive), “negative” (non-reactive), or “inconclusive” (indeterminate) for donor testing. If testing was not done, indicate “not tested.”

**Donor Hepatitis B viral load testing**

Hepatitis B viral load testing is used to quantify hepatitis B viral DNA in the blood. The diagnosis of hepatitis B infection, either acute or chronic, is generally made by serologic testing, though DNA testing may be useful in the diagnosis of early acute HBV. Additionally, DNA testing is useful to determine whether the
infection is active and to monitor response to anti-HBV therapies. Hepatitis B viral load testing is performed by PCR amplification of HBV DNA in the patient’s serum.

Report all instances of donor Hepatitis B viral load testing performed during the reporting period; create an instance for each test result. If no testing was performed, proceed with question 16.

**Question 14: Donor Hepatitis B viral load – date**

Specify the date donor Hepatitis B viral load testing was performed and continue with question 15.

**Question 15: Hepatitis B viral load level**

Report the result for donor viral load testing as indicated on the laboratory report. If necessary, convert values so they can be reported in the unit of measurement options available on the form.

**Donor Hepatitis C viral load testing**

Hepatitis C viral load testing is primarily used to monitor response to anti-viral therapy and confirm activity of infection; additionally, it may be used to diagnosis early acute HCV infection and to detect active chronic infection. Hepatitis C viral load testing is performed by RT-PCR amplification of HCV RNA in the patient’s serum.

Report all instances of donor Hepatitis C viral load testing performed during the reporting period; create an instance for each test result. If no testing was performed, proceed with question 18.

**Question 16: Donor Hepatitis C viral load – date**

Specify the date donor Hepatitis C viral load testing was performed and continue with question 17.

**Question 17: Hepatitis C viral load level**

Report the result for donor viral load testing as indicated on the laboratory report. If necessary, convert values so they can be reported in the unit of measurement options available on the form.
Q18-37: Antiviral Therapy for Hepatitis

This section is related to antiviral therapy given to the recipient.

**Question 18: Was therapy given for hepatitis since the date of the last report (or, if this is the first post-HCT report, since diagnosis)?**

Hepatitis antiviral therapy is intended to prevent progression of the disease and minimize sequelae of infection. The National Institutes of Health (NIH) in the United States recommends antiviral therapy for Hepatitis B patients with acute liver failure, cirrhosis or advanced cirrhosis with positive viral load, and for reactivation of chronic HBV during or after chemotherapy and/or immunosuppression. [2] Lamivudine, pegylated interferon alfa, entecavir, and tenofovir are medications currently used to treat Hepatitis B. Hepatitis C therapy has similar goals of sustaining a viral response and minimizing sequelae of infection. Therapy is recommended for patients with elevated liver enzymes and/or significant histologic damage on biopsy.

Indicate if the recipient received antiviral therapy for hepatitis at any time during the current reporting period; for the first post-transplant report, report any therapy since transplant. If “yes,” continue with question 19. If “no,” continue with question 25.


For each therapeutic agent below, create an instance for each course. A course is defined as the period from therapy start to discontinuation of therapy, during which the patient is regularly scheduled to receive a certain dose of medication; if the dose is changed, please continue the course and only report therapy stopped if the medication is discontinued for at least 14 consecutive days.

**Question 19: Lamivudine therapy – course given**

Indicate if the recipient received a course at any time during the current reporting period; create an instance for each course given. If “yes,” continue with question 20; if “no,” continue with question 25.

**Question 20: Date started**

Report the date therapy was initiated and continue with question 21.
Question 21: Daily dose

Report the daily prescribed dose at the start of the therapy.

Question 22: Reason started

This is a free text data field. Concisely document the rationale for starting this course of therapy; suggested examples include “prophylaxis” and “treatment.” If the patient received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”

Question 23: Therapy stopped?

Indicate if therapy was stopped during the current reporting period. If “yes,” continue with question 24. If “no,” continue with question 25.

Question 24: Date stopped

Report the date therapy was stopped and continue with question 25.

Question 25: Interferon therapy – course given

Indicate if the recipient received a course at any time during the current reporting period; create an instance for each course given. If “yes,” continue with question 26; if “no,” continue with question 31.

Question 26: Date started

Report the date therapy was initiated and continue with question 27.

Question 27: Daily dose

Report the daily prescribed dose at the start of the therapy.

Question 28: Reason started

This is a free text data field. Concisely document the rationale for starting this course of therapy; suggested examples include “prophylaxis” and “treatment.” If the patient received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”

Question 29: Therapy stopped?

Indicate if therapy was stopped during the current reporting period. If “yes,” continue with question 30. If
“no,” continue with question 31.

**Question 30: Date stopped**

Report the date therapy was stopped and continue with question 31.

**Questions 31-32: Other antiviral therapy – course given**

Indicate if the recipient received a course of any other (not Lamivudine or interferon) antiviral therapy for hepatitis infection at any time during the current reporting period; create an instance for each course of each agent given. If “yes,” continue with question 32 and specify the other antiviral therapy given; if “no,” continue with continue with signature section of the form.

**Question 33: Date started**

Report the date therapy was initiated and continue with question 34.

**Question 34: Daily dose**

Report the daily prescribed dose at the start of therapy.

**Question 35: Reason started**

This is a free text data field. Concisely document the rationale for starting this course of therapy; suggested examples include “prophylaxis” and “treatment.” If the patient received multiple courses of therapy, use this field to provide rationale for the dose change at onset of new course. If the rationale for therapy is not available in the records, document “unknown.”

**Question 36: Therapy stopped?**

Indicate if therapy was stopped during the current reporting period. If “yes,” continue with question 37. If “no,” continue with question signature lines, review of form, and form submission.

**Question 37: Date stopped**

Report the date therapy was stopped and continue with question signature lines, review of form, and form submission.
2150: Viral Infection Diagnosis and Treatment Form

The CMV / EBV / ADV / HHV-6 / BK Viral Infection Diagnostic Form captures information regarding the diagnosis, treatment, and status of the following infections:

- Cytomegalovirus (CMV)
- Epstein-Barr Virus (EBV)
- Adenovirus (ADV)
- Human Herpes Virus 6 (HHV-6)
- BK Virus (BK)

A Viral Infection Diagnostic Form will come due any time one of the above viral infections is reported on the Post-HCT Follow-Up Data Form (2100). For CMV and HHV-6, this form will come due only if there is at least one infection site other than "Blood." One form must be completed for each applicable infection reported. The reporting period for this form corresponds to the Post-HCT Follow-Up Data Form on which the infection was reported.

See the Post-HCT Follow-Up Data section of the manual for more information on reporting infections.

Links to Sections of Form
Q1-31: Infection Episode
Q32-50: Hematologic Findings at Diagnosis of Infection
Q51-76: Therapy
Q77: Infection Status at the Time of Evaluation for this Reporting Period

Manual Updates
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please reference the retired manual section on the Retired Forms Manuals webpage.
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| 6/25/18    | 2150: Viral Infections         | Modify   | Added (in red below) and removed (struck out below) text from the instructions for reporting infection status at the time of evaluation for this reporting period (question 77): If the status of the infection is not documented in the HCT / cellular therapy physician’s note summarizing their last evaluation performed during the reporting period, obtain documentation from the provider indicating which option to report. For reporting purposes, centers should indicate “Ongoing” if the infection is still present, but cannot be considered improved or resolved.  
  - Ongoing: Infection is still present, but cannot be considered improved or resolved  
  - Improved: Still on treatment, but responding to treatment and no longer showing signs / symptoms of infection  
  - Resolved: Treatment completed  
  - Unknown                                                                 |                                                                                                                                                                                                              |
| 6/25/18    | 2150: Viral Infections         | Modify   | Added (in red below) further instruction on reporting therapy (question 51): Report “Yes” if the recipient received any antiviral medication between seven days prior to the date of diagnosis (refer to question two) and the date of contact for the reporting period (refer to the date of contact reported on the corresponding Post-HCT Follow-Up Data Form). Report all therapy received regardless of the infection being treated.                                                                 |                                                                                                                                                                                                              |
Q1-31: Infection Episode

Question 1: Organism

This field is auto-populated to match the virus reported on the Post-HCT Follow-Up Data Form (Form 2100). Review the value to ensure it is accurate. A Viral Infection Diagnostic Form will come due for each CMV, EBV, ADV, HHV-6, and BK virus reported on the Post-HCT Follow-Up Data Form (Form 2100) so it is imperative to identify the viral infection to which this form will correspond. See the previously noted exception for CMV and HHV-6 infections.

If multiple infections of the same virus are reported during the same reporting period, the center must complete a Viral Infection Diagnosis and Treatment Form for each infection instance, or episode, reported.

Question 2: Date of diagnosis of infection

This field is auto-populated to match the date reported on the Post-HCT Follow-Up Data Form (Form 2100). Review the value to ensure it is accurate. See the Post-HCT Follow-Up Data section of the manual for further instructions on reporting the date of diagnosis.

If multiple infections of the same virus are reported in the same reporting period, the diagnosis date in question two will clarify for which infection episode the form is being completed.

Questions 3-25: Diagnostic Tests

Report all testing that had positive results and which indicated the viral infection was present. Do not report negative or indeterminate / equivocal testing in this section. As indicated in the instructions for question one, if the recipient was diagnosed with multiple viral infections prior to infusion, multiple CMV / EBV / ADV / HHV-6 / BK Viral Infection Diagnostic Forms must be completed (one for each organism). Ensure the testing reported in these questions only reflects the assessments used to identify the infection / organism being reported on this form. For reporting purposes, only report methods performed and samples collected (or sites assessed for radiological findings) between 7 days prior and 14 days after the diagnosis date reported in question two.

Links to specific instructions
- Methods of Assessment
- Sample / Tissue Sources
- Date Sample Collected
- Detection in Blood / Serum by PCR
Methods of Assessment:

A viral infection may be identified by multiple assessments near the time of diagnosis. A description of each method of assessment is provided below. Report “Yes” for any diagnostic method that detected the viral infection being reported on this form and complete all associated questions for that method. Report “no” for assessments which were never performed or were never considered to be positive for the fungal infection being reported on this form. Note, the time window provided in the initial instructions for questions 3-25. If the significance of the test result is not clear, obtain documentation from the recipient’s physician confirming whether the assessment was considered positive. A description of each test and some sample / tissue sources are provided below.

**PCR assay:** samples taken from the recipient are manipulated using polymerase chain reaction techniques. Presence and classification of virus is assessed by identifying known viral DNA fragments. A typical PCR report will document the viral copy load detected (quantitative) and a threshold for determining whether a viral infection was detected (positive, negative, or equivocal). Reports can generally be found in the microbiology / virology section or the molecular pathology section of the medical record. If the report is unclear, contact your center’s laboratory to confirm the result.

**Culture:** samples taken from the recipient are incubated in media containing cells the virus is able to infect. Presence of infection is assessed by identifying viral cytopathic effects via microscopy following incubation. The culture report will document whether cytopathic changes are detected (positive) or not detected (negative). Results are typically found in the microbiology / virology section of the medical record. For the purposes of this form, any culture results, including a shell viral culture, should be reported. This technique is less commonly used for virus identification.

**Histopathology / biopsy:** the presence of infection is assessed by identifying viral cytopathic effects via microscopy in the samples obtained via biopsy or fine needle aspirate from the recipient. No incubation techniques or additional growth media are used. The pathology report will document whether cytopathic changes are detected (positive) or not detected (negative). Results are generally found in the pathology section of the medical record. If staining was also done on the sample, report the stain results under immunohistochemical staining.

**Immunohistochemical staining (IHC):** tissue samples are treated with antibodies and dye. The antibodies bind to antigens on the surfaces of the cells, allowing for the identification of viral cytopathic changes. Testing results will be documented in the pathology report for the tissue sample, on which, IHC was used. If the report is unclear, obtain documentation from the HCT / cellular therapy physician clarifying how the assessment should be reported.

**Radiographic findings:** includes all imaging assessments. Examples include x-ray, CT scan, PET scan, ultrasound and / or MRI. These assessments are capable of identifying signs of a viral infection,
but cannot confirm the presence of a specific virus. Refer to the clinical interpretation of an imaging assessment to determine whether the test was considered positive or negative. If the provider’s notes do not confirm the assessment results, obtain documentation from the HCT / cellular therapy physician clarifying how the assessment should be reported.

Sample / Tissue Sources:

Only report sample / tissue sources that were collected during the time window specified above and, for which, the test method detected the infection.

**Blood**: whole blood, bone marrow, serum, plasma

**Bronchial fluid**: fluid from lungs typically collected via broncholar lavage

**Cerebrospinal fluid**: fluid from spinal column typically collected via spinal tap

**Pericardial fluid**: Fluid from pericardial cavity typically collected via pericardiocentesis

**Tissue**:

- **Central nervous system (CNS)**: brain, brain stem, spinal cord, cerebrospinal fluid
- **GI tract**: esophagus, stomach, jejunum, ileum, colon, rectum
- **Heart / myocardium**: endocardium, myocardium, epicardium, pericardium
- **Liver**: liver, gallbladder, biliary tract
- **Lung**: trachea, bronchi, bronchioles, lungs
- **Lymph node**: lymph nodes from any location
- **Skin**: hypodermis, dermis, and epidermis
- **Spleen**: capsule, white and red pulp

Report fluid and tissue samples taken from the oral cavity and joints using the “Other” option for sample or tissue source as appropriate.
Date Sample Collected:
The date of sample collection is only reported for PCR studies. A date must be reported for question six if any of the following sample sources were reported for question four:

- Bronchial fluid
- Cerebrospinal fluid
- Pericardial fluid
- Stool
- Urine
- Other

If samples from the above sources were collected on different dates (between seven days prior and 14 days after the date of diagnosis), report the earliest sample collection date in question six. See General Guidelines for Completing Forms for more information on reporting dates.

A date must be reported for question 11 if “Tissue” was reported as a sample source for question four. Only one tissue can be specified per instance (copy) of question nine. The date reported in question 11 should correspond to the collection date.

Detection in blood / serum by PCR:
Questions seven and eight must be completed if “Blood” was reported as a sample source for question four. For question seven, report the highest number of viral copies detected in any blood sample obtained between the date of diagnosis and the end of the reporting period. Also, report the date on which the sample with the highest number of viral copies was collected in question eight. See General Guidelines for Completing Forms for more information on reporting dates.

Question 26-31: Select all clinical signs present on the date (± 1 day) of diagnosis of infection
Report “Yes” for any symptoms documented at the time of diagnosis. Clinical signs are documented in provider notes as part of the patient narrative, review of systems, and / or physical exam findings.

- **Requiring oxygen**: inadequate oxygen saturation or labored respiration requiring supplemental oxygen (e.g., nasal cannula, non-rebreather mask, mechanical ventilation).
- **Hepatomegaly**: Enlargement of liver detected by physical exam or by radiographic imaging of the liver
- **Splenomegaly**: Enlargement of the spleen detected by physical exam or by radiographic imaging of the spleen
- **Neurologic symptoms**: confusion, irritability, seizures, drowsiness, etc.
• **Enlarged lymph nodes / lymphadenopathy**: palpable lymph nodes on examination or enlarged lymph nodes seen on radiographic imaging.
Q32-50: Hematologic Findings at Diagnosis of Infection

Question 32-50: Provide values closest to the date of diagnosis of the infection (±7 days)

All values reported in questions 32-50 must reflect testing performed within seven days of the date of diagnosis (question two). If multiple tests were performed during this time, report the results of the testing performed closest to the date of diagnosis (question two). If testing was not done within this period, report “Unknown” for that value.

For each laboratory test, indicate whether the result was “Known” or “Unknown” at the time of diagnosis. If “Known,” report the result and the unit of measure. If “Known” is reported for serum creatinine (question 42) or ALT (question 45), also specify the upper limit of normal and corresponding unit of measure.
Q51-76: Therapy

Question 51: Did the recipient receive any therapy between 7 days prior to the date of infection diagnosis and the date of contact for this reporting period?

Report “Yes” if the recipient received any antiviral medication between seven days prior to the date of diagnosis (refer to question two) and the date of contact for the reporting period (refer to the date of contact reported on the corresponding Post-HCT Follow-Up Data Form). Report all therapy received regardless of the infection being treated. If the recipient did not receive any antiviral medication during this time frame, report “No” and go to question 77.

Question 52-54: Antiviral drugs

Report “Yes” for question 52 and complete questions 53-57 if the recipient received any antiviral medication within the time window indicated in the instructions for question 51. Complete one instance of questions 53-57 for each drug administered. If the antiviral medication given is not listed as an option for question 53, report “Other antiviral drug” and specify the drug in question 54.

If no antiviral drugs were given during the specified time window, report “No” for question 52 and go to question 58.

Question 55-56: Was therapy started more than 7 days prior to the date of infection diagnosis?

Report “Yes” for question 55 and go to question 57 if the reported drug was started greater than seven days prior to the date of diagnosis.

If the drug was started within seven days prior to, on, or after the date of diagnosis, report “No” for question 55 and report the date it was started in question 56. Refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates. Check “Date Estimated” box next to question 56 if an estimated date was reported.

Question 57: Was therapy still being given at 30 days (± 3 days) after the date of diagnosis of infection?

If the infection was diagnosed less than 30 days prior to the end of the reporting period, report whether the drug was still being given within three days prior to the day of contact. Otherwise, report whether the drug was given, even once, between 27 and 33 days after the date of diagnosis.

If it is not known whether treatment was still being given within the time window specified above, leave question 57 blank and override the error in FormsNet3 using the code “Unknown”. 
Question 58-76: Other antiviral therapies:

Indicate if the recipient received a course of any other antiviral therapy between seven days prior to the date of diagnosis (refer to question two) and the date of contact for the reporting period (refer to the corresponding follow-up form).

Types of therapy

**Combination Chemotherapy:** This therapy is only applicable when reporting an EBV infection. For all other viruses, report “No” for this therapy. Do not report immunotherapy, radiation therapy, or cellular therapies as combination chemotherapy.

**Rituximab:** Immunotherapy drug targeting cells expressing CD20. Brand / trade names include Rituxan.

**IVIG (Intravenous immunoglobulin):** A blood product with multiple immunodulatory mechanisms of action. Brand / trade names include IgVena, Kiovig, Flebogamma, Gammagard-SD, Octagam, Sandoglobulin, Sandoglobulin NF, Vigam-S.

**Cytogam:** IgG specific to CMV. This therapy is only applicable when reporting a CMV infection. For all other viruses, report “No” for this therapy.

**Cellular Therapy:** Cellular infusions given to treat infection. Includes virus-specific T-cells (CTLs) and donor lymphocyte infusions. Do not report supportive therapies, such as platelet or whole blood transfusions, or HCT as a cellular therapy.

**Other drug:** Any treatment for the infection that cannot be reported as an antiviral drug (questions 53-54) or as one of the therapies described above.

For each therapy given within the time window specified above, also report whether therapy was started more than seven days prior to the date of diagnosis and whether the therapy was still being given at 30 days after the date of diagnosis.

Was therapy started more than 7 days prior to the date of infection diagnosis?

Report “Yes” if the therapy was started greater than seven days prior to the date of diagnosis.

If the therapy was started within seven days prior to, on, or after the date of diagnosis, report “No” and report the date it was started. Refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates. Check “Date Estimated” box if an estimated date was reported.
Was this therapy still being given at 30 days (± 3 days) after the date of diagnosis of infection?

If the infection was diagnosed less than 30 days prior to the end of the reporting period, report whether the therapy was still being given within 3 days prior to the day of contact. Otherwise, report whether the therapy was given, even once, between 27 and 33 days after the date of diagnosis. Note that the therapies of chemotherapy, Rituximab, IVIG, Cytogam, or cellular therapies are not generally given on a daily basis. However, these are often given weekly or monthly so looking out to 33 days after the date of the diagnosis will be critical to determine if the patient is still receiving.

If it is not known whether treatment was still being given within the time window specified above, leave this question blank and override the error in FormsNet3 using the code “Unknown”.
Q77: Infection Status at the Time of Evaluation for this Reporting Period

Question 77: What was the infection status at the time of evaluation for this reporting period?

Report the status of the viral infection on the date of contact for this reporting period (refer to the corresponding follow-up form) based on the primary care provider’s clinical judgement. If the status of the infection is not documented in the HCT / cellular therapy physician’s note summarizing their last evaluation performed during the reporting period, obtain documentation from the provider indicating which option to report.

- Ongoing: Infection is still present, but cannot be considered improved or resolved
- Improved: Still on treatment, but responding to treatment and no longer showing signs / symptoms of infection
- Resolved: Treatment completed
- Unknown
2540: Tepadina® Supplemental Data

Tepadina® Supplemental post-HCT Data Collection Form, Form 2540, must be completed for recipients who are enrolled onto CIBMTR study SC17-03. This is a multi-center, prospective, observational post-authorization long-term study of the use of thiotepa as part of a high-dose chemotherapy regimen followed by hematopoietic stem cell transplantation (HCT) in Canadian and American recipients. U.S. recipients are eligible if they have received an autologous HCT for primary CNS lymphoma or any lymphoma with CNS involvement. Canadian recipients are eligible after allogeneic or autologous HCT and have received Tepadina.

This supplemental data form, Form 2540, will come due for participating centers when thiotepa is reported as part of the conditioning regimen, and the Recipient Eligibility Form, Form 2500, indicates that “Adienne Tepadina®” was the brand of thiotepa given to the recipient. Supplemental data collection form will be completed at the 100 day through 5-year time points post-HCT.

Links to Sections of the Form:
Q1-2: Tepadina® Stop Date
Q3-35: Hematologic Findings
Q36-65: Organ Function
Q66-67: Data from Post-HSCT Follow-Up Form

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

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<th>Description</th>
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</table>
Q1-2: Tepadina® Stop Date

Questions 1 & 2: Tepadina® stop date

Indicate if Tepadina® stop date is “Known” or “Unknown” in question 1. Start date is reported on F2400 in the conditioning regimen section. Report the final administration date of Tepadina® in question 2. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, General Guidelines for Completing Forms.

If the date therapy stopped is “Unknown,” go to question 3.
Q3-35: Hematologic Findings

Questions 3-35: Hematologic Findings

These questions are intended to determine the hematological status of the recipient after the HCT. There are three sections to collect hematologic results at day +7, +14, and +21 post-HCT. Testing may be performed multiple times within the reporting period; however, report the laboratory values within +/-3 days of day +7, +14 and +21 post-HCT.

Report the laboratory value and unit (if applicable) for each hematologic finding. If a value is not known, select “unknown” and continue with the next laboratory value.

For platelets, check the box if platelets were transfused within seven days prior to the testing.
Questions 36 – 65: Organ Function

Report any disorder / impairment that can be directly attributed to Tepadina®

Hypersensitivity
Clinically significant hypersensitivity reactions, including anaphylaxis, have occurred following administration of TEPADINA. Hypersensitivity may include shortness of breath, hypotension, dizziness, and possibly syncope.

