Instructions for Post-Transplant Essential Data (Post-TED) Form (Revision 4)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Post-Transplant Essential Data (Post-TED) Form (Revision 4).

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: CIBMTRFormsManualComments@nmdp.org. Comments will be considered for future manual updates and revisions. For questions that require an immediate response, contact your transplant center's CIBMTR CRC.

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Post-Transplant Essential Data (Post-TED)

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 General Instructions, Center Type and Data Collection Forms.

The Post-TED must be completed at the following time points: 100 days, 6 months, annually for 6 years post-HCT, and biennially thereafter. 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.

NOTE:
If the Post-TED form is being completed for a 6-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, 6 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, and is, therefore, not considered a subsequent HCT.

Contact your center's CIBMTR CRC if the subsequent Pre-TED does not come due automatically.

NOTE:
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 FormsNet 3 for each reporting period in which no contact exists.

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; and
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other agencies.

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) and Indication for CRID Assignment (Form 2814). If errors are noted in the key fields, correct the Form 2804 and/or Form 2814 and then review it for accuracy. After the Form 2804 and/or Form 2814 has been corrected, verify the 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.

NOTE: HCT Date
The HCT date must be the same date as was reported on the Pre-TED. If the transplant date changed after the Pre-TED was submitted, use the error correction process to change the HCT date on the Pre-TED. The correct date should then be used on the Post-TED.

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.

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 this Post-TED is being completed for the Day+100 time point, the answers to all questions should reflect the clinical status of the recipient between the HCT infusion date and latest follow-up date. If this Post-TED is being completed for the 6-month or

annual time period, the answers to all questions should reflect the clinical status of the recipient between follow-up dates of the most recent Post-TED completed and the current Post-TED. If the recipient has not been seen by a clinician within the reporting period, but the survival status is known, submit the Post-TED reporting only the survival status and date of contact.

If the Post-TED 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.

NOTE: 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.

It is important to note that the date latest follow-up for the Form 2450 being completed should be *the date prior to the start of the preparative regimen* or *before the date of a subsequent HCT* if no preparative regimen is given. Also, even if the subsequent transplant date *falls outside of the reporting period for this form,* the answer to "did the recipient receive a subsequent HCT" must be "yes" (question 949 in the key fields).

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 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:

Form	Time Point	Approximate Range
Post-TED (Form 2450)	100 days	+/- 15 days (Day 85-115)
	6 months	+/- 30 days (Day 150-210)
	1 year, 2 year, 3 year, etc.	+/- 30 days (Months 11-13, 23-25, 35-37, etc)

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: A Loss to Follow-up Form Declaration (Form 2802) should be completed
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 and a Loss to Follow-Up Declaration (Form 2802) may need to be completed.

- 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 contact is also carefully chosen. If the recipient dies, 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 6 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 6 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 primary 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. 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.

NOTE: Aplastic Anemia
If the recipient received an HCT for aplastic anemia, and the primary cause of death is attributed to relapse/recurrence of disease, report "HCT related causes" and select "Rejection/Poor graft function" as the cause of death.

If the primary cause of death is unclear, consult with a physician for their best medical opinion.

Question 4: Specify
Specify 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.

If there were multiple contributing causes of death, enable an additional instance to report additional causes.

Question 6: Specify
Specify 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").

Questions 3-6: 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 GVHD. If reported as a primary or contributing cause of death, acute GVHD should also be reported in related data fields on the Post-TED.

Chronic GVHD. If reported as a primary or contributing cause of death, chronic GVHD should also be reported in related data fields on the Post-TED.

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. Also known as "cytokine storm" in severe cases, results in a systemic inflammatory response. This response can be a result of infusions of specific drugs or graft-versus-host disease; if related to graft-versus-host disease, GVHD should also be reported as a contributing cause of death.

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."

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).

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 viruses 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 4 or 6.

Diffuse alveolar damage (without hemorrhage) describes histological changes found in lung disease. It is 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.

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 4 or 6.

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).

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. Also report VOD/SOS in questions 46-48 on the Post-TED.

Cardiac: If a cause of death was cardiac failure.

Pulmonary: If a cause of death was pulmonary failure from non-infectious causes such as bronchiolitis obliterans (BO) or cryptogenic organizing pneumonia (COP).

Do not report pulmonary hemorrhage using this cause of death (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.

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, provide additional detail. Each organ system failure should be reported in the "specify" field (question 4 or 6).

If multiple organ failure was due to sepsis, report the infection as a cause of death.

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 in question 4 or 6.

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 questions 49-56 on the Post-TED.

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.

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 in question 4 or 6.

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 (primary cause of death) 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, provide detailed information on the cause of death.

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.) stem cell infusion. Stem cells are defined as mobilized peripheral blood stem cells, bone marrow, or cord blood. The source of the 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 O.

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)
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 DCI. For more information on how to distinguish infusion types (example: HCT versus DCI), see Appendix O.

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.

