2450: 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 an international center, has consented to participate in research, and has been assigned to the TED track by the Form Selection Algorithm.
- 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.

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, six months, and annually post-HCT. These forms should be completed as closely to these time points as possible. The structure of the TED Forms is such that each form should fit on a timeline with distinct start and stop dates that do not overlap any other forms, except in the case of a subsequent HCT. The Post-TED is considered past due 120 days after each of these time points.

* If the Post-TED form is being completed for a six-month or annual evaluation, the answers to all questions should reflect the clinical status of the recipient since the last report.

* 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.

Subsequent HCT:
If a recipient receives a subsequent HCT between Post-TED time points (100 day, six months, annually), the TED form sequence will start over again with another Pre-TED.

However, if the recipient receives an autologous HCT as a result of a poor graft or graft failure, the TED form sequence **will not** start over again. Generally this type of infusion (autologous rescue) is used to treat the recipient's poor graft response, rather than to treat the recipient's disease.

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

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, contacting the hospital billing department, or beginning a search request with the CIBMTR. 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 center should indicate this status in FormsNet for each reporting period in which no contact exists.

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

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

Date	Manual Section	Add/ Remove/ Modify	Description
4/6/16	2450: Post-TED	Modify	Changed the wording in questions 66-73 to reflect the possibility of multiple causes of death (i.e., select all that apply), rather than a single primary cause of death.
2/9/16	2450: Post-TED	Modify	Modified pediatric acute GVHD Gut guidelines to question 15. See table for details.
1/22/16	2450: Post-TED	Modify	Updated footnote 4 below acute GVHD staging and grading table: Persistent nausea with *or without* histologic evidence of GVHD in the stomach or duodenum.

12/3/15	2450: Post-TED	Modify	Updated description of DLI indication reporting in Questions 118-119: From the list provided, indicate the reason the cells were infused. *If there was more than one reason for the DCI, check all applicable indications.* ~~If the recipient received multiple DCIs for more than one indication, report the DCI and the new indication in the second DCI section.~~ ~~If multiple DCIs were given within the 10-week period, check all applicable indications.~~
9/27/15	2450: Pre-TED	Modify	language to question 65: Cause of death is considered the main disease, complication, or injury that leads to death. Do not report the mode of death (e.g., cardiopulmonary arrest). Only one primary cause of death may be specified; however, **under "HSCT-related causes,**" multiple contributing causes may be listed if relevant.
9/27/15	2450: Pre-TED	Remove	Removed the following phrase from "Subsequent Transplant" for clarification purposes. This does not change the intention of the question; if a recipient receives an autologous rescue, new forms should not come due: 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.~~
6/26/15	2450: Pre-TED	Modify	Added warnings to GVHD section that state autologous and sygeneic HCTs should skip the section.
6/12/15	Manual-wide	Modify	Language relating to the Lost-to-Follow-Up (2802) has been removed.
6/12/15	2450: Pre-TED	Add	Added explanatory text to question 106: The date reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). Indicate the date the sample was collected for examination for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments, or the date of physical examination.
6/5/15	2450: Post-TED	Add	Added pediatric acute GVHD Gut guidelines to question 15. See table for details.

Q1-7: 100 Day Report Only

* Question numbers correspond to the FormsNet3^{SM} application. Questions 1-7 should only be answered for the 100 day reporting period.

Question 1: Is "Date of HCT" the same as the date given on Pre-TED?

If the HCT occurred on the date reported on the Pre-TED (question 2, Date of this HCT), check “yes” and continue with question 2.

If the HCT **did not** occur on the date reported on the Pre-TED, you must update the HCT date you reported on the Pre-TED or, in the case of a subsequent transplant, on the form that you reported the subsequent transplant on. **The correction of the HCT date must be completed before the Post-TED is started.**

If the HCT did not occur, check “no” and continue with question 2.

Question 2: Was HCT infusion given?

If the HCT infusion was given, check “yes” and continue with question 8 (do not answer questions 3-7). If the HCT infusion was not given, check “no” and continue with question 3.

Question 3: At least one dose of the preparative regimen was given?

If at least one dose of the preparative regimen was administered (includes radiation and/or chemotherapy), check “yes” and continue with question 4. If the preparative regimen was not started, check “no” and continue with question 5.

Question 4: Patient died during preparative regimen?

If the recipient died after the start of the preparative regimen, but prior to the HCT infusion, check “yes” and continue with question 62. If “no,” continue with question 5.

> * **Questions 5-6**
> If the HCT did not occur, and the patient did not die during the preparative regimen, either question 5 or question 6 must be answered “yes.”