- Grade 1: systemic intervention not indicated
- Grade 2: oral intervention indicated
- Grade 3: Bronchospasm; hospitalization indicated for clinical sequelae; intravenous intervention indicated
- Grade 4: life-threatening consequences; urgent intervention indicated

Erythematous rash / toxic skin reaction
Symptoms- 
Erythematous rash: abnormal redness and inflation of the skin

Flushing: sudden redness of the skin

Photosensitivity: A disorder characterized by an increase in sensitivity of the skin to light

Stevens-Johnson syndrome / Toxic epidermal necrolysis: a severe allergic drug reaction

- Painful Blistering of the skin and mucous membrane involvement. Typical symptoms for both diseases include peeling skin, fever, body aches, a flat red rash, and blisters and sores on the mucous membranes.
- Ocular involvement includes severe conjunctivitis, iritis, palpebral edema, conjunctival and corneal blisters and erosions, and corneal perforation.
- Stevens-Johnson syndrome causes only small areas of peeling skin (affecting less than 10% of the body).
- Toxic epidermal necrolysis causes large areas of peeling skin (affecting over 30% of the body).

Grade 3-4 elevation of AST, ALT, and/or bilirubin
AST (Aspartate aminotransferase increased): A finding based on laboratory test results that indicate an increase in the level of aspartate aminotransferase (AST or SGOT) in a blood specimen.

- Grade 3: >5.0 – 20.0 x ULN if baseline was normal; >5.0 – 20.0 x baseline if baseline was abnormal
- Grade 4: >20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal

ALT (Alanine aminotransferase increased): A finding based on laboratory test results that indicate an increase in the level of alanine aminotransferase (ALT or SGPT) in the blood specimen.

- Grade 3: >5.0 – 20.0 x ULN if baseline was normal; >5.0 – 20.0 x baseline if baseline was abnormal
- Grade 4: >20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal

Bilirubin (Blood bilirubin increased): A finding based on laboratory test results that indicate an abnormally high level of bilirubin in the blood. Excess bilirubin is associated with jaundice.

- Grade 3: >3.0 – 10.0 x ULN if baseline was normal; >3.0 – 10.0 x baseline if baseline was abnormal
- Grade 4: >10.0 x ULN if baseline was normal; >10.0 x baseline if baseline was abnormal

Leukoencephalopathy: A disorder characterized by diffuse reactive astrocytosis with multiple areas of necrotic foci without inflammation.

Other neurological toxicity: F2100 captures CNS hemorrhage, encephalopathy (non-infectious), neuropathy, seizures, and stroke. The intent of this question to capture other neurological impairments outside of those options.

Confusion / delirium:

- Confusion: A disorder characterized by a lack of clear and orderly thought and behavior.
- Delirium: A disorder characterized by the acute and sudden development of confusion, illusions, movement changes, inattentiveness, agitation, and hallucinations. Usually, it is a reversible condition.

Hallucination: A disorder characterized by a false sensory perception in the absence of an external stimulus.
Hemorrhage: severe bleeding, other than cerebral, diffuse alveolar or CNS hemorrhage (captured on 2100).

Cerebral hemorrhage:
A disorder characterized by bleeding of the brain.
Date of onset: for each impairment / disorder, report the date the disorder / impairment was first documented by a physician or other health care provider in the progress note or chart.

For each impairment / disorder, indicate if the medical director believes the disorder / impairment to be directly related to the infusion of the drug.
Questions 66-67 refer to data reported on form 2100, Q441-615, please ensure data reported here matches with form 2100

Question 66 & 67: In the transplant physician's judgment, were any of the disorders / impairments reported on the form 2100 a direct result of the Tepadina® reported administration?

2100 Q441-615: Organ Function form instruction manual:

Indicate if the medical director believes the adverse event to be directly related to the infusion of Tepadina®, check all that apply.

- Acute renal failure requiring dialysis
- Bronchial obliterans
- Congestive heart failure
- Cryptogenic organizing pneumonia (COP / BOOP)
- Deep vein thrombosis (DVT) / Pulmonary embolism (PE)
- Diffuse alveolar hemorrhage
- GVHD (acute or chronic)
- Hypertension (HTN) requiring therapy
- Infection
- Mucositis requiring therapy
- New malignancy
- Non-infectious interstitial pneumonitis (IPn or ARDS) / idiopathic pneumonia syndrome (IPS)
- VOD
2553: VOD/SOS

The Veno-occlusive Disease (VOD) / Sinusoidal Obstruction Syndrome (SOS) Form, Form 2553, must be completed when VOD / SOS has been reported to have developed on the 100 Day Post-HCT Data Form (F2100) or the 100 Day Post-TED Form (Form 2450). Additionally, a Six Month VOD/SOS Form will come due if the center has reported VOD/SOS did not resolve during the 100 day reporting period (question 124). This form captures laboratory and pathologic studies at the time of diagnosis, treatment administered during the reporting period, and the maximum severity of VOD / SOS during the reporting period.

Q1-28: Diagnosis
Q29-42: Laboratory Studies at Diagnosis
Q43-98: Therapy
Q99-112: Maximum Severity
Q113-145: VOD / SOS Status
Q146-153: Management of Late Sequelae
Q154-163: Hospital Stay

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/7/2018</td>
<td>2553: VOD/SOS</td>
<td>Add</td>
<td>Added an example on how to report the <strong>planned total daily dose</strong> for Defibrotide</td>
</tr>
<tr>
<td>5/24/17</td>
<td>2553: VOD/SOS</td>
<td>Add</td>
<td>Updated the description of the VOD / SOS Form on the title page by adding the text in red below: <em>The Veno-occlusive Disease (VOD) / Sinusoidal Obstruction Syndrome (SOS) Form, Form 2553, must be completed when VOD / SOS has been reported to have developed on the 100 Day Post-HCT Data Form (F2100) or the 100 Day Post-TED Form (Form 2450). Additionally, a Six Month VOD/SOS Form will come due if the center has reported VOD/SOS did not resolve during the 100 day reporting period (question 124). This form captures laboratory and pathologic studies at the time of diagnosis, treatment administered during the reporting period, and the maximum severity of VOD / SOS during the reporting period.</em></td>
</tr>
<tr>
<td>7/26/16</td>
<td>2553: VOD/SOS</td>
<td>Add</td>
<td>Version 1 Released</td>
</tr>
</tbody>
</table>
Q1-28: Diagnosis

Veno-occlusive disease (VOD) or sinusoidal obstruction syndrome (SOS) may occur have HCT as a conditioning regimen injury to the hepatic venous endothelium, resulting in hepatic venous outflow obstruction due to occlusion of the hepatic venules and sinusoids. This typically results in a distinctive triad of clinical signs including hepatomegaly with right upper quadrant tenderness, third space fluid retention (e.g., sudden fluid weight gain (≥5%), ascites), and jaundice with a cholestatic picture. Ancillary features commonly seen include increased platelet transfusion needs, and coagulopathy. Pre-existing liver conditions may make development of VOD/SOS more likely. There is increased risk of development of VOD/SOS associated with prior history of hepatitis B, drug-induced hepatitis, or cirrhosis; second or greater hematopoietic cell transplant; ablative conditioning with high doses of radiation therapy or use of busulfan; and sirolimus given to recipients undergoing ablative conditioning. VOD/SOS may occur after autologous or allogeneic HCT. Agents such as low-dose heparin, ursodiol, or defibrotide may be given as prophylaxis against liver toxicities, including VOD/SOS. VOD/SOS occurs prior to D+100 post-transplant, and typically prior to D+30 post-transplant; diagnosis is based on clinical suspicion and supportive findings. Right upper quadrant (RUQ) ultrasound can be helpful to establish the diagnosis of VOD/SOS. The RUQ US is also helpful to rule out other causes of hyperbilirubinemia, such as bile duct obstruction and/or gall bladder disease. A liver biopsy is considered the gold standard for diagnosis VOD/SOS, but may be a risky procedure in patients with low platelets and is generally reserved for patients in whom a diagnosis of VOD/SOS is unclear and other diagnoses need to be excluded. Clinical diagnosis is generally based on the Seattle, modified Seattle, or Baltimore criteria.

Seattle Criteria (1984)

- Two or more of the following present prior to D+30:
  - Bilirubin ≥ 2 mg/dL (34 μmol/L)
  - Hepatomegaly and RUQ pain
  - Ascites with or without unexplained weight gain > 2% over baseline

Modified Seattle Criteria (1993)

- Two or more of the following present prior to D+20:
  - Bilirubin ≥ 2 mg/dL (34 μmol/L)
  - Hepatomegaly and RUQ pain
  - Ascites with or without unexplained weight gain > 2% over baseline

Baltimore Criteria (1987)
• Bilirubin ≥ 2 mg/dL (34 μmol/L) before D+21 and at least two of the following:
  ◦ Hepatomegaly (generally painful)
  ◦ Ascites
  ◦ Weight gain > 5% over baseline

Question 1: Was the date of diagnosis of VOD previously reported?
Indicate whether the date of VOD diagnosis has already been reported on the 100 day VOD/SOS Form. Report “yes” and continue with question 4 if the initial diagnosis date was previously reported. If indicating “no,” continue to question 2 and report the date of diagnosis.

Centers must indicate “no” if completing this insert for the 100 day reporting period.

Question 2: Date of diagnosis:
Report the date of clinical diagnosis of VOD/SOS. This may be well after signs and symptoms were first noted, but should reflect the time at which the recipient’s primary clinician made the determination that signs and symptoms were related to VOD/SOS; this may be the time at which other diagnoses on the differential are ruled out.

The diagnosis date reported in question 2 must match the diagnosis date reported on the Post-TED Form (F2450) in question 47 or on the Post-HCT Follow-up Data Form (F2100) in question 479.

When completing the diagnosis questions below (questions 3-42), “at the time of diagnosis” refers to any testing performed within approximately 7 days of the date of diagnosis and prior to the initiation of any treatment. Only report assessments which were performed within the reporting period. If multiple assessments by the same method were performed at the time of diagnosis, report the assessment closest to the diagnosis date.

Question 3: Was ultrasonography (with Doppler) performed?
Ultrasound may be abnormal in patients with VOD/SOS, but it is unlikely to be diagnostic for it. Ultrasound findings that are more common in VOD/SOS than other liver disorders occurring during HCT include the presence of ascites, an abnormal portal waveform, and marked thickening of the gallbladder wall. Ultrasonography techniques are enhanced when done with Doppler measurements which assess the direction of blood flow in the portal venous system. Reversal of flow in the portal vein is a common finding in patients with severe VOD/SOS.

Report whether an ultrasound study with Doppler was performed as part of the diagnostic work-up for VOD/SOS. If “yes” continue with question 4. Centers should also attach a copy of the ultrasound study report to the form. Refer to the FormsNet3SM Training Guide for more information on how to attach
documents in FormsNet.

If no ultrasound studies with Doppler were performed at the time of diagnosis, report “no” for question 3 and continue with question 9.

**Question 4: Date:**

Enter the date the ultrasonography assessment was performed.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

**Question 5-8: Specify results:**

Indicate whether the ultrasound study detected any abnormalities; these may include reversal of portal venous flow as well as hepatomegaly, ascites, and changes to gallbladder. If abnormalities were detected, indicated “yes” and continue with question 6. If “no,” continue with question 9.

**Question 9: Was a liver biopsy performed?**

A liver biopsy is not needed for the diagnosis of VOD/SOS. Report whether a liver biopsy was performed at the time of diagnosis.

If “yes,” specify the results in question 10. Centers should also attach a copy of the biopsy report to the form. Refer to the FormsNet3 SM Training Guide for more information on how to attach documents in FormsNet.

If “no,” continue with question 11.

**Question 10: Specify biopsy result:**

Report whether the liver biopsy was positive for signs of VOD/SOS. If the pathology report is not clear, refer to the progress notes to determine if the biopsy result is considered positive for signs of VOD/SOS.

**Question 11: Was an autopsy performed?**

Report “yes” if the diagnosis of VOD/SOS was made at the time of autopsy. The recipient’s survival status must be “Dead” on the Post-HCT Data Form if the center is reporting “yes.”

If an autopsy was performed, centers should attach a copy of the autopsy report to the form. Refer to the FormsNet3 SM Training Guide for more information on how to attach documents in FormsNet.
Indicate “no,” if the recipient started treatment for VOD/SOS prior to death. In this case, the autopsy would not have been performed “at the time of diagnosis” as defined in question 2.

**Question 12-15: Specify signs and symptoms at diagnosis of VOD / SOS:**

Report “yes” for any symptoms documented at the time of diagnosis.

- **Ascites**: Accumulation of fluid in the space between the lining of the abdomen and the abdominal organs (peritoneal cavity). This may be detected clinically on exam or seen on ultrasound.
- **Hepatomegaly**: Enlargement of liver detected by physical exam or by RUQ ultrasound.
- **Right upper quadrant pain**: One of the clinical features that may be associated with the onset of VOD/SOS.
- **Weight gain (>2% over baseline at time of diagnosis of VOD / SOS)**: Greater than 2% increase in the recipient’s weight compared to their baseline weight. The baseline weight is considered the weight prior to the start of the preparative regimen.

**Question 16: Was there concurrent organ dysfunction at the time of diagnosis?**

Indicate whether the recipient was diagnosed with concurrent organ dysfunction which required treatment at the time of diagnosis of VOD/SOS. If indicating “yes,” continue with question 17. If indicating “no,” continue with question 27.

**Question 17-26: Specify organ(s):**

- **Kidney**: Report “yes” for question 17 if the recipient has developed acute renal dysfunction with rising creatinine. If question 17 is “yes,” indicate whether the recipient required renal replacement therapy (e.g. dialysis) during the reporting period.
- **Lungs**: Report “yes” for question 19 if the recipient has developed any form of respiratory distress or requires new/additional oxygen supplementation. If reporting “yes” for lungs, indicate the highest level of oxygen support required at the time of diagnosis. If mechanical ventilation was required, indicate the first date ventilation was started and whether the recipient was extubated during the reporting period, report the date the procedure was performed.

- **Other organ:**
  - **Central nervous system**: mental status changes, confusion, seizure, or encephalopathy that is deemed to be related to the VOD/SOS
  - **Vascular**: Thrombotic microangiopathy, thrombotic thrombocytopenic purpura, or hemolytic uremic syndrome.
Question 27-28: Recipient weight (at diagnosis of VOD / SOS)

Report whether the recipient's weight at the time of diagnosis is known. If “yes,” report the recipient's weight in question 28. If “no,” continue with question 29.
Q29-42: Laboratory Studies at Diagnosis

Question 29-42: Laboratory studies at diagnosis

These questions are intended to determine liver function at the time of VOD/SOS diagnosis. Report testing performed on the date of diagnosis. If testing was not performed on the date of diagnosis, report the closest assessment performed prior to diagnosis.

For each laboratory study, report “known” if testing was performed at the time of diagnosis and indicate the result as well as the date testing was performed. Report “unknown” if testing was not performed or the results are not available.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.
Q43-98: Therapy

Treatment for VOD/SOS is generally intended to normalize flow through the hepatic vessels by resolving the central venous and sinusoidal obstruction and preventing fibrosis. Supportive therapies such as hypertransfusions may also be started to improve renal and pulmonary function. Do not report these supportive therapies in this section of the form. Report any treatment initiated as a result of the diagnosis of VOD/SOS.

Question 43: Was therapy given?

Report “yes,” if any treatment was given for the diagnosis of VOD/SOS. If “yes,” specify any treatment given during the reporting period in questions 44-98. If “no,” continue with question 99.

Question 44: Defibrotide

Report “yes,” if defibrotide was given for VOD/SOS during the reporting period. If “yes,” continue with question 45. If “no,” continue with question 66.

Question 45: Planned total daily dose

Indicate the planned total daily dose of defibrotide. The most common dose of Defibrotide used in the treatment of VOD/SOS is 6.25 mg/kg IV every 6 hours. The planned total daily dose would be 25 mg/kg. The planned dose will be documented prior to the initiation of therapy, usually in the orders. The actual dose may be adjusted based on reactions or complications experienced after treatment is started. Do not report dose adjustments made after treatment is started.

Question 46: Date started:

Report the date the first dose of defibrotide was administered. If defibrotide was continued from a prior reporting period, leave this field blank and override the error in FormsNet using the code “Verified Correct.”

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 47-48: Was this therapy still being given at the date of last contact (defibrotide)?

Indicate whether the recipient is still taking defibrotide on the date of contact. If “no,” report the date the last dose of defibrotide was administered.

If the recipient has died prior to the discontinuation of defibrotide used to treat VOD/SOS, select “yes”.
Question 49: Recipient weight: (at initiation of therapy)

Report the recipient’s weight on the first date defibrotide was administered. If the recipient’s weight was not measured at the initiation of defibrotide, report the weight used to determine the planned total daily dose.

Question 50-53: Lab results on therapy start date

For each laboratory study, report “known” if testing was performed on the date defibrotide was started followed by the result. Report “unknown” if testing was not performed or the results are not available.

Question 54-55: Specify the oxygen requirements (at initiation of therapy)

Indicate the highest level of oxygen support on the date defibrotide was started. If “Other oxygen requirement” is being reported, continue with question 55 and specify the type of support required.

Question 56-57: Specify the reason therapy stopped (defibrotide)

Indicate the reason defibrotide was stopped during the reporting period using one of the following options:

- **Death**: Currently, death appears as a reason for stopping therapy on the form. Centers should not use this option choice. Rather, if the recipient has died prior to the discontinuation of defibrotide, centers should report “yes” for question 47. This will cause questions 56-57 to be disabled, preventing the center from answering these questions.

- **Complete resolution**: The following guidelines are provided to assist data managers in determining whether the symptoms of VOD/SOS have completely resolved:
  - Bilirubin < 2.0 mg/dL (34 µmol/L)
  - Serum creatinine <1.5 times the upper limit of normal OR less than the upper limit of normal based on patient’s age.
  - Increase of greater than 80% in creatinine clearance/GFR compared to values at time of diagnosis and not currently on dialysis.
  - Greater than 90% oxygen saturation on room air AND no supplemental oxygen or ventilator requirements.

If a complete resolution of symptoms is documented in the progress notes, but the above guidelines have not been met, data managers should obtain documentation from the appropriate care provider clarifying whether any persistent symptoms are being attributed to VOD/SOS or another cause.

- **Completed prescribed course / end of treatment protocol**: The recipient has completed their full course of treatment without complete resolution of symptoms.
• **Discharged from hospital**: The recipient ended treatment early due so they could be discharged. Use this option for recipients who discontinue treatment as part of their transition to palliative care.

Do not use this option for recipients who have demonstrated a complete resolution of symptoms following treatment or recipients who completed their entire prescribed course of treatment prior to discharge.

• **Side effect(s)**: Treatment was completely stopped due to complications which are believed to be associated with that drug. Specify the side effects in questions 58-65.

• **Other**: Use this option choice for any reason not included above. Centers must specify the reason in question 57 when reporting "other."

**Question 58-63: Bleeding**

Indicate whether bleeding occurred as a side effect of treatment. If bleeding was a side effect, report the sites at which bleeding occurred in questions 59-63. If bleeding was not a side effect, continue with question 64.

This question should only be completed if the center has reported treatment was stopped due to side effects in question 56.

**Question 64-65: Other side effect**

Report "yes" if the recipient experienced any side effects of treatment other than bleeding. Specify other side effects in question 65. If no other side effects occurred, continue with question 66.

This question should only be completed if the center has reported treatment was stopped due to side effects in question 56.

**Question 66-98: Additional treatment for VOD/SOS**

These questions are intended to capture any other treatments initiated to manage or resolve complications associated with VOD/SOS.

For any drugs given as treatment for VOD/SOS, report the first date treatment was given during the reporting period and whether treatment is still being given on the date of contact. If treatment was stopped prior to the date of contact, report the last date treatment was given. For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

If a recipient received treatment for VOD/SOS and it was not discontinued prior to their date of death, report
“yes” for question 68 “Was this therapy still being given at the date of last contact?”

If the recipient received a therapy other than the drugs listed, report “yes” for “other therapy” and specify the treatment(s) in question 95.
Q99-112: Maximum Severity

The following section is intended to capture the maximum severity of VOD/SOS during the current reporting period. If this form is being completed for the six month follow-up report the maximum values obtained during the current reporting period. Do not report values from the 100 day reporting period on the 6-month follow-up form.

Question 99-100: Maximum recipient weight

Indicate whether the recipient’s maximum weight during the reporting period is known. If the maximum weight is known, report the weight in question 100. If the recipient was diagnosed with VOD/SOS during the current reporting period, report the maximum value between diagnosis and the end of the reporting period. If the maximum weight is not known, continue with question 101.

Question 101-103: Maximum total serum bilirubin

Indicate whether the recipient’s maximum total serum bilirubin during the reporting period is known. If the maximum total bilirubin is known, report the value in question 102 and indicate the date the sample was collected in question 103. If the recipient was diagnosed with VOD/SOS during the current reporting period, report the maximum value between diagnosis and the end of the reporting period. If the maximum total bilirubin is not known, continue with question 104.

Question 104-106: Maximum serum creatinine

Indicate whether the recipient’s maximum serum creatinine during the reporting period is known. If the maximum serum creatinine is known, report the value in question 105 and indicate the date the sample was collected in question 106. If the recipient was diagnosed with VOD/SOS during the current reporting period, report the maximum value between diagnosis and the end of the reporting period. If the maximum serum creatinine is not known, continue with question 107.

Question 107-110: Was the recipient placed on dialysis?

Indicate if the recipient underwent renal replacement therapy (e.g., dialysis or CVVH/ultrafiltration), even once, during the reporting period. If the recipient was diagnosed with VOD/SOS during the current reporting period, only report “yes” if the recipient underwent dialysis following the diagnosis of VOD/SOS. If dialysis was performed, report the first treatment date in question 108 and also indicate whether the recipient is still undergoing dialysis treatments at the time of the date of contact.

If the recipient stopped dialysis during the reporting period, report the date of the last run in question 110.
**Question 111-112: Specify the maximum oxygen requirements**

Report the maximum amount of oxygen support required during the reporting period. If the recipient was diagnosed with VOD/SOS during the current reporting period, only report the maximum requirement since the date of diagnosis.

If reporting “other oxygen requirement,” specify the type of oxygen support administered in question 112.
Q113-145: VOD / SOS Status

Question 113-115: Recipient weight (most recent)

Report “known” if the recipient’s weight was evaluated during the reporting period. If known, report the most recent weight documented during the reporting period and the date the measurement was taken. If the recipient’s weight was not evaluated during the reporting period, report “unknown” and continue with question 116.

Question 116-118: Total serum bilirubin

Report “known” if total serum bilirubin was evaluated during the reporting period. If known, report the most recent testing performed during the reporting period and the date of the sample was taken. If total serum bilirubin was not evaluated during the reporting period, report “unknown” and continue with question 119.

Question 119-121: Serum creatinine

Report “known” if serum creatinine was evaluated during the reporting period. If known, report the most recent testing performed during the reporting period and the date the sample was taken. If serum creatinine was not evaluated during the reporting period, report “unknown” and continue with question 122.

Question 122-123: Specify the oxygen requirements: (at date of last contact)

Report the amount of oxygen support required on the date of contact.

If reporting “other oxygen requirement,” specify the type of oxygen support administered in question 123.

Question 124-125: Did VOD / SOS resolve?