Initial ANC Recovery

NOTE: Initial ANC Recovery
Recovery, as reported in this section, does not distinguish between allogeneic engraftment (blood and stem cells of donor origin) and autologous engraftment (blood and stem cells of host origin). To demonstrate ***engraftment*** for allogeneic recipients, particularly non-myeloablative or reduced intensity approaches, chimerism tests must be done. These measure the quantity of donor cells relative to the quantity of host (recipient) cells. While ANC usually represents donor cells in allogeneic HCT, it cannot be proven without chimerism studies.

ANC recovery is defined as an absolute neutrophil count (ANC) of ≥ 0.5 x 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 ≥ 0.5 x 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:

Example 1: Calculating Absolute Neutrophil Count (ANC)

% segmented neutrophils
\+ % band neutrophils
= % neutrophils
x white blood cell count/mm^3
= absolute neutrophil count/mm^3

Example:
(Divide percentage by 100 to convert to decimal)

0.45 segmented neutrophils
\+ 0.05 band neutrophils
= 0.50 neutrophils
x $1000/mm^3$ white blood cell count
= $500/mm^{3*}$ absolute neutrophil count

ANC $500/mm^3$ = $0.5 \times 10^9/L$ = $0.5 \times 10^6/mL$ = $0.5 \times 10^3/mm^3$

*Traditionally, the definition of ANC recovery required selecting the first date of three consecutive days in which the recipient's ANC was ≥ $0.5x10^9/L$ ($500/mm^3$). 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 ≥ $0.5x10^9/L$ ($500/mm^3$).

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 $0.5 x10^9/L$. Do not begin counting ANC values of ≥ $0.5 \times 10^9/L$ 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 $0.5x10^9/L$ 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.

Example 2: Tracking ANC Recovery

Transplant Date = May 6				
Date	**WBC**	**% Neutrophils**	**ANC**	
May 7	900	0.6	540	
May 8	850	0.59	502	
May 9	720	0.7	504	
May 10	300	0.45	135	
May 11	15	No differential	--	
May 12	30	No differential	--	
May 13	50	No differential	--	
May 14	250	0.4	100	
May 15	800	0.7	560	Date of first recovery: ANC ≥ $0.5x10^9$/L
May 16	1050	0.8	840	
May 17	1000	0.7	700	
May 18	1800	0.6	1080	
May 19	2000	0.55	1100	
May 20	2500	0.53	1325	
May 21	2250	0.43	968	
May 22	1500	0.45	675	

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," continue with question 15.
- If "no," continue with question 16.
- Check "never below," if the recipient's ANC never dropped below 0.5 x 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 lab values):
Enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 0.5 x 10^9/L. For an example of tracking ANC recovery, see 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. The definition for late graft failure is taken from Appelbaum, F. R., & Thomas, E. D. (2009). Thomas' hematopoietic cell transplantation: Stem cell transplantation (4th ed.). Chichester, UK: Wiley-Blackwell.

If the recipient meets the criteria of late graft failure, indicate “yes” and continue.

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 x 10^9 L obtained on different days, as shown in example 3 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 3: Reporting Platelet Recovery

	Transfusion ↓										
Day	0	1	2	3	4	5	6	7	8	9	10
Platelet Count	10,000	35,000	30,000	25,000	10,000	15,000	19,000	23,000	25,000	40,000	50,000
Date	1/1/2008	1/2/2008	1/3/2008	1/4/2008	1/5/2008	1/6/2008	1/7/2008	1/8/2008	1/9/2008	1/10/2008	1/11/2008
								↑ 1st of 3			

Report 1/8/08 as date platelet count ≥ 20 x 10^9/L

Question 17: Was an initial platelet count ≥ 20 x 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 "never below," if the recipient's platelets never dropped below 20 x 10^9/L at any time post-HCT and a platelet transfusion was never required. If the recipient's platelet count drops below 20 x 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 6 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 ≥ 20 x 10^9/L

Enter the **first** date of three consecutive laboratory values obtained on different days where the platelet count was ≥ 20 x 10^9/L. Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in Example 3 above, when determining the recovery date.

If three laboratory values were not obtained on consecutive days, but a sequential rise of ≥ 20 x 10^9/L is demonstrated, follow the examples below when determining an estimated date.

Examples:

A. The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is 22 x 10^9/L on January 2, 24 x 10^9/L on January 3, and 28 x 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 x 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 ≥ 20 x 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 the day of the month as the *15th*. If the *15th* does not make logical sense in relation to the dates of the platelet counts obtained, use either the *1st* or *30th*. Report month and year as documented.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Graft versus Host Disease

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. Due to the rarity of this occurrence, the GVHD section should only be completed for allogeneic transplants. **For autologous or syngenetic HCT, leave questions 19-38 blank.**

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. Treatment-related factors include a myeloablative preparative regimen and inadequate post-HCT immune suppression (GVHD prophylaxis).

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.

This section is for allogeneic HCTs only. If this was an autologous or syngeneic HCT, continue to Liver Toxicity Prophylaxis.

Question 19: Did acute GVHD develop since the date of last report?
Indicate whether acute GVHD was clinically diagnosed during the reporting period in response to transplant or donor cellular infusion. If "yes," continue with question 20; indicate "yes" if there was a clinical diagnosis and approximate date is known, even if reported date must be estimated. Refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

If the recipient had a flare of acute GVHD occurring after period of symptom quiescence or immunosuppressive taper or discontinuation, report "yes" and continue with question 20.