Indicate whether VOD/SOS resolved during the current reporting period. The guidelines for determining whether a complete resolution was achieved are available in the instructions for question 56. If VOD/SOS symptoms resolved, continue with question 125. If VOD/SOS did not resolve during the reporting period, continue with question 146.

If VOD/SOS symptoms resolved and then returned less than 30 days later, report “no” for question 124 and continue with question 146.

If VOD/SOS resolved and recurred during the current reporting period, report “Yes” for question 124 and continue with question 125. For reporting purposes, recurrence of VOD/SOS is defined as a subsequent clinical diagnosis after demonstrating a complete resolution of all symptoms.
Question 126-127: Did VOD / SOS symptoms recur?

If a subsequent VOD/SOS clinical diagnosis was made following a complete resolution, report “yes” and continue with question 127. Otherwise, report “no” and continue with question 146.

Question 128-134: VOD / SOS symptoms at recurrence

Report “yes” for any symptoms documented at the time of recurrence.

- **Increased bilirubin**: ≥2.0 mg/dL (34 µmol/L)
- **Ascites**: Accumulation of fluid in the space between the lining of the abdomen and the abdominal organs (peritoneal cavity).
- **Weight gain**: Greater than 2% increase in the recipient’s weight compared to their weight prior to the onset of symptoms.
- **Hepatomegaly**: Abnormal enlargement of liver.
- **Right upper quadrant pain**: One of the clinical features that may be associated with the onset of VOD/SOS.

Question 135-145: Was therapy given for recurrent VOD / SOS?

Report “yes,” if any treatment was given for the recurrence of VOD/SOS. If “yes,” specify any treatment given during the reporting period in questions 136-145. If “no,” continue with question 146.

If the recipient received a therapy other than the drugs listed, report “yes” for “other drug” and specify the treatment(s) in question 145.
Q146-153: Management of Late Sequelae

**Question 146: Was management of late sequelae required?**

Report treatment for any complications associated with the diagnosis of VOD/SOS. Common treatments/procedures have been defined below.

**Question 147-153: Specify**

**Variceal banding**: An endoscopic procedure to place a band around a vessel to restrict flow in order to treat portal hypertension.

**Transjugular Intrahepatic Portosystemic Shunt (TIPS)**: An artificial tube is used to connect the portal vein to the hepatic vein in order to treat portal hypertension.

**Paracentesis**: A needle or catheter is inserted to remove ascites fluid from the peritoneal cavity in order to treat associated pressure and other complications. This is a typical treatment for ascites.

**Thoracentesis**: A needle is used to remove excess fluid from the pleural cavity in order to treat associated pressure and other complications. This is a typical treatment for ascites.

**Dialysis dependent**: Regular dialysis treatments to address chronic renal failure. Report “yes” for recipients receiving regular dialysis treatments.
Q154-163: Hospital Stay

The following questions are only completed for 100 Day follow-up forms. If this VOD/SOS Form is being completed for the six month follow-up, skip this section and submit the form (or continue to signature line if submitting a paper form).

**Question 154: Was the intent to complete the HCT procedure (conditioning, infusion, and period of recovery from neutropenia) as an outpatient?**

Indicate whether the plan for transplant was to perform all conditioning, infusion, and recovery in the outpatient setting. The recipient may be admitted after the start of the preparative regimen or infusion due to complications; however, centers should answer question 154 based on the plan at the time the transplant orders were created.

If the intent was to complete the entire HCT procedure in the outpatient setting, report “yes” and continue with question 155.

If any of part of the HCT procedure was planned to be done inpatient, report “no” and continue with question 156.

**Question 155: Did the recipient require an unplanned admission?**

Report “yes” if the recipient had to be admitted to the hospital for any reason during the reporting period. Otherwise, report “no” and submit the form (or continue to signature lines if submitting a paper form).

**Question 156-158: Was the recipient admitted to ICU during their hospital stay?**

Indicate whether the recipient was admitted to the ICU during their unplanned admission reported in question 155. If yes, report the date the patient was admitted to the ICU in question 157 and the date they were discharged from the ICU in question 158. If the patient had multiple ICU stays during their unplanned admission, report the start and end dates based on their first admission to the ICU.

If the recipient died prior to discharge from the ICU, leave question 158 blank and override the error using the code “Unable to Answer.”

**Question 159-160: Was the recipient discharged prior to the date of contact?**

Indicate whether the recipient was discharged from the hospital after HCT. If “yes,” continue with question 160 and report the discharge date. If “no,” skip question 160 and continue with question 161.
If the recipient died without ever being discharged from the hospital, report “no” for question 159 and submit the form (or continue to signature lines if submitting a paper form).

**Question 161: Total number of inpatient days (day 0 to day 100) in first 100 days post-HCT**

Enter the total number of inpatient days (starting from day 0). If the recipient was discharged and readmitted during the first 100 days, the total should include days hospitalized after being readmitted. When counting the total number of inpatient days, count either the day of admission or the day of discharge; do not count both.

**Question 162-163: Discharge status**

Questions 162-163 should only be completed if the center has reported “yes” for question 159. If the center has reported “no” for question 159, skip questions 162-163 and submit the form (or continue to signatures lines if submitting a paper form).

Indicate the recipient’s discharge status following their first inpatient stay. If reporting “other” as the discharge status, specify the other status in question 163.

**Signature Lines:**

The FormsNet3SM application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.
**2556/2557: Myelofibrosis**

The Myelofibrosis Pre- and Post-HCT Supplemental Data Forms (Forms 2556 and 2557) must be completed when the primary diagnosis for HCT is Primary Myelofibrosis (PMF) as reported on the Pre-TED Disease Classification Form (Form 2402). This includes essential thrombocythemia (ET) that has transformed to myelofibrosis (MF) at time of HCT or Polycythemia vera (PV) that has transformed to myelofibrosis (MF) at time of HCT. This form captures DIPSS Prognosis Score, laboratory studies prior to JAK1/JAK2 inhibitor therapy, JAK1/JAK2 inhibitor therapy, laboratory studies at last evaluation prior to HCT and disease assessment at time of HCT.
**2556: Myelofibrosis Pre-HCT Data**

The Myelofibrosis Pre-HCT Supplemental Data Form (Form 2556) must be completed when the primary diagnosis for HCT is Primary Myelofibrosis (PMF) as reported on the Pre-TED Disease Classification Form (Form 2402). This includes essential thrombocythemia (ET) that has transformed to myelofibrosis (MF) at time of HCT or Polycythemia vera (PV) that has transformed to myelofibrosis (MF) at time of HCT. This form captures DIPSS Prognosis Score, laboratory studies prior to JAK1/JAK2 inhibitor therapy, JAK1/JAK2 inhibitor therapy, laboratory studies at last evaluation prior to HCT and disease assessment at time of HCT.

Myeloproliferative neoplasms (MPN) is a category in the World Health Organization (WHO) classification of myeloid tumors. Subtypes include chronic eosinophilic leukemia, chronic neutrophilic leukemia, essential thrombocythemia (ET), mastocytosis, polycythemia vera (PV), primary myelofibrosis (PMF), etc.

Primary myelofibrosis (PMF) is characterized by a proliferation of predominantly megakaryocytes and granulocytes in the bone marrow (BM) that, in fully developed disease, is associated with reactive deposition of fibrous connective tissue and with extramedullary hematopoiesis. There is an evolution in the natural history of the disease from an initial prefibrotic phase characterized by a hypercellular BM with absent or minimal reticulin fibrosis to a fibrotic phase with marked reticulin or collagen fibrosis in the BM and often osteosclerosis. This fibrotic stage of PMF is characterized by a leukoerythroblastosis in the blood with teardrop-shaped red cells, hepatomegaly and splenomegaly.

Myelofibrosis can develop in patients with pre-existing ET or PV. The criteria for diagnosing post-ET MF or post-PV MF include a prior diagnosis of ET or PV and the subsequent development of two or more features including bone marrow fibrosis; leukoerythroblastosis; new anemia; splenomegaly; or constitutional symptoms (i.e., night sweats, fever, or inappropriate weight loss).

**Links to Sections of the Form:**

- **Q1-17: DIPSS Prognosis Score**
- **Q18-33: Pre-HCT JAK1 and JAK2 Inhibitor Therapy**
- **Q34-71: Laboratory Studies Prior to Therapy**
- **Q72-76: Laboratory Studies at Last Evaluation Prior to HCT**
- **Q77-90: Disease Assessment at the Time of HCT**

**Manual Updates:**

Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.
If you need to reference the historical Manual Change History for this form, please click [here](#) or reference the retired manual section on the [Retired Forms Manuals webpage](#).

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
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<td>2556: Myelofibrosis Pre-HCT Data</td>
<td>Remove</td>
<td>Removed text referencing the CMS study for Myelofibrosis. The 2556 and 2557 are required for all patients with Myelofibrosis, not just patients enrolled in the CMS study. The titles of the forms have already been changed to remove CMS study from the title.</td>
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<tr>
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<td>2556: Myelofibrosis CMS Study Pre-HCT Data</td>
<td>Add</td>
<td>Added instructions (highlighted red below) for questions 26-27. Indicate “yes” if the patient was treated with a different JAK1 or JAK2 inhibitor (other than ruxolitinib) and specify the drug in question 27. Also, indicate “yes” if the recipient started and stopped ruxolitinib multiple times prior to HCT. In this case, the center should use questions 26-31 to report each treatment interval not captured in questions 19-25.</td>
</tr>
<tr>
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<td>2556: Myelofibrosis CMS Study Pre-HCT Data</td>
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<td>Add</td>
<td>Version 1 of the 2556: Myelofibrosis CMS Study Pre-HCT Data section of the Forms Instructions Manual released. Version 1 corresponds to revision 1 of the Form 2556.</td>
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</table>
Q1-17: DIPSS Prognosis Score

The prognosis of myelofibrosis patients can be predicted by the Dynamic International Prognostic Scoring System (DIPSS) risk categorization as shown in studies conducted by the International Working Group for Myelofibrosis Research and Treatment. The DIPSS risk factors include patient age, constitutional symptoms, hemoglobin, leukocyte count and circulating blasts.

**Question 1: Specify the maximum DIPSS score the patient ever achieved:**

The DIPSS score is based on five variables including patient’s age, white blood count (WBC), hemoglobin, peripheral blood blasts and constitutional symptoms. Each variable is assigned a point value which are added together to determine the overall score. Refer to Tables 1 and 2. Report the maximum DIPSS score the patient ever achieved between diagnosis and the start of the preparative regimen (or infusion if no preparative regimen was given) in question 1. Note the maximum score that can be reported is 6.

**Table 1. DIPSS variables**

<table>
<thead>
<tr>
<th>Prognostic Variable</th>
<th>0 Points</th>
<th>1 Point</th>
<th>2 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>≤ 65</td>
<td>&gt; 65</td>
<td></td>
</tr>
<tr>
<td>WBC (x 10⁹ / L)</td>
<td>≤ 25</td>
<td>&gt; 25</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g / dL)</td>
<td>≥ 10</td>
<td>&lt; 10</td>
<td></td>
</tr>
<tr>
<td>Peripheral blood blasts</td>
<td>&lt; 1</td>
<td>≥ 1</td>
<td></td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. DIPSS risk category and prognosis**

<table>
<thead>
<tr>
<th>DIPSS score</th>
<th>DIPSS risk category</th>
<th>Median OS (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Low</td>
<td>Not reached</td>
</tr>
<tr>
<td>1-2</td>
<td>Intermediate – 1</td>
<td>14.2</td>
</tr>
<tr>
<td>3-4</td>
<td>Intermediate – 2</td>
<td>4</td>
</tr>
<tr>
<td>5-6</td>
<td>High</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**Question 2: Specify when maximum DIPSS score was documented**

Specify whether the maximum DIPSS score was documented “at diagnosis”, “between diagnosis and the preparative regimen” or “at last evaluation prior to the start of the preparative regimen.”
When completing questions 3-17, report the clinical and laboratory assessments used to determine the maximum DIPSS score. For example, if the maximum DIPSS score was documented at diagnosis, report the testing performed at diagnosis.

**Question 3-5: WBC**

Indicate whether the white blood count (WBC) is “known” or “unknown” at the time the maximum DIPSS score was documented. If “known,” report the WBC and unit of measure documented on the laboratory report in question 4; indicate the date sample was collected in question 5. If “unknown,” continue with question 6.

**Question 6-8: Hemoglobin**

Indicate whether the hemoglobin count is “known” or “unknown” at the time the maximum DIPSS score was documented. If “known,” report the hemoglobin and unit of measure documented on the laboratory report in question 7 and the date of sample collection in question 8. If “unknown,” continue with question 10.

**Question 9: Were RBC transfused < 30 days before date of test?**

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

Indicate if red blood cells were transfused less than or equal to 30 days prior to the testing.

**Question 10-12: Platelets**

Indicate whether the platelet count is “known” or “unknown” at the time when the maximum DIPSS score was documented. If “known,” report the platelet count and unit of measure documented on the laboratory report in question 11 and the date of sample collection in question 12. If “unknown,” continue with question 14.

**Question 13: Were platelets transfused < 7 days before date of test?**

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support the counts.

Indicate if platelets were transfused less than or equal to 7 days prior to the testing.

**Question 14-16: Blasts in blood**

Indicate whether the percentage of blasts in the blood is “known” or “unknown” at the time of when the
maximum DIPSS score was documented. If “known,” report the blast percentage documented on the laboratory report in question 15 and the date of sample collection in question 16. If “unknown,” continue with question 17.

If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.

Question 17: Did the recipient have constitutional symptoms? (>10% weight loss in 6 months, night sweats, unexplained fever higher than 37.5C)

If there was evidence of constitutional symptoms at the time the maximal DIPSS score was documented, select “yes”. If there was no evidence of constitutional symptoms, select “no.” If documentation is not clear or is not available to determine if constitutional symptoms were present, select “unknown.”
Q18-33: Pre-HCT JAK1 and JAK2 Inhibitor Therapy

Janus associated kinase inhibitors, also known as JAK inhibitors, are a type of medication that inhibits the activity of one or more of the Janus kinase family of enzymes (JAK1, JAK2, JAK3, TYK2) thereby blocking an enzyme that causes scar tissue to form in the bone marrow. These inhibitors are indicated for treatment of patients with intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF, and post-essential thrombocythemia MF.

Examples of JAK inhibitors include ruxolitinib (Jakafi / Jakavi) and tofacibinib (Xeljanz / Jakvinus).

*) Ruxolitinib (Jakafi)
If the recipient started and stopped ruxolitinib (Jakafi) therapy multiple times prior to transplant, report the most recent treatment interval in questions 19-25. Also, report the prior treatment interval(s) in questions 26-31.
Do not, however, report ruxolitinib (Jakafi) treatments given for past transplants that have previously been reported.

Question 18: Did the recipient receive JAK1 or JAK2 inhibitor therapy? (pre-HCT)?

Indicate “yes” if the recipient received JAK1 or JAK2 therapy prior to the current HCT (not including therapy given for past HCTs that have previously been reported) and continue with question 19. If “no,” continue with question 34.

Question 19: Ruxolitinib (Jakafi)

Indicate “yes” if the recipient received ruxolitinib, a Janus kinase inhibitor with selectivity for JAK1 and JAK2 of this enzyme and continue with question 20. Indicate “no” if the recipient did not receive ruxolitinib and continue with question 26.

Question 20-21: Date therapy started

Indicate “known” if the therapy start date is documented, and specify the first date of ruxolitinib therapy administration in question 21. If the date is unknown, indicate such and continue with question 22.

Question 22-23: Date therapy stopped

Indicate “known” if the therapy completion date is documented and specify the date therapy stopped in
question 23. If the patient is receiving systemic therapy in cycles, specify the first day of the last cycle of systemic therapy. If the treatment is not given in cycles (e.g., daily), indicate the last day systemic therapy was administered.

If the date is unknown, indicate such and continue with question 26.

**Question 24-25: Specify reason therapy stopped**

Indicate why the ruxolitinib therapy was stopped from the list of reasons provided. If “Other” is checked, specify “other reason” in question 25.

**Question 26-27: Other JAK1 or JAK2 inhibitor**

Indicate “yes” if the patient was treated with a different JAK1 or JAK2 inhibitor (other than ruxolitinib) and specify the drug in question 27. Also, indicate “yes” if the recipient started and stopped ruxolitinib multiple times prior to HCT. In this case, the center should use questions 26-31 to report each treatment interval not captured in questions 19-25.

If “no,” continue with question 32.

**Question 28-29: Date therapy started**

Indicate “known” if the therapy start date is documented, and specify the first date of systemic therapy administration in question 29. If the date is “unknown”, indicate such and continue with question 30.

**Question 30-31: Date therapy stopped**

Indicate “known” if the therapy completion date is documented. Continue with question 31 and specify the date therapy stopped. If the patient is receiving systemic therapy in cycles, specify the first day of the last cycle of systemic therapy. If the treatment is not given in cycles (e.g., daily), indicate the last day systemic therapy was administered.

If the date is unknown, indicate such and continue with question 32.

The FormsNet3SM application allows questions 26-33 to be reported multiple times. Complete these questions for each JAK1 or JAK2 inhibitor therapy administered prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given).

**Question 32: Response to therapy**

For each line of therapy given, indicate if there was “clinical improvement”, “stable disease”, “non-splenic disease progression”, “splenic disease progression” or “transformation to leukemia”.
Clinical improvement: defined as 50% improvement in palpable spleen length for spleen palpable by 10 cm, or complete resolution of splenomegaly for palpable spleen <10 cm

Non-splenic disease progression: increase in blasts to 10% to 19%, intolerance to treatment due to hematologic/non-hematologic side effects, or new onset transfusion-requiring anemia

Splenic disease progression: appearance of new splenomegaly palpable 5 cm below costal margin (BCM) or 100% increase in palpable distance BCM for baseline splenomegaly of 5 cm to 10 cm BCM, 50% increase in palpable distance BCM for baseline splenomegaly of 10 cm BCM, loss of spleen response, or symptomatic splenomegaly requiring splenectomy

Transformation to leukemia: peripheral blood or bone marrow blast count of 20%

Question 33: Date assessed

Report the date of the response to therapy reported in question 32 was assessed. Report the date of the pathological evaluation (e.g., bone marrow biopsy) or clinical evaluation. Enter the date the sample was collected for pathological and/or laboratory evaluation or report the date of the office visit in which the physician clinically assessed the recipient’s response.
Q34-71: Laboratory Studies Prior to Therapy

Specify the laboratory values immediately prior to JAK1 / JAK2 inhibitor therapy. If no JAK1 / JAK2 inhibitory therapy was given, report results at last evaluation prior to the start of the preparative regimen for HCT.

Question 34-35: Was presence of somatic mutations tested? (immediately prior to JAK1 / JAK2 inhibitor therapy initiation or prior to the start of the preparative regimen if no JAK1 / JAK2 inhibitor therapy was given)

Testing for somatic mutations may be performed by different methods including next generation sequencing, polymerase chain reaction, microarray, and fluorescence in situ hybridization. If testing was performed by any / all of these methods prior to the start of JAK1 / JAK2 inhibitor therapy was given (or prior to the start of the preparative regimen if no JAK1 / JAK2, capture the most recent test(s) in questions 37-56.

Indicate “yes” if somatic mutations were tested for and specify the date the sample was collected in question 35. Indicate “no” if somatic mutations were not tested for or “unknown” and go to question 57.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 36: Specify sample source

Indicate if the sample was from “bone marrow” or from “peripheral blood”.

Question 37-54: Was presence of somatic mutations tested? (immediately prior to JAK1 / JAK2 inhibitor therapy initiation)

For each gene mutation listed, Indicate “positive”, “negative” or “not done”.

Question 55-56: Other gene mutation

Indicate “positive” or “negative” if another gene mutation was tested for that was not listed in questions 37-54, and specify the other gene in Q56. If another gene mutation was not tested for, indicate “not done” and go to question 57.

Question 57-59: WBC

Indicate whether the white blood count (WBC) is “known” or “unknown” at the time of last evaluation prior to therapy. If “known,” report the WBC and unit of measure documented on the laboratory report in question 58; indicate the date sample was collected in question 59. If “unknown,” continue with question 60.
**Question 60-62: Hemoglobin**

Indicate whether the hemoglobin value is “known” or “unknown” at the time of last evaluation prior to therapy. If “known,” report the hemoglobin and unit of measure documented on the laboratory report in question 61 and the date of sample collection in question 62. If “unknown,” continue with question 64.

**Question 63: Were RBC transfused < 30 days before date of test?**

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

Indicate if red blood cells were transfused _less than or equal to_ 30 days prior to the testing.

**Question 64-66: Platelets**

Indicate whether the platelet count is “known” or “unknown” at the time of last evaluation prior to therapy. If “known,” report the platelet count and unit of measure documented on the laboratory report in question 65 and the date of sample collection in question 66. If “unknown,” continue with question 68.

**Question 67: Were platelets transfused < 7 days before date of test?**

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support the counts.

Indicate if platelets were transfused _less than or equal to_ 7 days prior to the testing.

**Question 68-70: Blasts in blood**

Indicate whether the percentage of blasts in the blood is “known” or “unknown” at the time of last evaluation prior to therapy. If “known,” report the blast percentage documented on the laboratory report in question 69 and the date of sample collection in question 70. If “unknown,” continue with question 71.

* If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.

**Question 71: Did the recipient have constitutional symptoms? (>10% weight loss in 6 months, night sweats, unexplained fever higher than 37.5°C)**

If there was evidence of constitutional symptoms at time of last evaluation prior to therapy, select “yes”. If there was no evidence of constitutional symptoms, select “no.” If documentation is not clear or is not
available to determine if constitutional symptoms were present, select “unknown.”
Q72-76: Laboratory Studies at Last Evaluation Prior to HCT

**Question 72-74: Total serum ferritin**

Ferritin is a blood cell protein that contains iron. Ferritin levels indicate how much iron a person’s body is storing. If the ferritin level is lower than normal, it indicates the body’s iron stores are low (iron deficiency). If the ferritin level is higher than normal it could indicate hemochromatosis, a condition that causes the body to store too much iron. Other causes of an elevated ferritin level include liver disease, acute and chronic inflammatory conditions, malignancy to name a few.

Indicate whether the total serum ferritin value is “known” or “unknown” at the time of last evaluation prior to the start of prep for HCT. If “known”, report the ferritin value documented on the laboratory report in question 73 and the date of sample collection in question 74. If “unknown”, continue with question 75.

**Question 75-76: CD34+ cells (peripheral blood)**

Indicate whether the CD34+ cell count is “known” or “unknown” at the time of last evaluation prior to the start of prep for HCT. If “known”, report the CD34+ cell count documented on the laboratory report in question 76. The reported value must be in units of cells / µL.
Q77-90: Disease Assessment at the Time of HCT

**Question 77: Did the recipient have evidence of pulmonary hypertension at HCT?**

Pulmonary hypertension (PH) refers to elevated pulmonary arterial pressure. PH can be due to a primary elevation of pressure in the pulmonary arterial system alone (pulmonary arterial hypertension), or secondary to elevations of pressure in the pulmonary venous and pulmonary capillary systems (pulmonary venous hypertension; post-capillary PH).

Indicate “yes” if the recipient has evidence of PH at the time of HCT or “no” if they did not. If documentation is not clear or is not available to determine if PH was present, select “unknown.”

**Question 78: Did the recipient have evidence of portal hypertension at HCT?**

Portal hypertension is high blood pressure in the hepatic portal system, which includes the portal vein and its branches. The hepatic portal system drains most of the intestines to the liver.

Indicate “yes” if the recipient has evidence of portal hypertension at the time of HCT or “no” if they did not. If documentation is not clear or is not available to determine if portal hypertension was present, select “unknown.”

**Question 79: Hepatomegaly**

Hepatomegaly is an enlargement of the liver. Indicate “yes” if the recipient has evidence of hepatomegaly at the time of HCT, and continue with question 80. Indicate “no” if they did not and go to question 82.

**Question 80: Specify the liver size**

Specify the number of centimeters the liver is below the right costal margin.

**Question 81: Specify the method used to measure the liver size**

Indicate if the liver size was measured by “physical assessment”, “ultrasound” or “CT scan”

**Question 82-83: Spleen size**

If the spleen size is “known” indicate the number of centimeters below the left lower costal margin in question 83. If the spleen size is “unknown” or “not applicable” (due to splenectomy), indicate the appropriate option and go to question 84.
Question 84: Iron overload

Indicate “yes” if the patient has documented iron overload and go to question 85. Indicate “no” if the patient doesn’t have documented iron overload and go to Signature Lines.

Question 85: Serum ferritin

Ferritin is a blood cell protein that contains iron. A ferritin level indicates how much iron a person’s body is storing. If the ferritin level is lower than normal, it indicates the body’s iron stores are low (iron deficiency). If the ferritin level is higher than normal it could indicate hemochromatosis, a condition that causes the body to store too much iron. Other causes of an elevated ferritin level include liver disease, acute and chronic inflammatory conditions, malignancy to name a few.

Indicate “yes” if the serum ferritin level indicated iron overload or “no” if it did not or wasn’t performed.

Question 86: Liver MRI

Indicate “yes” if a liver MRI was used to make the diagnosis iron overload or “no” if it did not or wasn’t performed.

Question 87-88: Other method

Indicate “yes” if another method was used to make the diagnosis of iron overload and indicate the method in question 88. Indicate “no” if another method was not used to make the diagnosis of iron overload.

Question 89: Iron chelation therapy

Iron chelation therapy is the removal of excess iron from the body using drugs such as deferoxamine.

Indicate “yes” if iron chelation therapy was used to treat the iron overload or “no” if it was not.

Question 90: Phlebotomy

Indicate “yes” if phlebotomy was used to treat the iron overload or “no” if it was not.

Signature Lines:

The FormsNet3SM application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.
2557: Myelofibrosis Post-HCT Data

The Myelofibrosis Post-HCT Supplemental Data Form (Form 2557) must be completed when the primary diagnosis for HCT is Primary Myelofibrosis (PMF) as reported on the Pre-TED Disease Classification Form (Form 2402). This includes essential thrombocythemia (ET) that has transformed to myelofibrosis (MF) at time of HCT or Polycythemia vera (PV) that has transformed to myelofibrosis (MF) at time of HCT. This form captures disease assessments performed since date of last report.

Myeloproliferative neoplasms (MPN) is a category in the World Health Organization (WHO) classification of myeloid tumors. Subtypes include chronic eosinophilic leukemia, chronic neutrophilic leukemia, essential thrombocythemia (ET), mastocytosis, polycythemia vera (PV), primary myelofibrosis (PMF), etc.

Primary myelofibrosis (PMF) is characterized by a proliferation of predominantly megakaryocytes and granulocytes in the bone marrow (BM) that in fully developed disease is associated with reactive deposition of fibrous connective tissue and with extramedullary hematopoiesis. There is an evolution in the natural history of the disease from an initial prefibrotic phase characterized by a hypercellular BM with absent or minimal reticulin fibrosis to a fibrotic phase with marked reticulin or collagen fibrosis in the BM and often osteosclerosis. This fibrotic stage of PMF is characterized by a leukoerythroblastosis in the blood with teardrop-shaped red cells, hepatomegaly and splenomegaly.

Myelofibrosis can develop in patients with pre-existing ET or PV. The criteria for diagnosing post-ET MF or post-PV MF include a prior diagnosis of ET or PV and the subsequent development of two or more features including bone marrow fibrosis; leukoerythroblastosis; new anemia; splenomegaly; or constitutional symptoms (i.e., night sweats, fever, or inappropriate weight loss).

Links to Sections of the Form:

Q1-25: Disease Assessment Since Date of Last Report

+Manual Updates: +

Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

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<tr>
<th>Date</th>
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<th>Description</th>
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<td></td>
</tr>
<tr>
<td>---------</td>
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<td></td>
</tr>
<tr>
<td>2/27/19</td>
<td>Remove</td>
<td>Removed text referencing the CMS study for Myelofibrosis. The 2556 and 2557 are required for all patients with Myelofibrosis, not just patients enrolled in the CMS study. The titles of the forms have already been changed to remove CMS study from the title.</td>
<td></td>
</tr>
<tr>
<td>1/31/17</td>
<td>Add</td>
<td>Version 1 of the 2557: Myelofibrosis CMS Study Post-HCT Data section of the Forms Instructions Manual released. Version 1 corresponds to revision 1 of the Form 2557.</td>
<td></td>
</tr>
</tbody>
</table>
Q1-25: Disease Assessment Since Date of Last Report

Question 1-2: Spleen size

If the spleen size is “known,” indicate the number of centimeters below the left lower costal margin in question 2. If the spleen size is “unknown” or “not applicable” (due to splenectomy), indicate the appropriate option and go to question 3.

Question 3-4: Was presence of somatic mutations tested?

Testing for somatic mutations may be performed by different methods including next generation sequencing, polymerase chain reaction, microarray, and fluorescence in situ hybridization. If testing was performed by any / all of these methods during the current reporting period, capture the most recent test(s) in questions 3-25.

Indicate “yes” if somatic mutations were tested for and specify the date the sample was collected in question 4. Indicate “no” if somatic mutations were not tested for or “unknown” and go to First Name.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 5: Specify the sample source

Indicate if the sample was from “bone marrow” or from “peripheral blood”.

Question 6-23:

For each gene mutation listed, Indicate “positive”, “negative” or “not done”.

Question 24-25: Other gene mutation

Indicate “positive” or “negative” if another gene mutation was tested for that was not listed in questions 6-23, and specify in Q25. If another gene mutation was not tested for, indicate “not done” and go to question First Name.

Signature Lines:

The FormsNet3SM application will automatically populate the signature data fields, including name and
email address of person completing the form and date upon submission of the form.
The Sanofi Mozobil Supplemental Data Collection Form (Form 2656) is designed to support a prospective, multicenter, observational registry of myeloma recipients undergoing hematopoietic progenitor cell mobilization and peripheral blood stem cell collection for upfront autologous transplantation. This form will come due for any recipients with upfront autologous transplants that have been identified as enrolled in this study. Upfront refers to the recipient’s first autologous HCT occurring no later than 12 months after the start of the first line of therapy used to treat myeloma. This form must be completed for all consecutive multiple myeloma upfront autologous transplants.

A Sanofi Mozobil Eligibility Form will come due based on certain criteria that will be determined by FormsNet. When answering question 1, did the HCT occur ≤ 12 months from the start of initial therapy for myeloma, also note that there should be NO progression between lines of therapy.

A Sanofi Mozobil Supplemental Data Collection Form will come due for each mobilization event performed prior to the recipient’s first autologous HCT. The way in which a mobilization event is defined for the purposes of this form is different from how mobilization events are defined for other CIBMTR forms. The examples below demonstrate how a single mobilization event is defined for the purposes of completing a Sanofi Mozobil Supplemental Data Form. The guidelines included in Appendix E: Definition of a Product do not apply when completing this form.

**Example 1:** An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. Since the collection and mobilization methods remained the same over the duration of the collection, this is considered one mobilization event.

**Example 2:** An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection, but the cell count was poor. GM-CSF was administered and the autologous recipient was re-collected. This is considered a single mobilization event for the purposes of completing a Sanofi Mozobil Supplemental Data Form.

**Example 3:** An autologous recipient was mobilized with G-CSF and underwent a one-day PBSC collection, but the cell count was poor. The recipient then received plerixafor to enhance the mobilization. This is considered a single mobilization event for the purposes of completing a Sanofi Mozobil Supplemental Data Form.

**Links to Form Sections**
- Q1-3: Mobilization
- Q4-56: Pre-Collection Therapy Given to Enhance Product Collection
- Q57-74: Mobilization Agents
## Q75-100: Apheresis Collection

### Manual Updates

Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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</tr>
</thead>
</table>
Q1-3: Mobilization

**Question 1-2: Did the recipient stay at a temporary location closer to the collection center for mobilization? (e.g., hotel)**

Report “Yes” for question one if the recipient stayed at a temporary location closer to the collection center for mobilization. If the recipient stayed at a temporary location, specify the number of days in question two.

Report “No” for question one and go to question three if the recipient did not stay at a temporary .

**Question 3: What was the intended method of stem cell mobilization for this recipient?**

Indicate the intended method of mobilization for this recipient. If, at the time of mobilization, the method was modified or an alternate method was used, report the actual method of mobilization in the ‘Mobilization Agents’ section.

- **Mobilization with G-CSF alone:** Select this option if the recipient received only G-CSF.
- **Mobilization with G-CSF + plerixafor:** Select this option if recipient received G-CSF and plerixafor as the planned method of mobilization.
- **Mobilization with G-CSF + as needed plerixafor rescue:** Select this option if the recipient received G-CSF and also received unplanned plerixafor due to insufficient mobilization with G-CSF alone.
- **Chemomobilization:** Select this option if the recipient received only chemomobilization.
Q4-56: Pre-Collection Therapy Given to Enhance Product Collection

**Question 4: Was pre-collection chemotherapy given to enhance product collection?**

Report “Yes” and go to question five if there was pre-collection chemotherapy given to enhance product collection.

If “No”, go to question 12.

**Question 5: Specify where chemotherapy was administered:**

Indicate whether the chemotherapy was administered in an inpatient hospitalization or in an outpatient setting. If any of the chemotherapy was administered while the recipient was admitted to the hospital, “Inpatient” must be reported.

**Question 6: Did the recipient receive antibacterial drugs(s) for infection prophylaxis during chemomobilization?**

Report “Yes” if the recipient received antibacterial drug(s) for infection prophylaxis during chemomobilization. If the recipient received more than one antibiotic during chemomobilization, complete an instance of questions 7-11 for each drug. Only three instances may be reported.

If the recipient did receive antibacterial drug(s), centers should specify the antibiotic(s) as defined in questions 7-8.

If “No”, go to question 12.

**Question 7-8: Specify antibiotic:**

Indicate which antibacterial drug was given to the recipient.

**Question 9: Total daily dose**

Report the total daily dose (in mg) of the drug specified in questions 7-8. For example, if a recipient receives 250 mg PO every 12 hours, the reported total daily dose would be 500 mg.

**Question 10: Date started**

Report the date the drug was started. If the exact date is not known, use the process described in General.
Instructions, General Guidelines for Completing Form.

**Question 11: Date stopped**

Report the date each drug was stopped. If the exact date is not known, use the process described in General Instructions, General Guidelines for Completing Forms.

**Question 12-14: Why was chemotherapy used for mobilization?**

Indicate why chemotherapy was used for mobilization.

If the chemomobilization was part of a clinical trial, centers should specify which trial as defined in question 13.

If "Other" has been reported for question 12, specify the other reason in question 14.

**Question 15-47: Specify chemotherapy agents given**

Report “Yes” for any chemotherapy agents / regimens administered as part of the recipient’s mobilization regimen. For any drugs / regimens where “Yes” has been reported, also report the total daily dose (see example calculation from question 9), the number of days administered, and the date started for the appropriate chemotherapy drugs.

If “Yes” has been reported for cyclophosphamide (question 15), centers must also report whether mesna was given during the mobilization regimen (question 19). Mesna is given to prevent cyclophosphamide induced hemorrhagic cystitis. If “Yes” has been reported for mesna (question 19), also report the total daily dose, number of days administered, and the date mesna was started.

Report chemotherapy agents not captured in questions 15-42 in the “Other drug” data fields (questions 43-47). Do not report supportive agents (e.g., mesna) in these data fields. If multiple “other drugs” were given, contact your center’s CRC to determine how to complete questions 43-47.

**Question 48: Were there complications from chemotherapy?**

Centers should report “Yes” if there were any complications from the chemotherapy reported in questions 15-47. If it is not clear whether a documented complication occurred as a result of chemotherapy, confirm with the appropriate care provider prior to reporting.

If no complications occurred, report “No” and go to question 58.
**Question 49: Specify complications from chemotherapy: (check all that apply)**

Using the available options, report all complications resulting from the chemotherapy reported in questions 15-47. The next question to be completed will depend on which options have been reported in question 49.

If "Hospitalization" is checked, questions 50-53 must be answered. If this option is not checked, questions 50-53 will be skipped.

If “Anemia requiring blood transfusion(s)” is checked, question 54 must be answered. If this option is not checked, question 54 will be skipped.

If “Thrombocytopenia requiring platelet transfusion(s)” is checked, question 55 must be answered. If this option is not checked, question 55 will be skipped.

If “Other” is checked, question 56 must be answered. If this option is not checked, question 56 will be skipped.

**Question 50: Specify date of admission**

Specify the date the recipient was admitted to the hospital due to complications from chemotherapy. If the exact date is not known, use the process described in General Instructions, General Guidelines for Completing Forms.

**Question 51: Was the recipient discharged prior to conditioning?**

Report “Yes” if the recipient was discharged from the hospital prior to conditioning and report the date of discharge asked in question 52.

If “No”, go to question 53.

**Question 52: Specify date of discharge**

Specify the date the recipient was discharged. If the exact date is not known, use the process described in General Instructions, General Guidelines for Completing Forms.

**Question 53: Specify where the recipient was hospitalized**

Specify whether the recipient was hospitalized at the transplant center or a local hospital. If the recipient was hospitalized at the transplant center and the transplant center is considered the recipient’s local hospital. Report “Transplant Center” for question 54.
**Question 54: Specify number of units transfused (blood)**

Specify the number of blood units transfused.

**Question 55: Specify number of units transfused (platelets)**

Specify the number of platelet units transfused.

**Question 56: Specify other complication**

Specify any other complications, not already reported in question 49, resulting from the chemotherapy reported in questions 15-47.
**Q57-74 Mobilization Agents**

**Question 57-74: Specify mobilization agents used**

Mobilization drugs are used to increase the number of hematopoietic progenitor cells in the recipient's peripheral blood prior to collection by apheresis. Report “Yes” for any mobilization drugs given as part of the mobilization regimen reported on this form. If multiple mobilization regimens were given prior to HCT, complete a separate Sanofi Mozobil Supplemental Data Collection Form for each regimen. Also, report the total daily dose (see example calculation from question 9), number of days administered, and the start date for any drugs given. See the examples included at the beginning of this manual for more information about mobilization regimens.

If “Yes” is reported for G-CSF, specify the drug given in questions 58-62. If more than one type of G-CSF is given (e.g., filgrastim and pegfilgrastim), complete a separate instance for each drug by clicking on the orange (+) sign in the ‘Mobilization Agents’ header.

If “Yes” is reported for plerixafor, indicate the reason this drug was given in question 67. If plerixafor was given as part of the original mobilization plan, indicate “Planned per protocol.” This is typically the case if plerixafor is given prior to any collection attempts or testing for CD34+ cells in the recipient’s peripheral blood. If, however, plerixafor was not started until a collection was attempted or was started as a result of a low CD34+ count in the peripheral blood, report “Recipient at risk of mobilization failure.” In this case, plerixafor is considered an unplanned agent which would not have been given if the first collection attempt(s) had yielded a sufficient number of hematopoietic stem cells or if peripheral blood testing demonstrated an adequate amount of CD34+ cells. The center would report “No” for plerixafor on the form being completed for the initial mobilization. A second form would be completed which would capture the use of plerixafor and any other concurrent mobilization agents.

If “Recipient at risk of mobilization failure” has been reported for question 67, also report the specific reason in questions 68-69.
Q75-100: Apheresis Collection

Question 75-76: Did the recipient receive blood transfusions (RBCs) during this apheresis collection?

Report “Yes” if the recipient received blood transfusions during this apheresis collection. Also, indicate the number of units of RBCs transfused during the collection in question 76.

If “No”, go to question 77.

Question 77-78: Did the recipient receive platelets during this apheresis collection?

Report “Yes” if the recipient received platelets during this apheresis collection. Also, indicate the number of units of platelets transfused during the collection in question 78.

If “No”, go to question 79.

Question 79-80: Was peripheral blood CD34+ checked the day prior to collection?

Report “Yes” if the peripheral blood CD34+ was tested the day prior to the first collection performed as part of this mobilization event. Also report the result of the test in question 81.

If “No”, go to question 81.

If the result of CD34+ testing is documented in units other than cells / uL, confirm the correct conversion with the center’s laboratory.

Question 81: Specify the total number of apheresis collection days for this mobilization

Report the total number of days the recipient underwent apheresis to collect the peripheral blood stem cell product. Do not include any days when collection was attempted, but no product could be collected (e.g., no product was collected because venous access could not be established).

Question 82-83: Was there a planned hospitalization for collection?

Report “Yes” if any collections, as part of this mobilization event, were planned to be done in the inpatient setting. If “Yes” is reported for question 82, specify the number of planned inpatient collection days in question 83.

If “No”, go to question 84.
Multiple Collection Days
A separate instance of questions 84-97 must be completed for each day of collection performed as part of the mobilization event being reported on this form.

Question 84: Date of collection

Indicate the date of collection. If multiple collections were done as part of this mobilization event, one instance of questions 84-97 must be reported for each day. The date reported in question 84 will clarify which date the reported values for questions 85-97 correspond to.

Question 85-87: Was there central venous access during collection? (i.e., central venous line (CVL))

Report “Yes” if central venous access was used for the purposes of the collection performed on the date reported in question 84. Access may be established prior to any collection attempt (planned) or after failed attempts (unplanned). If “Yes” is reported for question 85, indicate the type of access in question 86. If the type of access is reported as “Planned temporary CVL” or “Unplanned CVL,” also indicate in question 87 whether the central line was removed prior to the start of the preparative regimen for the recipient’s infusion.

If central venous access was not used for the purposes of collection, report “No” for question 85 and go to question 88.

Question 88-89: Peripheral blood CD34+ cells

Report “Known” if the peripheral blood CD34+ cell count was tested on the day of collection and prior to the initiation of leukapheresis. Also, specify the number of cells detected in question 89.

If the result of CD34+ testing is documented in units other than cells / uL, confirm the correct conversion with the center’s laboratory.

If “Unknown”, go to question 90.

Question 90-91: Absolute neutrophil count (ANC)

Report “Known” if the absolute neutrophil count was tested on the day of collection and prior to the initiation of leukapheresis. Also, specify the number of cells detected in question 91.

If “Unknown”, continue with question 92.

Question 92-94: Platelets

Report “Known” if the platelet count was tested on the day of collection and prior to the initiation of
leukapheresis. Also, specify the number of platelets detected and whether the recipient received a platelet transfusion within seven days prior to the test in questions 93 and 94 respectively.

Indicate whether or not platelets were transfused less than or equal to seven days before the date of test

**Question 95-96: Blood volume processed**

Indicate whether the blood volume processed during the collection being reported is “Known” or “Unknown.” This information is typically documented in a collection summary note or on an apheresis flowchart. If the blood volume cannot be found in the available documentation, confirm where this value would be documented with the appropriate apheresis staff prior to reporting “Unknown.” If the blood volume processed during the collection being reported is “Known,” report the volume in question 96.

The volume of blood processed may be documented as a total volume in liters or it may be documented in terms of the donor’s total blood volume. For example, 20 liters of blood may be processed during a single collection with a total blood volume of five liters. This may be recorded in the apheresis documentation as 20 total liters of blood processed or as four donor blood volumes.

**Question 97: Total CD34+ collected (on this day of collection)**

Report the total number of CD34+ cells (in units of cells / kg recipient weight) which were collected on the date reported in question 84.

**Question 98: Number of bags cryopreserved**

Report the total number of cryopreserved bags from all days of collection done as part of the mobilization event being reported.

**Question 99: Was this mobilization episode considered successful?**

Indicate whether or not this mobilization episode was considered successful. Consult the appropriate care provider if it is not clear whether the mobilization episode was considered successful.

If “No”, go to question 100.

**Question 100: Was remobilization done as a result?**

If another mobilization event was done, report “Yes” and submit the form. This will prompt another Sanofi Mozobil Supplemental Data Collection Form to come due. Report all data pertaining to the subsequent mobilization event on the new form.

If remobilization did not occur, report “No” and submit the form.
These sections include additional information referenced in other manuals.

Appendix A: Abbreviations and Definitions
Appendix B: Glossary of Terms
Appendix C: Cytogenetic Assessments
Appendix D: How to Distinguish Infusion Types
Appendix E: Definition of a Product
Appendix F: Response Evaluation Criteria in Solid Tumors
Appendix G: Tracking Disease Status for Multiple Myeloma
Appendix H: MDS/MPN Subtypes
Appendix I: Ethnicity and Race
Appendix J: Reporting Comorbidities
Appendix K: Key Fields
Appendix L: Karnofsky / Lansky Performance Status
Appendix M: Critical Data Fields
Appendix A: Abbreviations and Definitions

Appendix A provides definitions of common manual abbreviations and United States abbreviations.

Common Manual Abbreviations

YYYY: 4 digit year
MM: 2 digit month
DD: 2 digit day
AHOP: Adult, Hematology, Oncology or Pediatric Unit (select only one)
ALLO: Allogeneic
ANC: Absolute Neutrophil Count
AUTO: Autologous
BM: Bone Marrow
BMT-CTN: Blood & Marrow Transplant Clinical Trials Network
CIBMTR: Center for International Blood & Marrow Transplant Research
CIC: Center Identification Code
CMV: Cytomegalovirus
CR: Complete Remission
CRF: Comprehensive Report Form =

2000 Baseline
2004 IDM
2005 HLA
2006 INF
20xx Disease (pre-HSCT)
2100 Day-100
2200 Six month- two year
2300 Greater than two year
21xx Disease Follow-Up (Post-HSCT)
2046 FNG
2047, 2147 HEP
2048,2148 HIV
2900 Death

CTN: Blood & Marrow Transplant – Clinical Trials Network
d-0: Day zero, a.k.a. Date of HCT
DCI: Donor Cellular Infusion
**Product Form:** This was a transitional term used to temporarily describe the form pieces that came out of the '95/'02 CIBMTR Graft insert. The three Forms are IDM, HLA & INF. The term "Product Form" may have appeared in communication from Summer 2007; it is being retired.

**ProMISe:** Electronic data collection system for EBMT

**PTLD:** Posttransplant lymphoproliferative disorder

**Unit:** Adult, Hematology, Oncology, Pediatric (AHOP) Note: select only one.

**United States Abbreviations**

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1 The CIBMTR requests that the full name of U.S. Territories is used whenever possible.
Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for any of the appendices, please reference the retired appendix on the Retired Forms Manuals webpage.