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. 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 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 date is not documented, then report the date of histological confirmation.

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.

Question 21: Did acute GVHD persist since the date of last report?
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. If "yes," continue with question 29; indicate "yes" if there was a clinical diagnosis and approximate date is known, even if reported date must be estimated. Refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

Indicate "no" if the recipient has no history of acute GVHD or if all prior acute GVHD is inactive in the reporting period; continue with question 31. If the recipient previously had acute GVHD, which was resolved prior to the start of the current reporting period and flared in this reporting period, indicate "yes" in question 19 and "no" in question 21.

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

The acute GVHD grading scale is based on **clinical evidence** (physician observation), not histology. If there is a difference in the clinical grade recorded by the physician and a histological report, use the data from the clinical documentation. 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 table 1 below.

Table 1. GVHD Grading and Staging

Extent of Organ Involvement			
Stage	**Skin**	**Liver**	**Gut**
1	Rash on <25% of skin[1]	Bilirubin 2-3 mg/dl[2]	Diarrhea > 500 ml/day[3] or persistent nausea[4] *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

Grade[5]			
I	Stage 1-2	None	None
II	Stage 3 or	Stage 1 or	Stage 1
III	—	Stage 2-3 or	Stage 2-4
IV[6]	Stage 4	Stage 4	—

1. Use "Rule of Nines" (Table 2) 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 histological evidence of GVHD in the stomach or duodenum.
5. Criteria for grading given as minimum degree of organ involvement required to confer that grade.
6. Grade IV may also include lesser organ involvement with an extreme decrease in performance status.

Report the grade of the recipient's acute GVHD at the time of diagnosis; please note that this may not be the maximal grade for the reporting period. If acute GVHD was

present, but the maximum grade at diagnosis was not documented and it cannot be determined from the grading and staging table, report “not applicable.”

Questions 23-28: 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 Table 2 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.

Table 2. Percent Body Surfaces

Body Area	Percent	Total Percentage
Each Arm	9%	18%
Each Leg	18%	36%
Chest & Abdomen	18%	18%
Back	18%	18%
Head	9%	9%
Pubis	1%	1%

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/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.

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 another 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 reporting 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.

Question 29: Maximum overall grade of acute GVHD

The acute GVHD grading scale is based on **clinical evidence** (physician observation), not histology. If there is a difference in the clinical grade recorded by the physician and a histological report, use the data from the clinical documentation. 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 table 1 below.

Table 1 - Repeated. GVHD Grading and Staging

Extent of Organ Involvement			
Stage	**Skin**	**Liver**	**Gut**
1	Rash on <25% of skin[1]	Bilirubin 2-3 mg/dl[2]	Diarrhea > 500 ml/day[3] or persistent nausea[4]
2	Rash on 25-50% of skin	Bilirubin 3-6 mg/dl	Diarrhea >1000 ml/day
3	Rash on >50% of skin	Bilirubin 6-15 mg/dl	Diarrhea >1500 ml/day
4	Generalized erythroderma with bullous formation	Bilirubin >15 mg/dl	Severe abdominal pain with or without ileus

Grade[5]			
I	Stage 1-2	None	None
II	Stage 3 or	Stage 1 or	Stage 1
III	—	Stage 2-3 or	Stage 2-4
IV[6]	Stage 4	Stage 4	—

1. Use "Rule of Nines" (Table 2) 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 histological evidence of GVHD in the stomach or duodenum.
5. Criteria for grading given as minimum degree of organ involvement required to confer that grade.
6. Grade IV may also include lesser organ involvement with an extreme decrease in performance status.

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:

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 Table 1.
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 Table 1; "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).

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.

Question 31: Did chronic GVHD develop since the date of last report?
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 and as late as day 400 post-HCT. In chronic GVHD, the mechanism of tissue damage differs from acute GVHD and a greater variety of organs may be affected.

Indicate whether chronic GVHD was clinically diagnosed during the reporting period in response to transplant or donor cellular infusion. If "yes," continue with question 34; indicate "yes" if there was a clinical diagnosis and approximate date is known, even if reported date must be estimated. Refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

If the recipient had a flare of chronic GVHD occurring after period of symptom quiescence or immunosuppressive taper or discontinuation, report "yes" and continue with question 34.

Indicate "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 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 date is not documented, then report the date of histological confirmation.

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.

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 acute GVHD. If "yes," continue with question 34; indicate "yes" if there was a clinical diagnosis and approximate date is known, even if reported date must be estimated. Refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

Indicate "no" if the recipient has no history of chronic GVHD or if all prior chronic GVHD is inactive in the reporting period; continue with question 37. If the recipient previously had chronic GVHD, which was resolved prior to the start of the current reporting period and flared in the period, indicate "yes" in question 31 and "no" in question 33.

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. Clinical grade is based on the severity of signs and symptoms in organ systems involved by chronic GVHD, as well as the total number of organs or organ systems involved by chronic GVHD.

Mild: 1 or 2 organs involved with each organ involved having a score of 1; no lung involvement.
Moderate: 3 or more organs involved with each organ involved having a score of 1 **or** at least one organ, other than lung, involved with a score of 2 **or** lung involvement with a score of 1.
Severe: At least 1 organ involved with a score of 3 **or** lung involvement with a score of 2 or 3.

Table 3. Organ Scoring of Chronic GVHD

Organ	Score 0	Score 1	Score 2	Score 3
Skin - %BSA *Features to be scored by BSA:* Maculopapular rash, lichen planus-like features, sclerotic features, papulosquamous lesions or ichthyosis, keratosis pilaris-like GVHD	No BSA involved	1-18% BSA	19-50% BSA	>50% BSA
	No sclerotic features	N/A	Superficial sclerotic features, but not "hidebound"	Deep sclerotic features; "hidebound;" impaired mobility; ulceration
Mouth	No symptoms	Mild symptoms with disease signs but not limiting oral intake significantly	Moderate symptoms with disease signs with partial limitation of oral intake	Severe symptoms with disease signs with major limitation of oral intake
Eyes	No symptoms	Mild dry eye symptoms not affecting ADL (requirement of lubricant drops ≤ 3x/day)	Moderate dry eye symptoms partially affecting ADL (requiring lubricant drops > 3x/day or punctal plugs) without new vision impairment due to keratoconjunctivitis sicca (KCS)	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)
GI Tract	No symptoms	Symptoms without significant weight loss (< 5%) within 3 months	Symptoms associated with mild to moderate weight loss (5-15%) within 3 months	Symptoms associated with significant weight loss (> 15%) within 3 months, requires nutritional supplments for most caloric needs or esophageal dilation
Liver	Normal total bilirubin and ALT < 2 x ULN	Normal total bilirubin and ALT ≥ 2 x ULN	Elevated total bilirubin but ≤ 3 x ULN	Elevated total bilirubin > 3 x ULN

Lungs – symptoms	No symptoms	Mild symptoms (SOB after climbing one flight of steps)	Moderate symptoms (SOB after walking on flat ground)	Severe symptoms (SOB at rests; requires O2)
Lungs – FEV1	FEV1 ≥ 80%	FEV1 60-79%	FEV1 40-59%	FEV1 ≤ 39%
Joints and fascia	No symptoms	Mild tightness of arms or legs, normal or mild decreased range of motion and not affecting ADL	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	Contractures with significant decrease of range of motion and significant limitation of ADL (unable to tie shoes, button shirts, dress self, etc.)
Genital Tract	No signs	Mild signs and females with or without discomfort on exam	Moderate signs and may have signs of discomfort on exam	Severe signs with or without symptoms
Other features: 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	No GVHD	Mild	Moderate	Severe

NIH Consensus Criteria, 2005

Question 35: Specify if chronic GVHD was limited or extensive:
Report the date of maximum chronic GVHD involvement, based on chronic GVHD stage. 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; or,
- Liver histology showing chronic aggressive hepatitis, bridging necrosis, or cirrhosis; or
- Involvement of the eye with or without Schirmer's test; or
- Involvement of the salivary glands or oral mucous membranes with or without labial biopsy; or
- Involvement of any other target organ.

Reporting Stage of Chronic GVHD (Sullivan KM, *Blood* 1981; 57:267.)

Limited: Localized skin involvement resembling localized scleroderma with or without liver involvement; no other organ involvement.

Extensive: Generalized skin and/or multiple organ involvement.

Question 36: Date of maximum grade of chronic GVHD
Report the date 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.

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)
Indicate whether the recipient continues on systemic steroids for GVHD treatment or prophylaxis as of the end of the reporting period. If the recipient continues on steroids, report "yes." If the recipient received systemic steroids at any time post-transplant and steroids were discontinued in the current or previous reporting periods, indicate "no." If the recipient has never received systemic steroids for GVHD prophylaxis or treatment to date, report "not applicable." Do not report steroids given for adrenal insufficiency or in doses of ≤ 10 mg/day for adults or < 0.1 mg/kg/day for pediatric recipients. Do not report topical or locally acting steroids; topical steroids include creams and ointments, as well as inhaled (e.g., Pulmicort, Budesonide) or certain oral (e.g., Budesonide, Beclomethasone) forms. Indicate "unknown" if there is no information about the recipient's medication list and administration for the reporting period.

Question 38: Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for GVHD?
Indicate whether the recipient continues on immunosuppressive agents other than steroids for GVHD treatment or prophylaxis as of the end of the reporting period. If the recipient continues on non-steroidal immunosuppressive agents as of the end of the reporting period, report "yes." If the recipient received non-steroidal immunosuppressive agents at any time post-transplant and agents were discontinued in the current or previous reporting periods, indicate "no." If the recipient has never received non-steroidal immunosuppressive agents for GVHD prophylaxis or treatment to date, report "not applicable." Do not include steroids – systemic, topical, or local. Immunomodulatory agents or therapies, such as extra-corporeal photopheresis (ECP) and psoralen plus UVA (PUVA) therapy, should be included in this determination. Indicate "unknown" if there is no information about the recipient's medication list and administration for the reporting period.