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Appendix B: Glossary of Terms

General Terms

**absolute neutrophil count (ANC)**
Neutrophils are a type of white blood cell that helps protect the body from infection. The number of neutrophils in a recipient’s blood is used to track recovery after chemotherapy or HSCT. In some types of HSCT, the number of neutrophils is a marker of engraftment.

**allele**
One of the different forms of a gene that can occur at a single spot on a chromosome. A part of DNA representing a gene inherited from each parent to make a pair.

**allele code**
The NMDP uses allele codes to report the HLA allele combinations used to match recipients and donors. The codes reduce multiple allele combinations into an alphabetic term.

**allogeneic hematopoietic cell transplant**
Any cord blood, bone marrow or peripheral blood stem cell transplant that uses cells from a person other than the recipient. The donated cells can come from a family member or a donor who is not related to the recipient.

**antibody**
A protein in the blood that is created by the immune system in response to foreign substances like viruses, bacteria or tumor antigens. Each antibody recognizes a specific antigen unique to its target.

**antigens**
Substances capable of activating the immune system. Antigens include toxins, bacteria, foreign blood cells, and the cells of transplanted organs. Proteins found on most cells of the body are antigenic and therefore are the targets for graft-versus-host disease and graft rejection.

**apheresis**
A procedure where blood is taken from a person’s arm and passed through a machine. The machine separates and collects certain cells such as blood-forming cells, white blood cells or platelets. The rest of the blood is returned through the other arm.

**autologous hematopoietic cell transplant**
A transplant using blood-forming cells collected from the recipient. The recipient’s own blood-forming cells
are collected, stored and then returned to the body after the recipient receives high doses of chemotherapy and/or radiation therapy. The cells are generally collected when the recipient is in remission to minimize cancer cell contamination.

**blast phase**
The advanced stage of chronic myelogenous leukemia or chronic lymphocytic leukemia when the number of abnormal white blood cells in the bone marrow and blood is very high.

**cellular transplantation, cellular transplant therapy**
The process of replacing or supplementing a recipient’s diseased blood and immune system with healthy, blood-forming, immune or other hematopoietic-derived cells collected from marrow, peripheral blood or cord blood. This may include, but is not limited to, an infusion of donor lymphocytes or mesenchymal stem cells.

**chemotherapy**
A drug treatment that kills cancer cells. Used to prepare recipients for a marrow, PBSC, or cord blood transplant.

**confirmatory test (CT)**
An additional test designed to detect only a targeted substance (i.e., virus, protein, DNA, antibody, etc.) with high specificity and low sensitivity; generally done to confirm disease after a positive screening test, as it is more costly and time consuming than a screening test.

**contact date**
In order for a form (Pre-, Post-TED, and/or Comprehensive Report Form) to be entered into the database, the contact date must be at least a day greater than the contact date of the previous form. If the center has not had contact with the recipient since the contact date that was reported on the previous form, a Lost to Follow-up (Form 2802) should be submitted instead.

**cord blood unit (CBU)**
Cord blood that meets eligibility requirements and has been typed and stored for potential transplantation.

**cryopreservation**
A procedure for storing tissues or blood products at extremely low temperatures.

**cytomegalovirus (CMV)**
A virus that can cause pneumonia, gastroenteritis or urinary tract infection in people with weakened immune systems. Many healthy people infected with the virus have no signs of infection. CMV infection is a concern because of the risk of infection to people with weakened immune systems, such as transplant recipients and those with HIV.
disease
An abnormal condition of an organism that impairs bodily functions and can be deadly. Also defined as a way of the body harming itself in an abnormal way, associated with specific symptoms and signs.

disease specific forms
Previously called “inserts” by both the Minneapolis and Milwaukee campuses of the CIBMTR. These forms are due once the primary Comprehensive Report Form (i.e., Form 2000, 2100, 2200 or 2300) is complete.

DNA repository
A facility that stores NMDP volunteer donor blood samples for HLA testing. Blood samples are either frozen or spotted on filter paper cards for later DNA-based HLA typing.

engraftment
The stage when the transplanted blood-forming cells start to grow and make healthy new blood cells derived from the donor (including autologous).

enzyme immunoassay (EIA)
See ELISA

enzyme-linked immunosorbent assay (ELISA)
A biochemical technique used to detect the presence of specific substances such as antibodies or antigens. Because it can be performed to evaluate either the presence of antigen or the presence of antibody in a sample, it is a useful tool both for determining serum antibody concentrations (such as with the HIV or hepatitis) and also for detecting the presence of antigen.

false positive
Reactive test result not due to the presence of the substance being tested but rather to an interfering or cross-reacting substance; confirmatory testing is necessary to differentiate true positive from false positive.

filgrastim
A man-made version of a normal human protein that increases the number of blood-forming cells in the body. Filgrastim is used to treat neutropenia (a low number or neutrophils), stimulate the bone marrow to increase production of neutrophils. Filgrastim is also given to donors who have agreed to donate peripheral blood stem cells (PBSC). Filgrastim is also known as G-CSF (granulocyte-colony stimulating factor) or by the trade name Neupogen®.

good clinical practices (GCP)
An international ethical and scientific quality standard for designing, conducting, recording, and reporting, trials that involve the participation of human subjects.
**graft**
Tissue or organ transplanted from a donor to a recipient. In some cases the recipient can be both donor and recipient.

**graft failure**
When transplanted blood-forming cells fail to make enough white blood cells, platelets and red blood cells. There are several causes for graft failure, including graft rejection. Failure to engraft occurs when there is no recovery of donor (or autologous) stem cell function following the HSCT, and may be caused by inadequate numbers of blood-forming cells at the time of transplantation.

**graft-versus-host disease (GVHD)**
A condition where the transplanted marrow or blood stem cells react against the recipient’s tissues. GVHD is caused by the donor’s T cells. There are two types of GVHD, acute GVHD (aGVHD) and chronic GVHD (cGVHD). GVHD can be mild or serious and is sometimes life threatening. Recipients are given immunosuppressive medication after transplant to prevent and control GVHD.

**growth factor**
A substance that affects cellular growth, proliferation and cellular differentiation. Cytokines and hormones are examples of growth factors that bind to specific receptors on the surface of their target cells. Growth factors often promote cell differentiation and maturation. Filgrastim is one type of growth factor.

**HLA (human leukocyte antigen)**
The name of the major histocompatibility complex (MHC) in humans. The superlocus contains a large number of genes related to immune system function in humans. This group of genes resides on chromosome 6 and encodes cell-surface antigen-presenting proteins and many other genes. The proteins encoded by certain genes are also known as antigens, as a result of their historic discovery as factors in organ transplantations. The major HLA antigens are essential elements in immune function.

Different classes have different functions:

- **HLA class I** antigens (A, B & C) present peptides from inside the cell (including viral peptides if present). These peptides are produced from digested proteins that are broken down in the lysosomes. The peptides are generally small polymers, about 9 amino acids in length. Foreign antigens attract killer T-cells (also called CD8 positive cells) that destroy cells.

- **HLA class II** antigens (DR, DP, & DQ) present antigens from outside of the cell to T-lymphocytes. These particular antigens stimulate T-helper cells to reproduce and these T-helper cells then stimulate antibody producing B-cells, self-antigens are suppressed by suppressor T-cells.

HLA testing is used to match recipients and donors for marrow, blood stem cell and organ transplants.
human T-cell lymphotropic virus (HTLV)
A single-stranded RNA retrovirus that causes T-cell leukemia and T-cell lymphoma in adults and may also be involved in certain demyelinating diseases.

immunobiology
The study of the immune response and the biological aspects of immunity to disease.

indeterminate
Test results that do not meet criteria for either positive or negative; may require repeat or additional testing.

infectious disease markers (IDMs)
Proteins in the blood that show if a person has had an infectious disease that could be transferred to a recipient through a marrow or PBSC transplant.

informed consent
The process by which a person receives an explanation of the risks and benefits of a medical treatment or research study. If a person agrees to participate, he or she must indicate in writing that they understand and agree to the information provided. A person can provide informed consent at the age of 18.

institutional review board (IRB)
An IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the institution with which it is affiliated. The IRB has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified by both the federal regulations and local institutional policy.

neutralization test
A test that determines the power of an antiserum or other substance by testing its action on the pathogenic properties of a microorganism, virus, bacteria, or toxic substance.

non-myeloablative transplant
A type of transplant that uses lower doses of chemotherapy and/or radiation to prepare a recipient for transplant. In this type of preparative regimen, the recipient’s hematopoietic system is not expected to be completely destroyed.

nucleic acid amplification test (NAT/NAAT)
A test can detect evidence of infection by amplifying nucleic acid in a virus, allowing for early detection of minute quantities of viral genes in the blood. The NAT can detect disease at an earlier stage than antibody testing (e.g. ELISA) since the appearance of antibodies and antigens take time to be detectable. Also see: PCR.
polymerase chain reaction (PCR)
A method of NAT testing, PCR is a powerful method for amplifying specific DNA/RNA segments and is used in the diagnosis of both infections and genetic diseases.

radiation therapy
Treatment with high-energy rays used to destroy or shrink cancer cells, or suppress the immune system.

recombinant immunoblot assay (RIBA)
A confirmatory test for hepatitis C, RIBA can detect whether a positive anti-HCV test is due to exposure to HCV (positive RIBA) or represents a false signal (negative RIBA).

research sample repository
A facility operated by the NMDP that stores research blood samples collected from marrow, PBSC donors, cord blood units, and recipients whose transplants were facilitated through the NMDP. The research samples are used in studies designed to improve outcomes for future transplant recipients.

screening test
An inexpensive, easy and rapidly performed test with high sensitivity and low specificity; used with the intention of detecting early evidence of disease.

sensitivity
A measure of how well a test correctly identifies everyone who has a disease or condition; the proportion of individuals with a disease or condition that will have a positive test.

seroconversion
The development of detectable antibodies in the blood as a result of exposure to an infectious agent.

serology
The scientific study that tests the blood serum for antibodies. Prior to seroconversion, the blood tests seronegative for the antibody; after seroconversion, the blood tests seropositive for the antibody.

specificity
A measure of how well a test eliminates everyone who does not have a disease or condition; the proportion of individuals without a disease or condition that will have a negative test.

western blot
An immunoassay technique used to detect specific proteins in blood or tissue. Western blot is used as the confirmatory HIV test. A western blot is also used to detect other diseases such as bovine spongiform encephalopathy and Lyme disease.
**window period**
Time between infection with a virus and the time the immune system has produced enough antibodies for the antibody test to detect. This time period can vary from person to person.

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for any of the appendices, please reference the retired appendix on the [Retired Forms Manuals](#) webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
</table>


Appendix C: Cytogenetic Assessments

Introduction to Chromosomes

Cytogenetic Assessment Methods

Chimerism and Disease Assessment

Introduction to Chromosomes

A basic knowledge of chromosome abbreviations / terms is required to interpret cytogenetic test results. Typical human cells contain 23 chromosome pairs (46 total chromosomes). Twenty-two of these pairs are autosomal (non-sex) chromosomes. Each autosomal chromosome is referred to by its number, one through 22. The remaining two chromosomes (the 23rd pair) are referred to as sex chromosomes and are identified as either X (female) or Y (male). Females have two X chromosomes while males have one X and one Y chromosome.

Chromosomal abnormalities refer to changes in the amount or location of chromosomal material. Definitions of general categories of chromosomal abnormalities are provided below:

**Addition:** extra chromosomal material is present. This includes extra material within a specific region of a chromosome and entire extra chromosomes. Extra material is described by the location while extra whole chromosomes are described based on the quantity present. Trisomy refers to three chromosomes present (one extra) while tetrasomy refers to four chromosomes present (two extra).

**Deletion:** loss of chromosomal material. This includes loss of material within a specific region of a chromosome and entire missing chromosomes. Loss of material is described by location while entire missing chromosomes are described based on the quantity present. Monosomy refers to one chromosome present (one lost) while nullisomy refers to no chromosomes present (both lost).

**Translocation:** an exchange of chromosomal material between two or more chromosomes.

**Inversion:** the base pair order is reversed for a specific region of a chromosome.

**Hyperdiploidy:** the total number of chromosomes present is higher than normal. The definition of hyperdiploidy is typically further specified on the form being completed. For example, a form may require greater than 50 chromosomes be present to report hyperdiploidy.

**Hypodiploidy:** the total number of chromosomes present is lower than normal.

Abnormalities are described by identifying the involved chromosomes and specific locations, when applicable. The location is described when an abnormality involves only a specific section of a chromosome or when a translocation has occurred. The location is defined by two pieces of information, the chromosome arm and the arm region. The arm refers to the short (p arm) or long (q arm) end of the chromosome on
opposite sides of the centromere. The arm region describes the distance from the centromere. See Figure 1 below for a depiction of the chromosome arm and arm regions. Definitions of common cytogenetic abbreviations and terms are provided in Table 1.

**Figure 1. Chromosome Structure**

![Chromosome Structure Diagram](image)

**Table 1. Cytogenetic Abbreviations and Terms**

<table>
<thead>
<tr>
<th>Abbreviation/Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>p</td>
<td>short arm of a chromosome</td>
</tr>
<tr>
<td>q</td>
<td>long arm of a chromosome</td>
</tr>
<tr>
<td>p+ / add(p)</td>
<td>addition of chromosomal material to the short arm of a chromosome</td>
</tr>
<tr>
<td>q+ / add(q)</td>
<td>addition of chromosomal material to the long arm of a chromosome</td>
</tr>
<tr>
<td>p- / del(p)</td>
<td>loss of chromosomal material to the short arm of a chromosome</td>
</tr>
<tr>
<td>q- / del(q)</td>
<td>loss of chromosomal material to the long arm of a chromosome</td>
</tr>
<tr>
<td>t</td>
<td>translocation of chromosomes; e.g., t(1;19)</td>
</tr>
</tbody>
</table>
+ addition of an entire chromosome (trisomy); e.g., +21
-
deletion of an entire chromosome (monosomy); e.g., -7
Ph+ Philadelphia chromosome, arises from translocation t(9;22)
inv inversion of chromosomal material; e.g., inv(1)(p36q21)
der Derivative
metaphase cell phase at which chromosomes may be examined
karyotype designation of results of chromosome analysis; karyotype may be defined at the cell level, cell line or clone level, or at the level of the individual

Cytogenetic Assessment Methods

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing a sample of cells for the presence of chromosomal abnormalities. Cytogenetic assessment can also be done to determine chimerism following an allogeneic infusion when there is a sex mismatch between the donor and recipient. Specific methods of assessment include karyotyping and fluorescence in situ hybridization (FISH).

Karyotyping, also referred to as conventional cytogenetics, is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are performed to visualize chromosomes during cell division so various bands and reconfigurations are seen. Karyotype assessments typically examine around 20 cells. Figure 2 below shows an example of a karyotype. The chromosomes are arranged in numerical order with sex chromosomes included last.

Figure 2. Karyotype
Karyotype results are provided in a unique format which is demonstrated in Figure 3 below. Commas separate each finding within a karyotype. A slash separates different karyotypes identified in the sample. Different karyotypes are identified when findings are detected in some, but not all cells. In Figure 3, a slash is used to indicate two different karyotypes were identified from the examined cells. The number of cells demonstrating each karyotype is denoted in brackets following each karyotype description.

When reporting karyotype results, a data manager must distinguish between clonal and non-clonal findings. Clonal abnormalities are present in multiple cells and indicate a separate cell line, such as a malignant population, is present. If an abnormality is only detected in a single cell (or two cells in the case of deletions), it should not be reported. In this case, the finding could represent an isolated non-clonal abnormality or an inaccurate observation by the examiner. Refer to the general reporting guidelines below.
when determining which abnormalities to report.

**Additions:** must be present in at least two cells.

**Deletions:** must be present in at least three cells.

**Translocations:** must be present in at least two cells.

**Inversions:** must be present in at least two cells.

Karyotyping may also detect constitutional abnormalities. These are abnormalities present since birth. Examples include, but are not limited to, trisomy 21 and Klinefelter’s syndrome. It is not necessary to report constitutional abnormalities when reporting karyotyping results.

**Figure 3. Karyotype Results**

![Karyotype Result Diagram]

**Table 2. Karyotype Results**

<table>
<thead>
<tr>
<th>Number</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Number of chromosomes detected.</td>
</tr>
<tr>
<td>2</td>
<td>Sex chromosomes.</td>
</tr>
<tr>
<td>3</td>
<td>Deletion of chromosomal material on the long arm of chromosome 7 between regions 21 and 34.</td>
</tr>
<tr>
<td>4</td>
<td>Trisomy 8; extra chromosome 8.</td>
</tr>
<tr>
<td>5</td>
<td>Translocation of chromosomal material on the long arm of chromosome 8 and the long arm of chromosome 9.</td>
</tr>
<tr>
<td>6</td>
<td>Number of cells (metaphases) examined with these abnormalities.</td>
</tr>
<tr>
<td>7</td>
<td>Separates information about differing karyotypes.</td>
</tr>
<tr>
<td>8</td>
<td>Number of chromosomes detected.</td>
</tr>
<tr>
<td>9</td>
<td>Sex chromosomes.</td>
</tr>
</tbody>
</table>
**FISH** is a molecular cytogenetic technique using fluorescent probes that bind to a **specific** part of a chromosome (i.e., the probes recognize and bind to fragments of DNA). It is a sensitive technique that can assess hundreds of cells per test. The probes are mixed with cells from the tissue sample. A fluorescent “tag” is then used to visualize the binding of the probe to the cells. Probes can identify the number of chromosomes or gene copies within a cell as well as the relative locations of specific genes or chromosome regions. Unlike karyotype assessments, FISH can be done on non-dividing, or interphase, cells. A FISH assessment typically examines between 200 and 500 cells.

Each probe has a specific target or set of targets and is therefore only capable of detecting abnormalities associated with that area. Additionally, the type of probe used affects the interpretation of the results. See below for descriptions of common categories of FISH probes.

- **Centromere Enumeration Probe (CEP):** targets the centromere and is used to count the number of a specific chromosome in a cell (e.g., trisomy 8 or +8).
- **Locus Specific:** targets a single locus other than the centromere and is used to detect additions, deletions, or rearrangements.
- **Dual Fusion:** targets two loci and is used to detect translocations.
- **Break-apart:** used to confirm gene rearrangements. The 3’ portion of the gene or region is in one color and the 5’ is in another color. If rearranged, colors are separate.

It is important to know what a FISH assessment is testing for before trying to interpret the results. For instance, a probe specific to the p arm of chromosome 9 would not be capable of detecting a deletion anywhere on chromosome 4. In Figure 4 below, two cells were exposed to centromere enumeration probes (CEP) specific to chromosomes 6 and 8 in order to determine the number of each chromosome present. Both cells have two copies of chromosome 6 (green probes) and three copies of chromosome 8 (red probes). This FISH result indicates the presence of a trisomy of chromosome 8.

**Figure 4. FISH**
Cytogenetics results are usually provided as a percentage or ratio of cells, for which, an abnormality was detected. The result may also be accompanied by a normal range to define when the test is considered positive for the abnormality being assessed. An interpretation / impression section of the report is also common and should be referenced when reporting testing results. Figure 5 is an example FISH report. It includes the identity of each probe, the number of abnormal cells, the normal range, a result for each probe, and a final interpretation. The report confirms the TP53 and CEP12 probes detected abnormalities; however, the TP53 probe did not detect an abnormality at a rate above the normal cut off value (7%). The final interpretation indicates these findings represent a gain of chromosome 12 (trisomy).

Figure 5. FISH Results
### FLUORESCENCE IN SITU HYBRIDIZATION REPORT

**FISH Probes**: CLL [Abbott (Vysis), Inc.]

<table>
<thead>
<tr>
<th>PROBE SETS CHROMOSOME LOCI</th>
<th># CELLS ANALYZED</th>
<th>NORMAL CUTOFF VALUE (95% CI)</th>
<th>RESULTS</th>
<th>ISCN NOMENCLATURE 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>11q22.3 (ATM), 17p13 (TP53)</td>
<td>200</td>
<td>10</td>
<td><strong>Del 11q22.3 &gt; 0.0% Del 17p13 &gt; 7.0%</strong></td>
<td>Loss of 17p13 (TP53) detected (5%) Abnormal signal pattern.</td>
</tr>
<tr>
<td>CEP 12/13q14(D13S219),13q34</td>
<td>200</td>
<td>130</td>
<td><strong>Gain of 12 &gt; 2.5% Del 13q &gt; 5.5% Homozygous Del 13q &gt; 1.5% Loss of 13 &gt; 5.5%</strong></td>
<td>Gain of CEP 12 detected (65%). Abnormal signal pattern.</td>
</tr>
<tr>
<td>11q13(CCND1)/14q32 (IGH)</td>
<td>300</td>
<td>---</td>
<td>t(11;14) &gt; 1%</td>
<td>No CCND1/IGH rearrangement. Normal signal pattern</td>
</tr>
<tr>
<td>CEP6(D6Z1), 6q22-23(MYB)</td>
<td>300</td>
<td>---</td>
<td>Del(6q22-23) &gt; 3%</td>
<td>No deletion of MYB detected. Normal signal pattern.</td>
</tr>
</tbody>
</table>

* FISH only testing is not equivalent to conventional cytogenetic analysis of the patient's specimen, and is limited to the specific probe(s) and their corresponding DNA locations (genes) only.

**Summary**: Abnormal CLL FISH Panel

**Final Interpretation**: This fluorescence in situ hybridization (FISH) analysis showed an abnormal signal pattern with gain of chromosome 12 in 130 out of 200 (65%) cells, implying trisomy 12 consistent with CLL.


FISH reports may only refer to a probe by a gene name without indicating the chromosome number / region. For example, the report in Figure 5 could have only specified an ATM probe was used without also indicating the gene location was 11q22.3. It may be necessary, depending on the CIBMTR form, to know the gene location to accurately report the test results. The laboratory performing the study is the best resource for more information about the test that was done. A probe search can also be done using the HUGO Gene Nomenclature Committee’s website [genenames.org](http://genenames.org). This website provides gene symbols, approved names, associated names, and chromosomal locations for many of the probes in current use.
Chimerism and Disease Assessment

Cytogenetic assessments can be performed to identify markers of disease, determine chimerism following an allogeneic cellular infusion, or both. Cytogenetic assessment of chimerism is usually only done for sex mismatched pairs of recipients and donors. In these cases, a karyotype or FISH study can determine the ratio of cells containing female vs. male sex chromosomes. A unique form of karyotype assessment, Q banding, can also be used to assess chimerism for sex matched recipient and donor pairs; however, molecular techniques involving PCR amplification are much more common.

Disease assessment by cytogenetic methods involves the identification of disease-specific markers (e.g., -7, del(5q), Philadelphia chromosome). Once a marker is identified, cytogenetic assessments can be repeated to determine whether the marker, and therefore the disease, is still detectable. The types of markers identified can affect the disease classification and inform the treatment plan. A cytogenetic assessment cannot be considered a disease assessment until this method has detected a marker of disease. In other words, if cytogenetic studies have always been negative, the recipient's disease is not considered to be assessed by this method because there are no known cytogenetic abnormalities to evaluate. Pay attention to the wording of the question on the CIBMTR form being completed. "Was testing performed?" may be answered differently than “Was the disease assessed?"