Liver Toxicity Prophylaxis

Question 39: Was specific therapy used to prevent liver toxicity?
Liver toxicities in transplant patients may be related to drug toxicity, 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. For the 100-day reporting period, include 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 "yes," continue with question 40. If "no," continue with 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. For the 100-day reporting period, include 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 "other" therapy is reported in question 44, specify agent given as liver toxicity prophylaxis in question 45.

Veno-occlusive disease (VOD) / Sinusoidal obstruction syndrome (SOS)

Veno-occlusive disease (VOD) or 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. Ancillary features commonly seen include weight gain (≥ 5%), increased platelet transfusion needs, and coagulopathy. VOD/SOS is most commonly seen in recipients status post hematopoietic stem cell transplantation, and 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 stem cell transplant; ablative conditioning with high doses of radiation therapy or use of busulfan; and sirolimus given to recipients undergoing ablative conditioning. Agents such as low-dose heparin or ursodiol 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. Ultrasound may be used to exclude other disorders; liver biopsy is often a risky procedure, 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 either 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 46: Did veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS) develop since the date of last report?

Indicate whether the recipient had a diagnosis of VOD/SOS during the current reporting period. Indicate “yes” if there was a clinical diagnosis of VOD/SOS within the reporting period; indicate “no” if the recipient did not develop VOD/SOS within the reporting period. If VOD/SOS persists from the prior reporting period, indicate “no.”

Question 47: 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.

Question 48: Did veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS) persist or recur since the date of last report?
Indicate whether VOD/SOS was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report prior history of VOD/SOS without ongoing, active symptoms in the reporting period.

If VOD/SOS resolved during the previous reporting period and recurred during the current reporting period, report "Yes" for question 48. For reporting purposes, recurrence of VOD/SOS is defined as a subsequent clinical diagnosis after achieving and maintaining a complete resolution of all symptoms for at least 30 days.

New Malignancy, Lymphoproliferative or Myeloproliferative Disorder

Question 49: 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; also include the development of clonal cytogenetic abnormalities, uncontrolled proliferation of donor cells without malignant transformation, or post-transplant lymphoproliferative disorder. 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.

A new malignancy, lymphoproliferative disorder, or myeloproliferative disorder include but are not limited to:

- Skin cancers (basal, squamous, melanoma);
- New leukemia;
- New myelodysplasia;
- Solid tumors; and
- 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); and
- Transformation of MDS to AML post-HCT (report as disease progression).

NOTE: Skin Cancers

For most malignancies, one does 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.

However, in the case of a basal cell or squamous cell skin cancer, one needs to report each discreet episode. For example, a recipient had a basal cell skin cancer diagnosed on the neck four months post-HCT and 6 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 discreet lesion.

These discreet episodes should be reported in the "Other skin malignancy" questions on the Post-TED form.

If a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder has occurred following the HCT, check "yes" and continue with question 50. If not, check "no" and continue with question 57.

Questions 50-51: Specify new malignancy

Copy and complete questions 50-56 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 50, indicate "other new malignancy," and specify the type in question 51.

Question 52: 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 50.

Question 53: 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 54: Was documentation submitted to the CIBMTR? (e.g. pathology / autopsy report or other documentation)
Attaching a copy of the diagnostic pathology report for the new malignancy assists in disease confirmation and **reduces the need for later data queries**. Indicate "yes" if an attachment is added in FormsNet 3 to the Form 2450 supporting the diagnosis data reported in questions 49-53.

Question 55: Was the new malignancy donor / cell product derived?
In spite of stringent criteria for stem cell donors, there is some risk of donor derived malignancy. Donor related malignancy may be due to direct transmission of tumor or due to a tumor arising from cells of donor origin. Indicate the cell origin of the new malignancy. Cell origin may be inferred from karyotyping or FISH XX/XY testing the tumor cells following sex-mismatched transplantation, or from molecular methods of testing chimerism of the tumor cells, such as VNTR/STR or RFLP. If testing was performed to determine the origin of the tumor cells, indicate whether donor or product cells were detected by selecting "yes," or not, by selecting "no." If testing was not performed, indicate "not done."

Question 56: Was documentation submitted to the CIBMTR? (e.g. cell origin evaluation (VNTR, cytogenetics, FISH))
Attaching a copy of the evaluation for the cell origin of the new malignancy **reduces the need for later data queries**. Indicate "yes" if an attachment is added in FormsNet 3 to the Form 2450 supporting the diagnosis data reported in question 55.

Chimerism Studies (Cord Blood Units Only)

This section relates to chimerism studies from allogeneic HCTs using cord blood units only. If this was an autologous HCT, or an allogeneic HCT using a bone marrow or PBSC product, continue to disease assessment.

Chimerism studies are performed to determine the percent of blood or marrow cells post-transplant that are produced from donor stem cells and the perfect that are product from host (recipient) 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.

NOTE: 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. See Appendix S for an example.

Question 57: Were chimerism studies performed since the date of last report?
Indicate whether chimerism studies were performed within the reporting period. If "yes," continue with question 58. If "no," continue with question 76. This question will only apply for allogeneic HCTs with a cord blood unit source.

Question 58: Was documentation submitted to the CIBMTR? (e.g. chimerism laboratory reports)
Attaching a copy of chimerism study results **reduces the need for later data queries**. Indicate "yes" if an attachment is added in FormsNet 3 to the Form 2450 supporting the chimerism data reported.

Question 59: 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 though there may only be one donor for the current transplant.

Question 60-75: Provide date(s), method(s) and other information for all chimerism studies performed since the date of last report.
Copy question 60-75 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 reporting at a minimum:

- Studies performed on or at approximately Day+28
- Most recent prior to the date of contact, particularly for Day+100
- Most recent prior to and after an intervention (such as a donor cellular infusion)
- The first result to show complete / 100% donor chimerism

Table 4. Chimerism - Single Donor

Data Field	Description
60. NMDP donor ID	If the donor or one of the donors was an NMDP PBSC or marrow donor, enter the 9 digit NMDP donor ID.
61. 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.
62. 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.
63. 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.
64. 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.
65. Sex	If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry, provide the biological sex.
66. Date sample collected	Enter the date the sample was collected for the chimerism test.
67-68. Method	Report the test method used for the reported chimerism study. Karyotyping and FISH methods are only valid for sex mismatched transplants VNTR/STR is one of the most common molecular methods for assessing chimerism. See Table 6 for additional details on chimerism testing methods.
69. Cell source	Report whether the specimen taken for chimerism testing was from a marrow or peripheral blood source.
70-71. Cell type	Indicate the cell line or type tested. If the specimen was not sorted for a specific cell line, indicate "unsorted / whole." See table below for additional details on cell markers unique to certain cell lines.
72. 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.
73. Number of donor cells	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 and found to be of donor origin. If a non-cytogenetic test was used, leave these boxes blank.
74. 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.
75. Percent donor cells	Molecular testing methods include RFLP and VNTR/STR. Report the percentage of donor cells identified by RFLP or VNTR/STR or other 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 "> x%," report "x + 1" percent donor cells. If the test detected donor cells but indicated donor cells "< x%," report "x - 1" percent donor cells.

Table 5. Chimerism Cell Types

Cell Type	Description
Unsorted / whole	The peripheral blood or bone marrow sample has not been sorted or selected for a certain cell line.
Red blood cells	Also known as RBCs or erythrocytes; carry the CD235a cell marker
Hematopoietic progenitor cells	Includes CD34+ cells
Total mononuclear cells	Total mononuclear cells would be a specimen containing only and both lymphocytes and monocytes
T cells	Includes CD3+, CD4+, and/or CD8+ cells
B cells	Includes CD19+ or CD20+ cells
Granulocytes	Also known as polymorphonuclear leukocytes (PMNs, PMLs) and includes neutrophils, eosinophils, and basophils. Includes CD33+ cells
NK cells	Includes CD56+ cells
Other, specify	Use this option to report cell types that do not fit in a category above.

Table 6. Chimerism Methods

Method	Description
Karyotyping for XX/XY	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.
Fluorescent in situ hybridization (FISH) for XX/XY	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.*
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.*

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.

Note: 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 disease status criteria for the disease on which you are reporting.

Question 76: 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 99.

If the recipient achieved CR post-HCT (excluding unplanned therapy), check "complete remission (CR)" and continue with question 78.

If the recipient has not achieved a post-HCT CR to date, check "not in complete remission" and continue with question 77.

If the recipient's disease status was not evaluated post-HCT, check "not evaluated" and continue with question 99. 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 77: 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% 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 76, and "no disease detected by incomplete evaluation to establish CR" for question 77.
>
> **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 relapse 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 76, and "disease detected" in question 77.
>
> **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 x 10^9/L. In this case, "not in complete remission" should be selected for question 76, and "no disease detected by incomplete evaluation to establish CR" in question 77.

Question 78: Was the date of best response previously reported?
Indicate whether complete remission was reported in a previously reporting period; if "yes," continue with question 99 and if "no," continue with question 79. This question does not apply for "not in complete remission" responses to question 76.

Question 79: 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.

Question 80: 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. RFLP testing (with PCR amplification) is an example of a molecular test method used to detect the molecular marker BCR/ABL.

For recipients with "complete remission" selected for question 76: Select "yes" if a molecular disease assessment was performed at the time complete remission was established; if no molecular disease assessment was performed at the time of complete remission assessment, report the molecular study nearest that time and within the reporting period in which complete remission was established. Do not report a molecular disease assessment performed at the time of relapse or progression, if applicable. Indicate "no" if molecular disease assessments were not performed in the reporting period or were only performed at the time of relapse or progression. Indicate "not applicable" if molecular studies have never previously been performed, or have been performed but never shown molecular abnormalities associated with the recipient's primary transplant disease.

For recipients "not in complete remission" selected for question 76: Select "yes" if a molecular disease assessment was performed within the reporting period. Report the results of the most recent study if multiple assessments were performed during the reporting period. Indicate "no" if there were no molecular disease assessments performed within the reporting period. Indicate "not applicable" if molecular studies have never previously been performed, or have been performed but never shown molecular abnormalities associated with the recipient's primary transplant disease.