CIBMTR forms generally capture chimerism data separately from disease assessment data. Therefore, it is important to know what information can be reported based on the assessment performed.

Example: Consider a recipient of an allogeneic product obtained from a sex mismatched donor as part of treatment for AML. The cytogenetic abnormality t(8;21) was identified as a marker of this recipient’s disease on previous cytogenetic assessments. Would the following cytogenetic assessments be reported in chimerism data fields, disease assessment data fields, or both?

- **Karyotype**: report this assessment in both chimerism and disease assessment data fields. A karyotype is capable of detecting autosomal and sex chromosomes. The test would confirm whether the t(8;21) abnormality was still present and also provide a ratio of female to male cells.
- **FISH [X / Y probe(s) only]**: only report this assessment in chimerism data fields. The probes are able to provide a ratio of female to male cells, but are not capable of detecting the t(8;21) abnormality.
- **FISH [t(8;21) probes only]**: only report this assessment in disease assessment data fields. The probes are able to detect the t(8;21) abnormality, but are not capable of providing a ratio of female to male cells.
- **FISH [X / Y probe(s) and t(8;21) break apart probe]**: report this assessment in both chimerism and disease assessment data fields. The X / Y probe(s) will provide chimerism data while the t(8;21) probe results will be captured as a disease assessment.
Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

<table>
<thead>
<tr>
<th>Date</th>
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<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/20/18</td>
<td>Appendix C: Cytogenetic Assessments</td>
<td>Add</td>
<td>Added table below figure 3 to explain karyotype findings.</td>
</tr>
<tr>
<td>2/12/18</td>
<td>Appendix C: Cytogenetic Assessments</td>
<td>Add</td>
<td>Added the following description of constitutional abnormalities. <em>Karyotyping may also detect constitutional abnormalities. These are abnormalities present since birth. Examples include, but are not limited to, trisomy 21 and Klinefelter’s syndrome. It is not necessary to report constitutional abnormalities when reporting karyotyping results.</em></td>
</tr>
</tbody>
</table>
Appendix D: How to Distinguish Infusion Types

This appendix includes definitions of Hematopoietic Stem Cell Transplant (HCT), Cellular Therapies, Supplemental Infusions, and Autologous Cells Given for Graft Failure. For more information see Table 1.

Table 1. Distinguishing Infusion Types*

<table>
<thead>
<tr>
<th>Purpose of infusion</th>
<th>HCT Definitions</th>
<th>Autologous Cells Given for Graft Failure (Cell therapy)</th>
<th>HCT Supporting Solid Organ Transplant (Cell therapy)</th>
<th>Cellular Therapy (e.g. DCI/DLI)</th>
<th>Post-HCT Cellular Therapy (with HCT)</th>
<th>Co-infusion (with HCT)</th>
<th>Micro-transplants</th>
<th>Regenerative Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Resuscitate or repopulate recipient marrow, facilitate hematopoietic recovery, restore donor graft in case of autologous recovery or graft failure.</td>
<td>Restore autologous hematopoietic system, if given after an allologeneic transplant, this often is a temporary measure until next course of action is determined.</td>
<td>Develop tolerance to solid organ graft via HCT.</td>
<td>The intent is either to restore hematopoiesis.</td>
<td>The intent is either to restore hematopoiesis.</td>
<td>The intent is either to restore hematopoiesis.</td>
<td>The intent is either to restore hematopoiesis.</td>
<td>Restoration of organs/tissues excluding blood and marrow.</td>
</tr>
<tr>
<td>Composition of infusion</td>
<td>Must contain HPCs (hematopoietic progenitor cells) also known as CD34+ cells.</td>
<td>Must contain HPCs (hematopoietic progenitor cells) also known as CD34+ cells.</td>
<td>Must contain HPCs (hematopoietic progenitor cells) also known as CD34+ cells.</td>
<td>The cells of action are not stem cells, but the infusion may contain residual stem cells (insufficient to cause engraftment).</td>
<td>The cells of action are not stem cells, but the infusion may contain residual stem cells (insufficient to cause engraftment).</td>
<td>The cells of action are not stem cells, but the infusion may contain residual stem cells (insufficient to cause engraftment).</td>
<td>The cells of action are not stem cells, but the infusion may contain residual stem cells (insufficient to cause engraftment).</td>
<td>CD34 dose adequate to produce/restore hematopoiesis.</td>
</tr>
<tr>
<td>CIBMTR Form Where Data is Reported</td>
<td>HCT forms</td>
<td>No additional forms required</td>
<td>Report as HCT</td>
<td>Cell Therapy forms (4000 series)</td>
<td>Cell Therapy forms (4000 series) and HCT forms. Follow up as patient based on product type. Must be reported if Alogenic donor.</td>
<td>Report infusion data on KDS.</td>
<td>Cell Therapy forms (4000 series)</td>
<td>Cell Therapy forms (4000 series)</td>
</tr>
</tbody>
</table>

*A preparative regimen may or may not be given in all scenarios and is no longer used to define infusion type.

Granulocyte Infusions
Granulocyte infusions given solely to fight infection should not be reported as a HCT or cellular therapy. Contact your center’s liaison for further clarification regarding how to correctly report granulocyte infusions.

HCT Definitions

Hematopoietic Stem Cell Transplant (HCT) – Primary or Subsequent

A HCT is an infusion of a product (see Appendix E) that contains CD34+ cells. The intention of a HCT is
generally to restore hematopoiesis by replacing or repopulating the recipient marrow. A HCT is often preceded by a preparative regimen, which is used to kill normal cells, malignant cells (if present), and to prevent rejection. However, a preparative regimen may not always be used prior to a stem cell infusion. Examples of this may include a “boost” or infusions given for non-malignant diseases. These indications are still considered a HCT if they fit primary criteria used to define a transplant: the product infused contains CD34+ cells and there is intent to restore hematopoiesis.

*Report infusions of bone marrow, cord blood, and mobilized PBSC as a HCT; as a general rule of thumb, infusion of portions of original HCT product without further manipulation would be considered subsequent transplants. The intent of these infusions is generally to restore hematopoiesis.*

---

### HCT Examples Outside of Standard Context

1. Recipient receives an allogeneic related HCT. The product is collected via a standard G-CSF mobilization. A portion of cells from the first HCT are saved for a second infusion. The portion of cells are then manipulated for CD34+ selection and infused. This second infused is considered an HCT because there are sufficient CD34+ cells for engraftment.

2. Recipient receives an allogenic HCT. They never engrafted post-HCT & receive additional HPCs (hematopoietic progenitor cells, CD34+) to restore hematopoiesis. This infusion should be reported as a subsequent HCT because the intent is to restore hematopoiesis.

3. FCRx product is comprised of donor peripheral blood-derived bioengineered hematopoietic stem cells. Mature graft versus host disease (GVHD)-producing and antigen-presenting cells were removed from the donor blood, for induction of immunological tolerance during organ transplantation and enriched for facilitating cells. Kidney transplant patients treated with FCRx were fully withdrawn from immunosuppression without loss of engraftment and achieved durable chimerism. Product contains high dose of CD34+ cells that could/would lead to engraftment, this in fusion should be reported as an HCT. Source: [http://discovery.lifemapsc.com/regenerative-medicine/cell-therapy-applications/blood-fcrx-bioengineered-hematopoietic-stem-cells-for-immunological-tolerance](http://discovery.lifemapsc.com/regenerative-medicine/cell-therapy-applications/blood-fcrx-bioengineered-hematopoietic-stem-cells-for-immunological-tolerance)

4. Recipient receives an allogeneic unrelated (MUD) HCT. The PBSC product was collected in a total of
6 bags. Five of these bags were infused as the first HCT. The last bag was infused 6 months later as a “boost”. This infusion should be reported as a subsequent HCT because the intent is to restore hematopoiesis.

**Autologous Cells Given for Graft Failure**

A recipient may receive an infusion of autologous cells as a result of poor hematopoietic recovery or graft failure/rejection following prior allogeneic or autologous transplant; this is generally referred to as “autologous rescue.” The CIBMTR defines this type of infusion as a subsequent HCT; however, because the research value of these data does not justify the additional reporting burden to transplant centers, CIBMTR does not currently require additional forms in the event of these transplants. Necessary data are adequately captured on the routine follow-up forms.

**HCT Supporting Solid Organ Transplant**

In an effort to achieve organ tolerance and potentially avoid long term systemic immunosuppression, a recipient may receive an infusion of cells prior to a subsequent solid organ transplant. These infusions contain sufficient CD34 cells to result in engraftment and should be reported as an HCT.

**Cellular Therapy Definitions**

**Cellular Therapy vs. Donor Cellular Infusion**

For reporting purposes, cellular therapy infusions given to recipients who have never received a HCT are referred to as Cellular Therapies. If the recipient received a HCT and then received a cellular therapy, the infusion is referred to as a post-HCT cellular therapy, such as a donor cellular infusion (DCI). For further assistance to determine how to correctly report a cellular therapy, contact your center’s liaison.

**Cellular Therapy (Alone or Post-HCT)**

Cellular therapy is a form of immunotherapy that is commonly used to treat infections (e.g. viral), recurrent disease or mixed chimerism. Treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g. cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g. CAR T-cells).

The infused product does not contain sufficient CD34 cells to result in engraftment and the intent is not to restore hematopoiesis. The recipient does not routinely receive a preparative regimen prior to receiving a cellular therapy; however, chemotherapy or immunotherapy that is not sufficient to ablate the marrow to the point where stem cell support is required may be given prior to a cellular therapy.
A cellular therapy should not be reported if additional donor cells (containing CD34+ cells) are given for failed ANC recovery, partial or poor ANC recovery, loss of graft, or late graft failure. Hematopoietic progenitor cell products infused for these indications would be considered a subsequent HCT.

The types of cells used for a cellular therapies include, but are not limited to the following:

- **Lymphocytes**: A therapeutic product from any source containing a fixed or prescribed dose of T-cells
- **Peripheral blood mononuclear cells**: Whole blood collected as a source of nucleated cells (not hematopoietic progenitor cells) intended for therapeutic use other than restoring hematopoiesis
- **Dendritic cells from the original donor**: A therapeutic cell product containing dendritic cells for therapeutic use
- **Mesenchymal cells**: A therapeutic product containing mesenchymal stromal cells for therapeutic use

**Examples of Cellular Therapy Alone**


**Examples of Post-HCT Cellular Therapy (e.g., DCI / DLI)**

1. Recipient receives autologous-derived marrow-infiltrating lymphocytes (MILs) after an autologous HCT for multiple myeloma. The protocol randomizes the infusion of this product to be post-HCT or at relapse. This infusion should be reported as a post-HCT cellular therapy.
2. Recipient receives an autologous HCT and as part of the protocol will also receive a planned NK cell infusion from the same donor on Day 10. This infusion should be reported as a post-HCT cellular therapy.

**Co-Infusion (with HCT)**

A co-infusion (or supplemental infusion) is defined as an infusion of cells given prior to clinical Day 0 (after the start of the prep regimen) of an HCT or on Day 0 for any reason other than to produce engraftment. An infusion of supplemental cells may be given in conjunction with a preparative regimen for a HCT. A co-infusion is distinct from a post-HCT cellular therapy (e.g. DCI) as it is given prior to an HCT or on the day of HCT, whereas a post-HCT cellular therapy is always given after an HCT.

Examples of supplemental infusions include, but are not limited to the following:
Co-infusion cells should be reported in the “Product Type” section of the Pre-TED, in the “Other” and “Specify cell source” fields. The cell source that is intended to produce engraftment should also be reported in the “Product Type” section of the Pre-TED. When reporting co-infusions, the Cellular Therapy Infusion form (4006) is required for all recipients. The HCT Infusion form (2006) will capture information regarding the product intended for engraftment.

**Co-Infusion Reporting Scenario**

A recipient is scheduled to receive an allogeneic HCT infusion along with infusions of alpha / beta depleted T cells.

**Three infusions**

1. CD34+ HPCs and alpha / beta depleted T cells on 3/1/2016
2. HPCs (pure product) 3/2/2016

**How to report**

1. The infusion of CD34+ HPCs on 3/1/2016 is the event date of HCT
2. The infusion of T cells also on 3/1/2016 would be reported as a co-infusion on the pre-TED
3. The T cells infused on 3/23/2016 would be reported as a post-HCT cellular therapy on the appropriate HCT follow up form

**Micro-transplant**

An example of a micro-transplant is provided below. For further assistance identifying and reporting micro-transplants, contact your center’s liaison.

**Micro-transplant Example**

A recipient receives an HLA-mismatched related donor micro-transplant as treatment to maintain remission for AML. Donor GCSF-mobilized donor peripheral stem cells (GPBSCs) are infused at a target dose of 1.0 ×108 CD3+ cells / kg (recipient weight). Since the target dose is of CD3+ cells, the dose of CD34+ is insufficient for engraftment. This is reported as a cellular therapy.
Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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<thead>
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</thead>
<tbody>
<tr>
<td>7/11/17</td>
<td>Appendix D: How to Distinguish Infusion Types</td>
<td>Modify</td>
<td>Version 3 of Appendix D: How to Distinguish Infusion Types of the Forms Instructions Manual released. Note, versions 1 &amp; 2 of this appendix were referred to as Appendix O: How to Distinguish Infusion Types.</td>
</tr>
</tbody>
</table>
Appendix E: Definition of a Product

The intention of this appendix is to define the term **product**, and provide several examples of infusions using single and multiple products. This appendix will also provide direction with regard to reporting product infusion on the CIBMTR Infusion Form 2006.

**The Infusion Form 2006 must be submitted for each product.** In order for a Form 2006 to become due in the FormsNet³ application, each product must be reported as a separate instance (including any supplemental cells given prior to clinical day 0) on the Pre-TED Form 2400. If the patient received multiple products of the same type (e.g. multiple PBSC products), the transplant center must contact the center’s liaison to request an additional Form 2006 in FormsNet³. Additionally, whenever multiple products are reported on the Comprehensive Report Forms, the transplant center must also contact the liaison to request additional Form 2006s in FormsNet³.

**Single Product vs. Multiple Products**

**Single Product:** For the purposes of this manual, the CIBMTR defines a single product (i.e. stem cell product) as **cells collected from a single donor using the same mobilization cycle and collection method regardless of the number of collection days.**

If a **single** product is infused, then complete a single (i.e. one) **Form 2006.** For more information, see Example 1 and Table 1 below.

**Example 1 – Multiple Bags:** GCSF-stimulated donor had two PBSC collections on subsequent days. The products collected over the two days were divided into four bags. Although the product is contained in multiple bags, this collection is considered a single product, as there was no change in mobilization technique or collection method. Therefore, one Form 2006 should be submitted.

**Multiple Products:** For the purposes of this manual, the CIBMTR defines multiple products as cells collected using more than one donor, mobilization technique, and/or collection method.

If a **multiple** products are infused, then multiple (i.e. two or more) **Form 2006s must be completed.** For more information, see Examples 2-5 and Table 1 below.

**Example 2 – Double Cord Blood Units:** A recipient receives an infusion of two cord blood units. Two Form 2006s must be submitted as each cord blood unit is from a different donor.
Example 3 – Multiple Collection Methods: GCSF-stimulated donor had a PBSC collection and the product was cryopreserved. One month later, the donor had a marrow collection and both products were infused at the time of transplant. Two Form 2006s must be submitted as these products were collected using two different methods.

Example 4 – Change in Mobilization: GCSF-stimulated donor had a PBSC collection, but cell count was poor. GM-CSF was added and the donor was recollected. Each collection is considered a separate product due to the change in mobilization. Therefore, a Form 2006 is due for the GCSF-stimulated cells and a second Form 2006 is due for the GM-CSF-stimulated cells.

Example 5 – Re-Mobilization: GCSF-stimulated donor had a PBSC collection, but cell count was poor. The donor was re-mobilized with GCSF and a second PBSC collection was performed. Each collection is considered a separate product due to the re-mobilization of the recipient.

Table 1. Single Product vs. Multiple Products

<table>
<thead>
<tr>
<th>Definition</th>
<th>Number of Form 2006s Required:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single Product</strong></td>
<td>All of the following criteria must be met:</td>
</tr>
<tr>
<td></td>
<td>• Single donor/cell source</td>
</tr>
<tr>
<td></td>
<td>• Single mobilization method</td>
</tr>
<tr>
<td></td>
<td>• Single collection method</td>
</tr>
<tr>
<td></td>
<td>One</td>
</tr>
<tr>
<td><strong>Multiple Products</strong></td>
<td>One or more of the following criteria must be met:</td>
</tr>
<tr>
<td></td>
<td>• Multiple donors/cell sources</td>
</tr>
<tr>
<td></td>
<td>• Multiple mobilization methods</td>
</tr>
<tr>
<td></td>
<td>• Multiple collection methods</td>
</tr>
<tr>
<td></td>
<td>Multiple – one to represent each donor/cell source, mobilization method, and/or collection method</td>
</tr>
</tbody>
</table>

Manual Updates:
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</thead>
<tbody>
<tr>
<td>6/</td>
<td>Appendix E: Definition</td>
<td>Modify</td>
<td>Appendix P: Definition of a Product has been renamed as</td>
</tr>
</tbody>
</table>
of a Product

Appendix E: Definition of a Product.
Appendix F: Response Evaluation Criteria in Solid Tumors (RECIST)

Response Evaluation Criteria in Solid Tumors (RECIST)

The Response Evaluation Criteria in Solid Tumors (RECIST) were published in February 2000 by the European Organization for Research and Treatment of Cancer (EORTC), the National Cancer Institute of the United States, and the National Cancer Institute of Canada Clinical Trials Group. RECIST criteria are used to evaluate a patient's response to the therapy used to treat their disease.

The content of this appendix has been modified to fit the needs of the CIBMTR data collection forms. For the complete text and more detailed information regarding confirmation of response, methods of measurement, and use of RECIST in clinical trials, see [http://ctep.cancer.gov/protocolDevelopment/docs/quickrcst.doc](http://ctep.cancer.gov/protocolDevelopment/docs/quickrcst.doc) and [http://ctep.cancer.gov/protocolDevelopment/docs/therasserecistjnci.pdf](http://ctep.cancer.gov/protocolDevelopment/docs/therasserecistjnci.pdf).

Baseline documentation of Target and Non-Target lesions:

- All measurable lesions up to a maximum of five lesions per organ and 10 lesions in total that are representative of all involved organs should be identified as target lesions recorded, and measured at baseline. Target lesions should be selected on the basis of their size (lesions with the longest diameter) and their suitability for accurate repeated measurements (either by imaging techniques or clinically). A sum of the longest diameter (LD) for all target lesions will be calculated and reported as the baseline sum LD. The baseline sum LD will be used as the reference by which to characterize the objective tumor.
- All other lesions (or sites of disease) should be identified as non-target lesions and should also be recorded at baseline. Measurements of these lesions are not required, but the presence or absence of each should be noted throughout follow-up.

Response Criteria for Target and Non-Target lesions:

Table 1. Evaluation of target lesions

<table>
<thead>
<tr>
<th>Disease Status</th>
<th>Evaluation of Target Lesions</th>
<th>Evaluation of Non-Target Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>Disappearance of all target lesions for a period of at least one month.</td>
<td>Disappearance of all non-target lesions and normalization of tumor marker</td>
</tr>
<tr>
<td>Response Level</td>
<td>Description</td>
<td>Date</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Complete response with persistent imaging abnormalities of unknown significance.</td>
<td>No definition available.</td>
<td></td>
</tr>
<tr>
<td>At least a 30% decrease in the sum of the longest diameter of measures lesions (target lesions), taking as reference the baseline sum of the longest diameter.</td>
<td>No definition available.</td>
<td></td>
</tr>
<tr>
<td>Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum of the longest diameter since the treatment started.</td>
<td>Persistence of one or more non-target lesion(s) or/and maintenance of tumor marker level above the normal limits.</td>
<td></td>
</tr>
<tr>
<td>A 20% or greater increase in the sum of the longest diameter of measured lesions (target lesions), taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions.</td>
<td>Appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions.¹</td>
<td></td>
</tr>
</tbody>
</table>

¹ Although a clear progression of “non target” lesions only is exceptional, in such circumstances, the opinion of the treating physician should prevail and the progression status should be confirmed later on by the review panel (or study chair).

**Manual Updates:**

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</tr>
</thead>
<tbody>
<tr>
<td>6/30/17</td>
<td>Appendix F: Response Evaluation Criteria in Solid Tumors (RECIST)</td>
<td>Add</td>
<td>Added all retired content from Appendix N: Response Evaluation Criteria in Solid Tumors (RECIST) to Appendix F.</td>
</tr>
<tr>
<td>6/30/17</td>
<td>Appendix F: Response Evaluation Criteria in Solid Tumors (RECIST)</td>
<td>Modify</td>
<td>Appendix N: Response Evaluation Criteria in Solid Tumors (RECIST) has been renamed to Appendix F: Response Evaluation Criteria in Solid Tumors (RECIST).</td>
</tr>
</tbody>
</table>
Appendix G: Tracking Disease Status for Multiple Myeloma

Successfully tracking and reporting disease status for multiple myeloma requires an understanding of the different methods of assessment, away of organizing relevant test results, and the ability to identify the correct baseline against which changes in test results can be compared. For training on how to identify and interpret myeloma disease assessment, refer to the myeloma learning modules available on the CIBMTR website under Online Training. For examples of ways to track disease assessments, refer to the documents included under Disease Status Tracking Examples below. Finally, for instructions on how to choose the correct baseline, refer to Determining a Baseline below.

Disease Status Tracking Examples

Tracking Disease Status for Multiple Myeloma – Word Document
Tracking Disease Status for Multiple Myeloma – PDF

The links above go to a flowsheet to aid in the determination of disease status for patients with multiple myeloma.

Determining a Baseline

HCT is planned as part of initial therapy w/out prior disease progression or relapse.
The baseline used to determine the best response to HCT is the disease parameters obtained at the time of diagnosis.

Patients who have not received any chemotherapy within 6 months of HCT, untreated relapse/progression or if the recipient has never been treated (rare).
The baseline used to determine the best response to HCT would be the disease parameters obtained immediately prior to the start of the preparative regimen (not the disease parameters at time of diagnosis).

What if the patient had a disease progression or relapse of disease before HCT?
If a patient had disease progression or relapse of disease & was treated to reduce the myeloma burden before any preparative regimen was given for HCT, the baseline used to determine the best response to HCT would be the disease parameters obtained at the time of the relapse or progression. In other words, the baseline is the reset to the time of the relapse or progression. Therefore, the disease parameters obtained at diagnosis or immediately prior to the start of the preparative regimen would not be used as the baseline to determine the best response to HCT.
What if the patient had 2 or more disease progressions before HCT?
The appropriate baseline to use would be the disease parameters documenting the most recent disease progression.

What if the patient's initial therapy was changed to a different regiment due to toxicity & there was not a disease progression or relapse at any time prior to HCT, what baseline is used to determine the best response to HCT?
The baseline used to determine the best response to HCT is the disease parameters obtained at the time of diagnosis.

Tandem Transplantation w/out disease progression or relapse in between.
Since this is considered one treatment, the pre-HCT baseline for determining the best response following the second HCT would be the same baseline used prior to the first HCT (i.e. the disease parameters at diagnosis).

Example 1: A 62-year-old man is diagnosed with IgG Kappa multiple myeloma. He receives initial therapy with 6 cycles of bortezomib and lenalidomide/dexamethasone; and achieves a near complete remission (nCR). The values used to determine disease status at transplant are the values obtained at diagnosis.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>BMBX</th>
<th>SPEP</th>
<th>SIFE</th>
<th>UPEP</th>
<th>UIFE</th>
<th>Skeletal Survey</th>
<th>Treatment</th>
<th>Disease Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/31/08</td>
<td>27% plasma cells</td>
<td>3.3 g/dL</td>
<td>+</td>
<td>336 mg/24 hours</td>
<td>+</td>
<td>Negative</td>
<td>Bortezomib/ Lenalidomide/ Dexamethasone</td>
<td>Diagnosis: IgG Kappa</td>
</tr>
<tr>
<td>4/3/09</td>
<td>3% plasma cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/17/09</td>
<td>Negative</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td>nCR</td>
</tr>
<tr>
<td>5/13/09</td>
<td>Negative</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td>nCR (confirmatory)</td>
</tr>
<tr>
<td>5/17/09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Autologous HCT</td>
<td></td>
</tr>
</tbody>
</table>

Example 2: A 59-year-old woman is diagnosed with IgA Lambda multiple myeloma. She receives bortezomib and thalidomide/dexamethasone as initial treatment and achieves a CR. A few months later she has evidence of relapse. She is then treated with lenalidomide/dexamethasone and achieves a PR. The patient receives high-dose cyclophosphamide as part of an autologous stem cell harvest. The values used to determine disease status at transplant would be the values obtained at the time of relapse.
<table>
<thead>
<tr>
<th>Time Point</th>
<th>BMBX</th>
<th>SPEP</th>
<th>SIFE</th>
<th>UPEP</th>
<th>UIFE</th>
<th>Skeletal Survey</th>
<th>Treatment</th>
<th>Disease Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/27/10</td>
<td></td>
<td>4.5 g/dL</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/01/10</td>
<td></td>
<td>Aspirate=18% plasma cells; biopsy= sheets of plasma cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Diagnosis: IgA lambda</td>
</tr>
<tr>
<td>2/05/10</td>
<td></td>
<td></td>
<td></td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>3/05/10</td>
<td></td>
<td>2.6 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bortezomib/ Thalidomide/ Dexamethasone</td>
</tr>
<tr>
<td>4/5/10</td>
<td></td>
<td>1.7 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/5/10</td>
<td></td>
<td>0.5 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/4/10</td>
<td></td>
<td>0.03 g/dL</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/18/10</td>
<td>1% plasma cells</td>
<td>0.01 g/dl</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/15/10</td>
<td></td>
<td>Not detected</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/15/10</td>
<td></td>
<td>Not detected</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CR</td>
</tr>
<tr>
<td>11/15/10</td>
<td></td>
<td>Not detected</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CR (confirmatory)</td>
</tr>
<tr>
<td>12/15/11</td>
<td></td>
<td>Not detected</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/15/11</td>
<td></td>
<td>1.9 g/dL</td>
<td>+</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
<td>Relapse</td>
</tr>
<tr>
<td>2/15/11</td>
<td>7% plasma cells</td>
<td>2.2 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>3/15/11</td>
<td></td>
<td>1.4 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lenalidomide/ Dexamethasone</td>
</tr>
<tr>
<td>4/15/11</td>
<td></td>
<td>0.9 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Relapse (confirmatory)</td>
</tr>
<tr>
<td>5/15/11</td>
<td></td>
<td>0.7 g/dL</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PR</td>
</tr>
</tbody>
</table>

**Note:** The data captures the following key points:
- **Time Points:** 1/27/10, 2/01/10, 2/05/10, 3/05/10, 4/5/10, 5/5/10, 6/4/10, 8/18/10, 9/15/10, 10/15/10, 11/15/10, 12/15/11, 1/15/11, 2/15/11, 3/15/11, 4/15/11, 5/15/11
- **Skeletal Survey:** Aspirate=18% plasma cells; biopsy= sheets of plasma cells
- **Treatment:** Bortezomib/ Thalidomide/ Dexamethasone, Lenalidomide/ Dexamethasone
- **Disease Status:** CR, Relapse, PR
6/15/11  3% plasma cells  0.5 g/dL  +  

7/31/11  Autologous HCT  

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<tbody>
<tr>
<td>6/30/17</td>
<td>Appendix G: Tracking Disease Status for Multiple Myeloma</td>
<td>Add</td>
<td>Added all information pertaining to Determining a Baseline. This information was taken from the retired Appendix V: Multiple Myeloma – Defining What Baseline to Use When Determining Disease Status.</td>
</tr>
<tr>
<td>6/30/17</td>
<td>Appendix G: Tracking Disease Status for Multiple Myeloma</td>
<td>Modify</td>
<td>Appendix W: Tracking Disease Status for Multiple Myeloma has been renamed as Appendix G: Tracking Disease Status for Multiple Myeloma.</td>
</tr>
</tbody>
</table>
Appendix H: MDS/MPN Subtypes

The following MDS/MPN subtypes are used on the Pre-TED, AML Pre-HCT Disease Specific Form, and the MDS/MPN Pre-HCT Disease Specific Form. For subtypes only appearing in the Pre-TED MDS Disease Classification (Q480) section and the AML Pre-HCT Disease Specific Form, see the section toward the bottom of the page.

Refractory Cytopenia with Unilineage Dysplasia (RCUD)

- Includes Refractory Anemia (RA), Refractory Neutropenia (RN), and Refractory Thrombocytopenia (RT)
- Unilineage dysplasia in ≥ 10% affected lineage
- Of erythroid precursors, < 15% are ringed sideroblasts
- Myeloblasts are not increased (< 5%)
- Unicytopenia or bicytopenia of peripheral blood with < 1% blasts

Refractory Anemia with Ringed Sideroblasts (RARS)

- Unilineage, erythroid dysplasia in ≥ 10% of red blood cell precursors
- Ringed sideroblasts comprise ≥ 15% nucleated erythroid precursors
- Myeloblasts are not increased (< 5%)
- Peripheral blood anemia with no blasts

Refractory Anemia with Excess Blasts (RAEB-1)

- 5-9% blasts in the bone marrow and < 5% blasts in the peripheral blood
- If < 5% blasts in the bone marrow, then 2-4% blasts in the peripheral blood
- Unilineage or multilineage dysplasia
- Absence of auer rods
- Multiple peripheral blood cytopenias
- Peripheral blood with < 1 × 10^9/L monocytes

Refractory Anemia with Excess Blasts (RAEB-2)

- 10-19% blasts in the bone marrow or 5-19% blasts in the peripheral blood
- Unilineage or multilineage dysplasia
- Auer rods may be present
- Multiple peripheral blood cytopenias
- Peripheral blood with < 1 × 10^9/L monocytes
Refractory Cytopenia with Multilineage Dysplasia (RCMD)

- One or more blood cytopenias with dysplasia in two or more lines
- Multilineage dysplasia in ≥ 10% precursors
- Absence of auer rods
- Blasts are not increased (< 5% marrow, < 1% peripheral blood)
- Multiple peripheral blood cytopenias
- Peripheral blood with < 1 x 10^9/L monocytes

Childhood myelodysplastic syndrome, aka Refractory Cytopenia of Childhood (RCC)

- Multilineage dysplasia in ≥ 10% of precursors
- Blasts are not increased (< 5% marrow, < 2% peripheral blood)
- Dysplastic changes in ≥ 10% of neutrophils on peripheral blood smear

Myelodysplastic syndrome with isolated del(5q), aka 5q-syndrome

- Peripheral blood anemia
- Frequently hypolobated small megakaryocytes
- Blasts are not increased (< 5% blasts in marrow, < 1% blasts in peripheral blood)
- Deletion of part of the long arm of chromosome 5, del(5q)
- Must not meet criteria of any other specific category

Myelodysplastic Syndrome, Unclassifiable (MDS-U)

MDS that cannot be classified into any other defined category due to one or more atypical features
Examples include:

- Hypocellular MDS
- MDS with myelofibrosis
- < 5% blasts in the marrow with Auer rods present
- MDS with unilineage dysplasia with associated pancytopenia

Chronic neutrophilic leukemia

- Peripheral blood leukocytosis, ≥ 25 x 10^9/L with segmented neutrophil > 80% and immature granulocytes < 10%
- Blasts are not increased (< 5% marrow, < 1% peripheral blood)
- Normal granulocytic maturation
- No Ph+ or BCR-ABL fusion and no abnormalities of PDGFRα, PDGFRβ, or FGFR1
- Reactive neutrophilia, PV, PMF, ET, MDS, and MDS/MPN must be ruled out
Chronic eosinophilic leukemia, NOS

- Peripheral blood eosinophilia ≥ 1.5 × 10^9/L
- Evidence of clonal abnormality but must not be Ph+ or BCR-ABL fusion, rearrangement of PDGFRα, PDGFRβ, or FGFR1, or inversion or translocation of (16)(p13.1,q22)

or

- 3-19% blasts in the peripheral blood or 6-19% blasts in the bone marrow.
- Reactive and secondary Eosinophilia must be ruled out

Essential thrombocythemia

- Includes primary thrombocytosis, idiopathic thrombocytosis, and hemorrhagic thrombocythemia
- Bone marrow with megakaryocytic hyperplasia; may have minimal fibrosis. Typically no erythroid or granulocytic hyperplasia. No ringed sideroblasts or increased blasts.
- JAK2 mutation or other clonal marker
- Peripheral blood thrombocytosis, ≥ 450 × 10^9/L
- CML, PMF, PV, MDS, and other myeloid neoplasms must be ruled out

Polycythemia Vera (PCV)

Presence of two major and one minor criterion, or presence of one major and two minor criterion

Major

- Increased hemoglobin (> 18.5 g/dL in men, > 16.5 g/dL in women)
- JAK2 mutation

Minor

- Low serum erythropoietin (EPO)
- Hypercellular bone marrow with panmyelosis
- In vitro endogenous erythroid colony formation

Primary myelofibrosis

- Includes chronic idiopathic myelofibrosis (CIMF), agnogenic² myeloid metaplasia (AMM), myelofibrosis/sclerosis with myeloid metaplasia (MMM), and idiopathic myelofibrosis
- Megakaryocytic hyperplasia with fibrosis (MF 2-3) or hypercellular marrow with granulocytic hyperplasia
• JAK2 mutation or other clonal marker
• PV, CML, MDS, and other myeloid neoplasms must be ruled out
• At least two of the following: splenomegaly, anemia, increased serum LDH, and leukoerythroblastosis

Myeloproliferative Neoplasm, Unclassifiable (MPN, U)

• Definite clinical, laboratory, and morphological features that fail to meet criteria for specific MPN classification, or overlap two or more MPN categories
• No Ph+ or BCR-ABL fusion and no abnormalities of PDGFRA, PDGFRB, or FGFR1
• MPN, U should not be used when clinical data is insufficient or not available for proper classification of disease

Chronic Myelomonocytic Leukemia (CMMoL)

• Blasts and promonocytes < 20% in peripheral blood and bone marrow
• Peripheral blood monocytes, > 1 x 10^9/L
• Dysplasia in one or more lines; typically seen, but not an absolute requirement for diagnosis
• No Ph+ or BCR-ABL fusion and no abnormalities of PDGFRA or PDGFRB

Myelodysplastic/Myeloproliferative Neoplasm, Unclassifiable (MDS/MPN, U)

• Clinical, laboratory, and morphological features that overlap MPN and MDS; this includes blasts < 20% in peripheral blood and bone marrow, platelet count ≥ 450 x 10^9/L, and WBC ≥ 13 x 10^9/L
• No Ph+ or BCR-ABL fusion and no abnormalities of PDGFRA, PDGFRB, or FGFR1
• MDS/MPN, U should not be used for patient with a previous, well-defined MPN who develop dysplastic features consistent with transformation to a more aggressive histology

The options below are used only on the Pre-TED form in the MDS Disease Classification Section (Q480) and/or the AML Pre-HCT Disease Specific Form.

Juvenile Myelomonocytic Leukemia (JMML, JCML, JCMML)

• Blasts < 20% in bone marrow
• Peripheral blood monocytes, > 1 x 10^9/L
• No Ph+ or BCR-ABL fusion
• Splenomegaly
• May exhibit clonal chromosomal abnormality (may include monosomy 7)
• May have GM-CSF hypersensitivity
• May have peripheral blood leukocytosis, > 10 x 10^9/L
• May have increased fetal hemoglobin
Atypical chronic myeloid leukemia, Ph-/BCR- (CML, NOS)

- Peripheral blood leukocytosis, ≥ 13 × 10^9/L
- Blasts < 20% in peripheral blood and bone marrow
- Dysgranulopoiesis is present in the bone marrow
- Myelodysplastic and myeloproliferative features
- No abnormalities of PDGFRA or PDGFRB.
- No Ph+ or BCR-ABL fusion

Atypical chronic myeloid leukemia, Ph-/BCR unknown (CML, NOS)

- Peripheral blood leukocytosis, ≥ 13 × 10^9/L
- Blasts < 20% in peripheral blood and bone marrow
- Dysgranulopoiesis is present in the bone marrow
- Myelodysplastic and myeloproliferative features
- No abnormalities of PDGFRA or PDGFRB.
- No Ph+ and BCR-ABL fusion unknown

Atypical chronic myeloid leukemia, Ph unknown/BCR- (CML, NOS)

- Peripheral blood leukocytosis, ≥ 13 × 10^9/L
- Blasts < 20% in peripheral blood and bone marrow
- Dysgranulopoiesis is present in the bone marrow
- Myelodysplastic and myeloproliferative features
- No abnormalities of PDGFRA or PDGFRB.
- Ph chromosome unknown and no BCR-ABL fusion

Atypical chronic myeloid leukemia, Ph unknown/BCR unknown (CML, NOS)

- Peripheral blood leukocytosis, ≥ 13 × 10^9/L
- Blasts < 20% in peripheral blood and bone marrow
- Dysgranulopoiesis is present in the bone marrow
- Myelodysplastic and myeloproliferative features
- No abnormalities of PDGFRA or PDGFRB.
- Ph chromosome and BCR-ABL fusion unknown

Aplastic anemia

- Markedly hypocellular marrow with pancytopenia
- Peripheral blood cytopenia(s)
- Diagnosis of exclusion
Other hematologic disorder

If the recipient had an antecedent hematologic disorder not specified in the above options, specify in question text field.


2 There is a typo on the form; the form should read “agnogenic” rather than angiogenic.

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for any of the appendices, please reference the retired appendix on the [Retired Forms Manuals](https://www.cibmtr.org/forms-instruction-manual) webpage.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/Remove/Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/30/17</td>
<td>Appendix H: MDS/MPN Subtypes</td>
<td>Modify</td>
<td>Appendix X: MDS/MPN Subtypes has been renamed as Appendix H: MDS/MPN Subtypes.</td>
</tr>
</tbody>
</table>
Appendix I: Ethnicity and Race

Ethnicity

Ethnicity is the heritage or nationality of a group, but it is not connected to a specific race. For the purposes of the NMDP Consent for Participation Form and general NMDP work, ethnicity is viewed as an environmental influence on a person, versus a genetic trait. People who identify themselves as Spanish, Hispanic or Latino may be of any race.

Hispanic or Latino
Hispanic or Latino refers to people whose ancestors or descendants originated in Central and South America and in the Caribbean, who follow the customs and cultures of these areas and who may speak Spanish.

The phrase Hispanic or Latino excludes people born in Europe whose language is Spanish or Portuguese, and non-Spanish speaking people born in Brazil, Belize, French Guyana, Guyana, Surinam and other non-Spanish speaking territories.

- Chicano – Includes people born in the United States with Mexican ancestry.
- Latino – This term can be used by individuals who live throughout the United States. Many Latinos have come from Puerto Rico, Dominican Republic, Cuba and/or South America.
- Mexican – Includes all citizens of Mexico regardless of race.
- Puerto Rican – Includes all persons of Puerto Rican descent.

Not Hispanic or Latino
A member of any ethnicity, other than Hispanic.

Race

Race is the descendants of a common ancestor, or a group of people with distinct physical and genetic traits or characteristics that are passed on through birth.

American Indian or Alaska Native
Includes persons having origins in any of the original peoples of North, South or Central America.

- Alaska Native – Includes persons who originated from Alaska.
- Aleut – Includes persons who ancestors were Aleut, Alutiiq, Egegik or Pribilovan.
• North American Indian – Includes persons who indicate their race as American Indian, Canadian Indian, French-American Indian or Spanish-American Indian.
• Eskimo – Includes persons who indicate their origin as Eskimo, Arctic Slope, Inupiat and Yupik.
• South or Central American Indian – Includes persons who have origins from any of the original people of South or Central America such as Mayans or Incas.

Asian
Includes persons with ancestors in any of the original peoples of the Far East, the Indian subcontinent including Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, Philippine Islands, Thailand, Vietnam, Hmong, East India, Laos, Bangladesh, Indonesia, Sri Lanka, Nepal, Bhutan, Sikh, Burma and other South and Southeast Asian.

• Chinese – Includes persons who indicated their race as Chinese, or who identified themselves as Cantonese, Tibetan, or Chinese American. In standard census reports, persons who reported as Taiwanese or Formosan are included here with Chinese.
• Filipino – Includes persons who indicated their race as Filipino, Pilipino, or Philippine.
• Japanese – Includes persons who indicated their race as Japanese, Nipponese or Japanese American.
• Korean – Includes persons who indicated their race as Korean or Korean American.
• Vietnamese – Includes persons who indicated their race as Vietnamese or Vietnamese American.
• Other Southeast Asian – Includes persons from one of the Southeast Asian countries or groups including Laos, Hmong, Laohmong, Mong, Cambodia, Thailand, Siamese, Malaysia.
• South Asian – Includes persons from one of the South Asian countries including Afghanistan, India, Pakistan, Bangladesh, Nepal and Sri Lanka.
• Other Asian – Includes persons from or considering themselves to be Burmese, Indonesian, Bengali, Bharat, Dravidian, East India, Goanese or Asian Indian.

Black or African American
Includes persons having origins in any of the Black racial groups of Africa, including Black Americans, Africans, Haitians, and residents of Caribbean Islands of African descent.

• African – Includes people from countries such as Ghana, Nigeria, Niger, Liberia, etc.
• African American – All persons having origins in any of the Black racial groups of Africa and born or living in the United States.
• Caribbean – Includes persons who indicated their race from the area of the Caribbean.
• Black South or Central American – Includes people indicating Black with their origins from South or Central America. Includes countries such as Honduras, Cuba, Guatemala, Nicaragua, Panama, Costa Rica, Chile, Peru, Brazil, Colombia, Venezuela, and Bolivia.
Native Hawaiian and Other Pacific Islander

Native Hawaiian refers to persons having origins in any of the original peoples of the Hawaiian Islands, Guam or Samoa. Pacific Islander refers to persons having origins in any of the peoples of the Pacific Islands.

This category also includes the following groups: Carolinian, Fijian, Guamanian, Kosraean, Marshallese, Melanesian, Micronesian, New Guinean, Northern Mariana Islander, Palauan, Papua, Polynesian, Ponapean (Pohnpelan), Samoan, Solomon Islander, Tahitian, Tarawa Islander, Tokelauan, Tongan, Trukese (Chuukese) and Other Pacific Islanders.

This category does not include individuals who consider themselves “native” to the state of Hawaii simply by virtue of being born there.

- Hawaiian – Includes persons who identify their origins from the Hawaiian Islands chain in the Pacific Ocean.
- Guamanian – Includes persons who identify their origins as being from Guam.
- Samoan – Includes persons who identify their origins as being from Samoa.
- Other Pacific Islander – Includes persons who identify their origins as being from any other island in the Pacific Ocean.

White

Includes persons who indicate their race as White such as Canadian, German, Italian, Lebanese, Near Easterner, Arabian, Eastern European, etc.

- North American – Includes persons whose ancestors came from the continent of Europe, the Middle East or North Africa.
- White South or Central American – Includes persons who ancestors came from Europe to South Central American countries such as Argentina, Brazil and Mexico.
- White Caribbean – Includes persons who ancestors came from Europe to Puerto Rico, Cuba or consider themselves Chicano.
- Mediterranean – Includes persons who identify their origins from countries such as Italy, Greece, Turkey and Bulgaria.
- Northern European – Includes persons who are Belgian, Danish, German Austrian, Swiss, Scandinavian or British.
- Eastern European – Includes persons who identify their origins from countries such as the Czech Republic, Slovakia, Poland, Croatia, Hungary, Slovenia, former Soviet Union or Finland. Also includes persons who call themselves Gypsies from this region.
- Western European – Includes persons who identify their origins from countries such as Spain, Portugal and France.
• **Middle East or Near East** – A region of southwest Asia, between the India subcontinent and Europe, includes Kuwait, Turkey, Lebanon, Israel, Iraq, Iran, Jordan, Saudi Arabia, lands west of Pakistan and the other countries of the Arabian Peninsula. Also includes people of Jewish ethnicity including Sephardic and Ashkenazic.

• **North Coast of Africa** – Includes the northern countries of Africa such as Egypt, Sudan, Libya, Algeria, Morocco and Tunisia.
Appendix J: Reporting Comorbidities

CIBMTR collects comorbidities data based on criteria from the Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI), which was developed and validated by investigators at the Fred Hutchinson Cancer Research Center in Seattle, Washington. The HCT-CI was developed to identify comorbidities relevant to transplant and act as a tool for risk assessment before allogeneic hematopoietic stem cell transplantation. While the criteria were originally developed for use in the adult, allogeneic population, there is utility in collecting these data for all transplant populations, and, used in conjunction with other relevant risk factors, these data are useful in determining risk for transplant for the purposes of predicting expected outcomes.

What to Report

Report a comorbidity in all of the following areas if any of the specified criteria are met.