Question 81: Date assessed:
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 82: Was disease detected?
Report whether molecular markers for the primary transplant disease were identified. In order to be considered positive for a molecular marker, 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.

Question 83: Was the disease status assessed via 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.

For recipients with "complete remission" selected for question 76: Select "yes" if a flow cytometry disease assessment was performed at the time complete remission was established; if no flow cytometry disease assessment was performed at the time of complete remission assessment, report the flow cytometry study nearest that time and within the reporting period in which complete remission was established. Do not report a flow cytometry disease assessment performed at the time of relapse or progression, if applicable. Indicate "no" if flow cytometry disease assessments were not performed in the reporting period or were only performed at the time of relapse or progression. Indicate "not applicable" if flow cytometry studies have never previously been performed, or have been performed but never previously shown abnormalities associated with the recipient's primary transplant disease, or if < 5% plasma cells are detected by flow cytometry for recipients with multiple myeloma.

For recipients "not in complete remission" selected for question 76: Select "yes" if a flow cytometry disease assessment was performed within the reporting period. Report the results of the most recent study if multiple assessments were performed during the reporting period. Indicate "no" if there were no flow cytometry disease assessments performed within the reporting period. Indicate "not applicable" if flow cytometry studies have never previously been performed, have never previously shown abnormalities associated with the recipient's primary transplant disease, or if < 5% plasma cells are detected by flow cytometry for recipients with multiple myeloma.

Question 84: Date assessed
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 85: Was disease detected?
Report whether an abnormal cellular population associated with the recipient's primary transplant disease was detected. 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.

Question 86: 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 "yes" if FISH or karyotyping was performed within the reporting period and was considered relevant to the recipient's disease assessment. Select "no" if neither FISH nor karyotyping was performed to assess disease status within the reporting period. Report "not applicable" if FISH and karyotyping studies have never previously been performed, or have been performed but never previously shown cytogenetic abnormalities associated with the recipient's primary transplant disease.

Question 87: 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.

For recipients with "complete remission" selected for question 76: Select "yes" if a FISH disease assessment was performed at the time complete remission was established; if no FISH disease assessment was performed at the time of complete remission assessment, report the FISH study nearest that time and within the reporting period in which complete remission was established. Do not report a FISH disease assessment performed at the time of relapse or progression, if applicable. Indicate "no" if FISH disease assessments were not performed in the reporting period or were only performed at the time of relapse or progression. Indicate "not applicable" if FISH studies have never previously been performed, or have been performed but never previously shown FISH abnormalities associated with the recipient's primary transplant disease.

For recipients "not in complete remission" selected for question 76: Select "yes" if a FISH disease assessment was performed within the reporting period. Report the results of the most recent study if multiple assessments were performed during the reporting period. Indicate "no" if there were no FISH assessments performed within the reporting period. Indicate "not applicable" if FISH studies have never previously been performed, or had been performed but never previously shown FISH abnormalities associated with the recipient's primary transplant disease.

Question 88: Date assessed
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 89: Was disease detected?
Report whether FISH abnormalities associated with the primary transplant disease were detected.

Question 90: Was the disease status assessed via karyotyping?
For recipients with "complete remission" selected for question 76: Select "yes" if karyotyping was performed at the time complete remission was established; if no karyotyping was performed at the time of complete remission assessment, report the karyotyping performed nearest that time and within the reporting period in which complete remission was established. Do not report karyotyping performed at the time of

relapse or progression, if applicable. Indicate "no" if karyotyping was not performed in the reporting period or was only performed at the time of relapse or progression. Indicate "not applicable" if karyotyping has never previously been performed, or has been performed but never previously shown abnormalities associated with the recipient's primary transplant disease.

For recipients "not in complete remission" selected for question 76: Select "yes" if a karyotyping was performed within the reporting period. Report the results of the most recent study if multiple assessments were performed during the reporting period. Indicate "no" if karyotyping was not performed within the reporting period. Indicate "not applicable" if karyotyping had never previously been performed, or had been performed but never previously shown abnormalities associated with the recipient's primary transplant disease.

Question 91: Date assessed
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 92: Was disease detected?
Report whether cytogenetic abnormalities associated with the primary transplant disease were detected by karyotyping. 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.

Question 93: 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.

For recipients with "complete remission" selected for question 76: Select "yes" if radiologic assessment was performed at the time complete remission was established; if multiple imaging techniques relevant to determination of recipient's disease status were performed, report the imaging assessment performed nearest that time and within the reporting period in which complete remission was established. Do not report radiologic assessment performed at the time of relapse or progression, if applicable. Indicate "no" if radiologic assessment was not performed in the reporting period or was only performed at the time of relapse or progression. Indicate "not applicable" if radiologic assessment was never previously been performed, or was not pertinent to determination of recipient's disease status, based on primary transplant disease type.

For recipients "not in complete remission" selected for question 76: Select "yes" if a radiologic assessment was performed within the reporting period. Report the results of the most recent study if multiple assessments were performed during the reporting period. Indicate "no" if radiologic assessment was not performed within the reporting period. Indicate "not applicable" if radiologic assessment was never previously been performed, or was not pertinent to determination of recipient's disease status, based on primary transplant disease type.