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Definition and/or criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmia</td>
<td>Any history of:</td>
</tr>
<tr>
<td></td>
<td>• Atrial fibrillation</td>
</tr>
<tr>
<td></td>
<td>• Atrial flutter</td>
</tr>
<tr>
<td></td>
<td>• Sick sinus syndrome</td>
</tr>
<tr>
<td></td>
<td>• Ventricular arrhythmias</td>
</tr>
<tr>
<td>Cardiac</td>
<td>The presence of one or more of the following:</td>
</tr>
<tr>
<td></td>
<td>• Any history of coronary artery disease (one or more vessels requiring medical treatment, stent, or bypass),</td>
</tr>
<tr>
<td></td>
<td>• Any history of myocardial infarction, or</td>
</tr>
<tr>
<td></td>
<td>• congestive heart failure, or LVEF ≤ 50% (or a shortening fraction (SF) of &lt; 26% for pediatric cases) on most recent evaluation prior to the start of the preparative regimen</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>Any history of:</td>
</tr>
<tr>
<td></td>
<td>• Transient ischemic attack</td>
</tr>
<tr>
<td></td>
<td>• Cerebrovascular accident/stroke</td>
</tr>
<tr>
<td></td>
<td>• Subarachnoid, subdural, epidural, or intraparenchymal hemorrhage</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Current (within 4 weeks prior to HCT) history of diabetes or steroid-induced hyperglycemia requiring insulin or oral hypoglycemics, not controlled by diet alone.</td>
</tr>
<tr>
<td>Heart valve disease</td>
<td>The presence of one or more of the following:</td>
</tr>
<tr>
<td></td>
<td>• At least a moderate or severe degree of valve stenosis or insufficiency as determined by echo, whether the valve is mitral, aortic, tricuspid or pulmonary;</td>
</tr>
<tr>
<td></td>
<td>• Prosthetic mitral or aortic valve;</td>
</tr>
<tr>
<td></td>
<td>• Symptomatic mitral valve prolapse</td>
</tr>
<tr>
<td>Hepatic, mild</td>
<td>Any of the following:</td>
</tr>
<tr>
<td></td>
<td>• Chronic hepatitis</td>
</tr>
<tr>
<td>Condition</td>
<td>Criteria</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Hepatic, moderate/severe</td>
<td>Any of the following:</td>
</tr>
<tr>
<td></td>
<td>• Liver cirrhosis</td>
</tr>
<tr>
<td></td>
<td>• Bilirubin &gt; 1.5 x ULN*</td>
</tr>
<tr>
<td></td>
<td>• AST or ALT &gt; 2.5 x ULN*</td>
</tr>
<tr>
<td>Infection</td>
<td>The presence of one or more of the following requiring continuation of therapeutic antimicrobial/antifungal treatment after Day 0:</td>
</tr>
<tr>
<td></td>
<td>• Documented infection</td>
</tr>
<tr>
<td></td>
<td>• Fever of unknown origin</td>
</tr>
<tr>
<td></td>
<td>• Pulmonary nodules suspicious for fungal pneumonia</td>
</tr>
<tr>
<td></td>
<td>• A positive PPD test requiring prophylaxis against TB</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Any history of:</td>
</tr>
<tr>
<td></td>
<td>• Crohn’s disease or</td>
</tr>
<tr>
<td></td>
<td>• Ulcerative colitis requiring treatment</td>
</tr>
<tr>
<td>Obesity</td>
<td>Body mass index (BMI) &gt; 35 kg/m2 or BMI-for-age ≥ 95% (pediatric recipients only) during pre-transplant work-up period.</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>Any history of peptic ulcer (gastric or duodenal) confirmed by endoscopy or radiologic diagnosis and the patient has or is receiving treatment.</td>
</tr>
<tr>
<td>Psychiatric disturbance</td>
<td>Any psychiatric illness requiring treatment within four weeks prior to the pre-transplant work-up period. Examples include depression, anxiety, schizophrenia, or bipolar disorder.</td>
</tr>
<tr>
<td>Pulmonary, moderate</td>
<td>Any of the following at the time of pre-transplant evaluation:</td>
</tr>
<tr>
<td></td>
<td>• Adjusted DLCO 66-80%</td>
</tr>
<tr>
<td></td>
<td>• FEV1 66-80%</td>
</tr>
<tr>
<td></td>
<td>• Dyspnea on slight activity attributed to pulmonary disease and not anemia</td>
</tr>
<tr>
<td>Pulmonary, severe</td>
<td>Any of the following at the time of pre-transplant evaluation:</td>
</tr>
<tr>
<td></td>
<td>• Adjusted DLCO ≤ 65%</td>
</tr>
<tr>
<td></td>
<td>• FEV1 ≤ 65%</td>
</tr>
<tr>
<td></td>
<td>• Dyspnea at rest attributed to pulmonary disease and not anemia</td>
</tr>
<tr>
<td></td>
<td>• Requires intermediate or continuous supplemental oxygen</td>
</tr>
<tr>
<td>Renal, moderate/severe</td>
<td>Any of the following:</td>
</tr>
<tr>
<td></td>
<td>• Serum creatinine &gt; 2 mg/dL or 177 µmol/L</td>
</tr>
<tr>
<td></td>
<td>• On dialysis in pre-transplant evaluation period</td>
</tr>
<tr>
<td></td>
<td>• Prior renal transplantation</td>
</tr>
<tr>
<td>Rheumatologic</td>
<td>Any history of rheumatologic disease requiring treatment including:</td>
</tr>
<tr>
<td></td>
<td>• Systemic lupus erythematosus</td>
</tr>
<tr>
<td></td>
<td>• Rheumatoid arthritis</td>
</tr>
<tr>
<td></td>
<td>• Sjogren’</td>
</tr>
<tr>
<td></td>
<td>• Polymyositis</td>
</tr>
<tr>
<td></td>
<td>• Dermatomyositis</td>
</tr>
<tr>
<td></td>
<td>• Mixed connective tissue disease</td>
</tr>
<tr>
<td></td>
<td>• Polymyalgia rheumatic</td>
</tr>
<tr>
<td></td>
<td>• Polychondritis</td>
</tr>
</tbody>
</table>
• Sarcoidosis
• Vasculitis syndromes

<table>
<thead>
<tr>
<th>Solid tumor, prior</th>
<th>Report any history of solid tumor that required receiving a specific treatment (including surgery, radiotherapy and/or drug therapy). Do not include non-melanoma skin cancer, leukemia, lymphoma, or multiple myeloma at this time.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other co-morbid condition</td>
<td>Report any other co-morbid condition with significant potential impact to recipient’s transplant outcome or overall survival; examples would be those co-morbid conditions which do not fit in the above options but require modifications to the recipient’s transplant plan or course.</td>
</tr>
</tbody>
</table>

(*) ULN refers to upper limit of normal for respective laboratory study

---

**Hepatic and Renal Comorbidities**

In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities:

**Hepatic Comorbidity:** The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

**Renal (Moderate/Severe) Comorbidity:** Serum creatinine > 2 mg/dL or > 177 μmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

---


Determine relevant comorbidities through careful review of the recipient medical record. Reviewed documentation should include the recipient’s past medical history and objective data from the pre-transplant work-up, including pulmonary function tests, echocardiogram, body weight, and laboratory results. The recipient medication list should be correlated with the past medical history to verify there are not any medications that do not align with the patient’s medical history; if there were to be medications commonly used for a certain purpose not listed in the medical history, further clarify if a relevant comorbidity is present. However, if the medical record remains ambiguous, after careful review, as to whether a condition meets the criteria for reporting comorbidity, do not report.

Report all comorbidities meeting criteria at time of pre-transplant evaluation. This may include comorbidities secondary to the primary transplant disease or conditions resulting from prior therapy and persisting or meeting criteria for reporting at the time of transplant.
Example 1. A recipient with a past medical history of depression, treated with Celexa, is undergoing their pre-transplant work-up. Review of the medication list shows they also take Novolog and Lantus. Pre-transplant work-up reveals BMI 27.2 kg/m², EF 58%, unremarkable laboratory results, and adjusted DLCO 62%. In this case, the recipient would have psychiatric, diabetes, and severe pulmonary comorbidities, identified in the past medical history, medication list, and pre-transplant work-up data respectively.

For instances in which the pulmonary function testing report does not correct diffusing capacity of carbon monoxide for hemoglobin, use the Dinakara equation to correct.

To correct an uncorrected DLCO:

\[
\text{corrected DLCO} = \frac{\text{uncorrected DLCO}}{(0.06965 \times \text{hemoglobin})}
\]

where hemoglobin is measured in g/dL.

What not to report

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Do not report the following</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmia</td>
<td>Transient arrhythmia never requiring treatment.</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Syncope; tachycardia; bradycardia</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>Prior history of traumatic brain injury; syncope; concussions; seizure disorder</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Resolved gestational diabetes; glucose intolerance</td>
</tr>
<tr>
<td>Heart valve disease</td>
<td>Asymptomatic mitral valve prolapse</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Elevated liver enzymes not meeting criteria for hepatic comorbidity and without diagnosis of cirrhosis or chronic hepatitis.</td>
</tr>
<tr>
<td>Infection</td>
<td>History of significant infection not requiring treatment after day of transplant (Day 0)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>GERD; gastric bypass surgery; irritable bowel syndrome (IBS); neutropenic colitis</td>
</tr>
<tr>
<td>Obesity</td>
<td>Overweight but not meeting BMI criteria for reporting; pediatric patient in upper weight-for-age percentile not meeting criteria for reporting</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>Gastritis; GERD; ulcerative colitis (ulcerative colitis would be reported as an inflammatory bowel disease comorbidity)</td>
</tr>
<tr>
<td>Psychiatric disturbance</td>
<td>Behavioral issues</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Sleep apnea</td>
</tr>
<tr>
<td>Renal, moderate/</td>
<td>Nephritis; nephrolithias</td>
</tr>
</tbody>
</table>
### Severe

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatologic</td>
</tr>
<tr>
<td>Osteoarthritis; osteoporosis; vasculitis</td>
</tr>
<tr>
<td>Solid tumor, prior</td>
</tr>
<tr>
<td>Basal cell carcinoma; squamous cell carcinoma</td>
</tr>
<tr>
<td>Other co-morbid condition</td>
</tr>
<tr>
<td>Any of the above conditions in this table; any of the conditions listed below not fitting well into the above categories</td>
</tr>
</tbody>
</table>

Below are additional examples of conditions seen reported in the ‘other co-morbidity’ section that are not necessary or beneficial to report. This is not a comprehensive list and is intended to serve as a reference for determining whether to report using the ‘Other, comorbidity’ data field.

If the following conditions existed previously in the patient’s history but are now corrected, they do not need to be reported as an ‘other co-morbid condition.

- ASD repair
- Facial weakness
- Head trauma
- HSV+
- Hydronephrosis
- Kidney stones
- Knee surgery
- Seizure (single event)
- TAH
- TB
- Traumatic brain injury
- Truncus arteriosis
- Typhlitis
- Vascular disease

The following conditions are not relevant transplant outcomes or risk, and should not be reported under the comorbidities section.

- Acne
- Benign tumor (removed)
- Bradycardia
- Bulging discs
- Cataracts
- Concussions
- Congenital alopecia
- Deafness or hearing loss
- Fractures
- Gallbladder (stones, sludge)
- Gastric bypass surgery
- Glaucoma
- Glomerulosclerosis (assume Cr okay)
- Glucose-6-phosphate dehydrogen
- Glucose intolerance
- Gout
- Headaches (chronic)
- Hemorrhoidectomy
- Hemorrhoids
- Hernia
- Kidney stones
- Knee arthritis
- Knee surgery
- Lyme disease
- Macular degeneration
- Malabsorption
- Malnutrition
- Meniere’s disease
- Menorrhagia
- Microalbuminuria
- Migraines
- Mitral valve insufficiency (mild)
- Mitral valve prolapsed (asymptomatic)
- Mitral valve regurgitation (mild)
- Non-alcoholic steatohepatitis (NASH)
- Prior h/o necrotizing fasciitis
- Neonatal jaundice
- Nephritis
- Restless leg syndrome
- Rosacea
- Scoliosis
- Shingles
- Sleep apnea
- Solitary kidney
- Spastic colon
- Splenectomy
- Syncope
- Tachycardia
- Thalassemia (minor or trait)
- Thyroidectomy
- Thyroid nodules
- Tonsillectomy
- Tracheoesophageal fistula
- Traumatic brain injury
- Tremors
- Tubal ligation
- Uterine fibroids
• Hypercholesterolemia
• Hyper-eosinophilia (if not disease related)
• Hyperlipidemia
• Hyperparathyroidism
• Hypertension
• Hypertriglyceridemia
• Hysterectomy
• Insomnia
• Iron deficiency anemia
• Iron deposition or overload

<table>
<thead>
<tr>
<th>Date</th>
<th>Manual Section</th>
<th>Add/ Remove/ Modify</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/16/17</td>
<td>Appendix J: Reporting Comorbidities</td>
<td>Modify</td>
<td>Updated the Hepatic and Renal Comorbidities note box to match the note box included in the Form 2400 section of the manual. For review of renal and hepatic comorbidities, criteria are met when the patient has two or more laboratory values meeting the threshold for reporting between days -24 and -10 (or the date of the last test prior to start of the preparative regimen). If the laboratory values are only assessed once in that period, extend review to between days -40 and -10. In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities: <strong>Hepatic Comorbidity:</strong> The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 &amp; -25 as the second value. <strong>Renal (Moderate/Severe) Comorbidity:</strong> Serum creatinine &gt; 2 mg/dL or &gt; 177 μmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 &amp; -25 as the second value.</td>
</tr>
<tr>
<td>6/30/17</td>
<td>Appendix J: Reporting Comorbidities</td>
<td>Modify</td>
<td>Appendix M: Reporting Comorbidities has been renamed as Appendix J: Reporting Comorbidities.</td>
</tr>
<tr>
<td>7/24/17</td>
<td>Appendix M: Reporting</td>
<td>Add</td>
<td>Appendix M has been revised and combined with the former appendix U. Appendix U has been retired.</td>
</tr>
<tr>
<td>15</td>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix K: Key Fields

⚠️ This section is undergoing revision. For an archived copy of this information, please see Retired Form Manuals.
Appendix L: Karnofsky/Lansky Performance Status

Karnofsky/Lansky Performance Status

The CIBMTR uses Karnofsky/Lansky performance status to determine the functional status of a recipient. Recipient performance status is a critical data field that has been determined to be essential for all outcome-based analyses. The Karnofsky Scale is designed for recipients aged 16 years and older, and the Lansky Scale is designed for recipients one year old to less than 16 years old. Use this scale (see table 1) to determine the score (10-100) that best represents the recipient’s activity status at the requested time point.

Table 1. Karnofsky/Lansky Scale

<table>
<thead>
<tr>
<th>Karnofsky Scale (recipient age ≥ 16 years)</th>
<th>Lansky Scale (recipient age ≥ 1 year and &lt;16 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Able to carry on normal activity; no special care is needed</td>
<td>Able to carry on normal activity; no special care is needed</td>
</tr>
<tr>
<td>100 Normal, no complaints, no evidence of disease</td>
<td>100 Fully active</td>
</tr>
<tr>
<td>90 Able to carry on normal activity</td>
<td>90 Minor restriction in physically strenuous play</td>
</tr>
<tr>
<td>80 Normal activity with effort</td>
<td>80 Restricted in strenuous play, tires more easily, otherwise active</td>
</tr>
<tr>
<td>Unable to work, able to live at home, cares for most personal needs, a varying amount of assistance is needed</td>
<td>Mild to moderate restriction</td>
</tr>
<tr>
<td>70 Cares for self, unable to carry on normal activity or to do active work</td>
<td>70 Both greater restrictions of, and less time spent in active play</td>
</tr>
<tr>
<td>60 Requires occasional assistance but is able to care for most needs</td>
<td>60 Ambulatory up to 50% of time, limited active play with assistance/supervision</td>
</tr>
<tr>
<td>50 Requires considerable assistance and frequent medical care</td>
<td>50 Considerable assistance required for any active play, fully able to engage in quiet play</td>
</tr>
<tr>
<td>Unable to care for self, requires equivalent of institutional or hospital care, disease may be progressing rapidly</td>
<td>Moderate to severe restriction</td>
</tr>
<tr>
<td>40 Disabled, requires special care and assistance</td>
<td>40 Able to initiate quite activities</td>
</tr>
<tr>
<td>30 Severely disabled, hospitalization indicated, although death not imminent</td>
<td>30 Needs considerable assistance for quiet activity</td>
</tr>
<tr>
<td>20 Very sick, hospitalization necessary</td>
<td>20 Limited to very passive activity initiated by</td>
</tr>
<tr>
<td>Date</td>
<td>Manual Section</td>
</tr>
<tr>
<td>------</td>
<td>----------------</td>
</tr>
<tr>
<td>4/4/17</td>
<td>Appendix L</td>
</tr>
</tbody>
</table>

**Karnofsky/Lansky Performance Score vs. ECOG performance score:**

Some transplant centers may prefer to collect and use the ECOG performance score as opposed to the Karnofsky/Lansky score. Although the ECOG and Karnofsky/Lansky performance score systems are based on similar principles, the scales are not the same. For centers that collect only the ECOG performance score, see the memorandum and worksheet example here.

**Manual Updates:**
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.
Appendix M: Critical Data Fields

The following list of data fields have been identified as being critical to accurate outcome analyses. These fields are audited for each recipient selected for audit. The table below is a summary of many of the critical data points grouped by data field type. Critical fields are regularly reviewed and updated; therefore, the list below includes the critical fields for the most current revisions of the forms. Since the audit process reviews data reported over four years (including older form revisions), critical fields reviewed as part of the audit may differ from the summary below. For a complete list of current data collection forms (including form numbers and names) visit the CIBMTR website.

<table>
<thead>
<tr>
<th>Field</th>
<th>Form(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics Data</strong></td>
<td></td>
</tr>
<tr>
<td>Recipient Date of Birth</td>
<td>2400</td>
</tr>
<tr>
<td>Recipient Race and Ethnicity</td>
<td>2400</td>
</tr>
<tr>
<td><strong>Product and Infusion Data</strong></td>
<td></td>
</tr>
<tr>
<td>Infusion date</td>
<td>Appears on multiple CIBMTR forms</td>
</tr>
<tr>
<td>Previous transplants</td>
<td>2010 – 2045 (comprehensive disease specific pre-transplant forms), 2055, 2400</td>
</tr>
<tr>
<td>Infusion times</td>
<td>2006</td>
</tr>
<tr>
<td>Total volume infused</td>
<td>2006</td>
</tr>
<tr>
<td>Entire volume of product infused (what happened to the reserved)</td>
<td>2006</td>
</tr>
<tr>
<td>Adverse events associated with infusion</td>
<td>2006</td>
</tr>
<tr>
<td>HCT product type</td>
<td>Appears on multiple CIBMTR forms</td>
</tr>
<tr>
<td>Donor identification</td>
<td>2006</td>
</tr>
<tr>
<td>Pre-collection therapy</td>
<td>2006</td>
</tr>
<tr>
<td><strong>Consent</strong></td>
<td></td>
</tr>
<tr>
<td>IRB-approved consent for submitting research</td>
<td>2400</td>
</tr>
<tr>
<td>IRB-approved consent to donate research blood samples</td>
<td>2400</td>
</tr>
<tr>
<td><strong>Product Manipulation and Analysis</strong></td>
<td></td>
</tr>
<tr>
<td>Product manipulation and thaw</td>
<td>2006, 2400</td>
</tr>
<tr>
<td><strong>Methods of manipulation</strong></td>
<td>2006</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------</td>
</tr>
<tr>
<td><strong>Product thaw information</strong></td>
<td>2006</td>
</tr>
<tr>
<td><strong>Tumor cells detected in recipient or product prior to HCT (autologous HCT)</strong></td>
<td>2006</td>
</tr>
<tr>
<td><strong>Selected product analysis data including timepoint, volume, and certain cell counts</strong></td>
<td>2006</td>
</tr>
</tbody>
</table>

**Clinical Status of Recipient**

| **Karnofsky / Lansky score** | 2100, 2400 |
| **Recipient blood type** | 2000 |
| **Hematologic findings prior to preparative regimen** | 2000 |
| **CMV** | 2000 |
| **Disease specific staging** | 2013, 2016 |

**Pre-HCT Preparative Regimen and Lines of Therapy**

| **Preparative regimen prescribed** | 2000, 2400 |
| **Classify recipient's prescribed preparative regimen** | 2000, 2400 |
| **Date preparative regimen began** | 2000, 2400 |
| **Preparative regimen drugs** | 2000, 2400 |
| **Irradiation performed** | 2000 |
| **Pharmacokinetics performed to determine dosing** | 2000 |
| **Pre-HCT or pre-infusion therapy** | Appears on multiple pre-HCT CIBMTR forms |

**GVHD**

| **Select GVHD prophylaxis drugs** | 2400 |
| **Acute and chronic GVHD develop / persist** | 2100, 2450 |
| **Grading, staging, onset, and extent of GVHD, including dates** | 2100, 2450 |
| **Preventative therapy used after preparative regimen** | 2100 |
| **Recipient still receiving therapy at date of contact** | 2100, 2450 |
### Post-HCT Disease Therapy

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional post-HCT therapy planned</td>
<td>2400</td>
</tr>
<tr>
<td>Subsequent transplant / cellular therapy</td>
<td>2100, 2400, 2450</td>
</tr>
<tr>
<td>Therapy / intervention given in reporting period</td>
<td>2110-2145 (comprehensive disease specific post-transplant forms), 2450</td>
</tr>
</tbody>
</table>

### Primary Disease for HCT

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of diagnosis</td>
<td>2010-2045, 2055, 2402</td>
</tr>
<tr>
<td>Primary disease for which the HCT was performed, including classification / subtype</td>
<td>2010-2045, 2110-2145, 2402</td>
</tr>
<tr>
<td>Predisposing condition / therapy related</td>
<td>2010-2045, 2402</td>
</tr>
<tr>
<td>Laboratory studies, cytogenetic abnormalities, molecular markers, immunohistochemical stains, and flow cytometry assessed prior to HCT</td>
<td>2010-2045, 2402</td>
</tr>
<tr>
<td>Histologic transformation (date of transformation and disease classification)</td>
<td>2010-2045</td>
</tr>
</tbody>
</table>

### Disease Status

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease status at diagnosis and prior to preparative regimen including remission status</td>
<td>2010-2045, 2402</td>
</tr>
<tr>
<td>Laboratory studies prior to preparative regimen (monocyte, blasts, etc.)</td>
<td>2010-2045</td>
</tr>
<tr>
<td>Disease status at day 30</td>
<td>2127</td>
</tr>
<tr>
<td>Clinical / hematologic, molecular, flow, and cytogenetic relapse or progression including pertinent dates</td>
<td>2010-2045, 2110-2145, 2402, 2450</td>
</tr>
<tr>
<td>Best response to HCT and date best response first began</td>
<td>2110-2145, 2450</td>
</tr>
<tr>
<td>Best response: Clinical / hematologic assessment</td>
<td>2110-2145, 2450</td>
</tr>
<tr>
<td>Best response and disease assessment at the time of evaluation: Molecular, flow, cytogenetic, FISH, and cytogenetics</td>
<td>2110-2145</td>
</tr>
<tr>
<td>Current disease status and date assessed</td>
<td>2110-2145, 2155, 2450</td>
</tr>
<tr>
<td>Survival</td>
<td>Date of actual contact and survival status</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>Date of death and cause of death</td>
</tr>
<tr>
<td>ANC Recovery</td>
<td>Evidence of initial hematopoietic recovery and date</td>
</tr>
<tr>
<td></td>
<td>ANC subsequent decline after recovery</td>
</tr>
<tr>
<td>Other</td>
<td>Diagnosis of new malignancy, lymphoproliferative or myeloproliferative disease / disorder, development of VOD / SOS</td>
</tr>
<tr>
<td></td>
<td>Solid organ transplant in reporting period</td>
</tr>
<tr>
<td></td>
<td>Who is being tested for IDM/HLA</td>
</tr>
<tr>
<td></td>
<td>History of infection at any time prior to start of preparative regimen</td>
</tr>
</tbody>
</table>

Appendix M – Critical Data Fields