Question 94: Date assessed
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 95: Was disease detected?
Report whether radiological abnormalities associated with the primary transplant disease were detected.

Question 96: 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 96.

For recipients with "complete remission" selected for question 76: Select "yes" if clinical/hematologic assessment was performed at the time complete remission was established; if clinical/hematologic assessment was performed at the time of complete remission assessment, and clinical/hematologic assessment(s) were relevant to determination of recipient's disease status, report the clinical/hematologic assessment performed nearest that time and within the reporting period in which complete remission was established. Do not report clinical/hematologic assessment performed at the time of relapse or progression, if applicable. Indicate "no" if clinical/hematologic assessment was not performed in the reporting period or was only performed at the time of relapse or progression.

For recipients "not in complete remission" selected for question 76: Select "yes" if a clinical/hematologic assessment was performed within the reporting period. Report the results of the most disease-specific assessment performed within approximately 30 days of the contact date. Indicate "no" if a clinical/hematologic assessment was not performed within the reporting period.

Question 97: Date assessed
Report the date of clinical/hematologic assessment. For recipients with "complete remission" reported in question 76, this will likely match the date CR was achieved reported in question 79, since complete remission criteria generally require clinical or hematologic assessment to confirm. If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

Question 98: Was disease detected?
Report whether clinical/hematologic abnormalities associated with the primary transplant disease were detected. In general, if the clinical/hematologic assessment date is that same as that reported in question 79 for recipients achieving complete remission in the reporting period, the answer to question 98 should be "no."

Post-HCT Therapy

Report therapy given since the date of last report to prevent relapse or progressive disease. This may include maintenance and consolidation therapy. Do not report any therapy given for relapse, persistent, or progressive disease.

Question 99: 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 100: 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 101-156: Specify systemic therapy
Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Treatment may consistent 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 155 and specify in question 156.

Table 7. Drug Classes

Drug Class	Description
Monoclonal antibody (mAb)	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) *Do not report PD1 or tyrosine kinase inhibitors under this class. These drugs are captured separately.*
Tyrosine kinase inhibitors (TKI)	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. *Do not report FLT3 or BTK inhibitors under this class. These drugs are captured separately.*
FLT3 inhibitor	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.
Hypomethylating agent	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.
Proteasome inhibitor	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.
Immune modulating agent	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. *Do not report mAb therapy or PD1 inhibitors under this class. These drugs are captured separately.*
PD1 inhibitor	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.
BTK inhibitor	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 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.*

Question 157: 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 158: Cellular therapy
Cellular therapy refers to the infusion of human or animal derived cells, which may be modified or processed to achieve a specific composition. Examples include T-cell, NK cell, and mesenchymal cell 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 159: 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 160-161: 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 161.

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 162: 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 163.

If clinical/hematologic evidence of relapse/progressive disease was not found at any time post-transplant, check "no" and continue with question 165.

Question 163: 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 165. If this is the report of first instance of clinical/hematologic relapse or progression, indicate "no" and continue with question 164.

Question 164: 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 165: 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 relapsed, persistent, or 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.

Question 166: 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 for both persistent disease *and* decreased / loss of donor chimerism or both relapsed / progressive disease *and* decreased / loss of donor chimerism, and in these cases, the disease status related justification should be selected.

Question 167-172: 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. For each option, select "yes" if last assessment by that method was consistent with the rationale reported in question 166. 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 166; 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 167, 169, and 170 would be answered "yes" on the Post-TED form in the 6-month reporting period.

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 166, 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 173: Date intervention started
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.

Question 174: 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.

Questions 175-230: Specify systemic therapy
Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Treatment may consistent 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 Table 7 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 229 and specify in question 230.

Question 231: 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 232: Cellular therapy
Cellular therapy refers to the infusion of human or animal derived cells, which may be modified or processed to achieve a specific composition. Examples include T-cell, NK cell, and mesenchymal cell infusions. Indicate "yes" if the recipient received any form of cellular therapy for relapsed, 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 233: Blinded randomized trial
A blinded, randomized trial refers to a research 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 234-235: 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 intrathecal therapy or surgery. Specify the other therapy given in question 235.

Current Disease Status

Question 236: 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 99. 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.

Question 237: 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 236, and "no disease detected by incomplete evaluation to establish CR" for question 237.
>
> **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 relapse 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 236, and "disease detected" in question 237.
>
> **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 x 10^9/L. In this case, "not in complete remission" should be selected for question 236, and "no disease detected by incomplete evaluation to establish CR" in question 237.

Question 238-239: 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 disease assessment consistent with disease status reported in questions 236-237. The reported date may reflect a disease assessment by any method – molecular, cytogenetic, FISH, flow cytometry, radiologic, or clinical/hematologic. If there are multiple disease assessments within the 30 days prior to or on the date of contact, report the most recent that is consistent with the disease status reported in questions 236-237. If there are no disease specific assessments

within the 30 days prior to or on the date of contact, report the latest assessment in which the recipient was clinically assessed by a physician or midlevel clinician.

Signature Lines
The FormsNet3^{SM} 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.

Manual Change History

Version Number	Date of Change	Type of Change (Add / Remove / Modify)	Description of Change