Question 5: This HCT is cancelled?

If the HCT was cancelled, check “yes,” and continue with question 62, and submit the form. If “no,” continue with question 6.

Question 6: This HCT is postponed?

If this HCT was postponed, check “yes” and continue with question 7. The “no” should never be chosen for this question, as the HCT will either have been cancelled (question 5) or postponed.

Question 7: New estimated date:

Enter the new estimated date of the HCT, complete questions 62-74, and submit the form. A postponed HCT does not count as an HCT event. If the postponed event is re-scheduled and completed, then another Pre-TED will be requested and the follow-up process will start with the subsequent Pre-TED.

Do not change the date on the previously submitted Pre-TED via the error correction process. A new Pre-TED must be completed for the re-scheduled HCT.

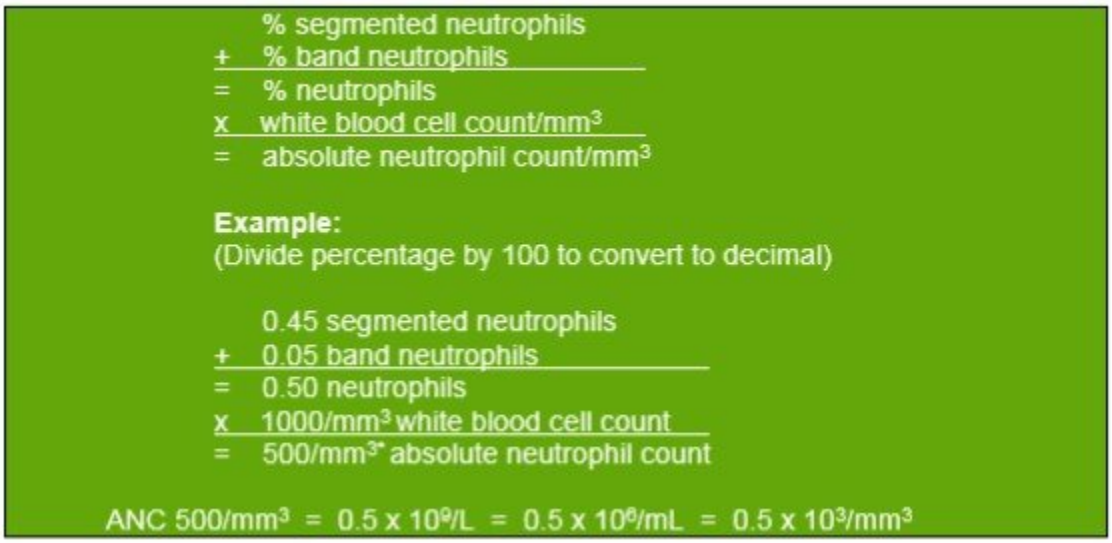
For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Q8-11: Initial ANC Recovery

* **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 × 10^9/L (500/mm3) 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 × 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)



Traditionally, the definition of ANC recovery required selecting the first date of three consecutive days in which the recipient's ANC was ≥ 0.5×10^9/L (500/mm^3). For various reasons it may not be possible to obtain daily laboratory values. Under those circumstances, report ANC recovery based upon three consecutive laboratory values (drawn more than a day apart) as long as the ANC remains ≥ 0.5×10^9/L (500/mm^3).

Tracking the date of ANC recovery may not always be straightforward. In some cases the ANC may fluctuate for a period of time before the recipient fully recovers. In other cases the ANC may remain above 0.5×10^9/L for several days immediately post-HCT and then fall below 0.5×10^9/L. Do not begin counting ANC values of ≥ 0.5×10^9/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 0.5×10^9/L. If this is the case, an ANC recovery date will not be reported, and the "never below" option should be chosen. However, if the recipient's ANC drops below 0.5×10^9/L for even one day, this should be considered the nadir and "never below" should not be chosen. See the following example for more information regarding tracking the date of ANC recovery.

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 ≥ 0.5×10^9/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 8: Was ≥ 0.5 × 10^9/L achieved for 3 consecutive labs?

Indicate whether or not there was evidence of **initial** ANC recovery following this HCT.

Check only **one** response:

- If “yes,” continue with question 9.
- If “no,” continue with question 10.
- Check “never below,” if the recipient’s ANC never dropped below 0.5 × 10^9/L at any time post-HCT.
- Check “previously reported” if this is the six-month or annual follow-up, and the initial ANC recovery has already been reported.
- Check “unknown” if there is no documentation of ANC recovery and/or laboratory reports cannot be obtained. This answer should rarely be used, as ANC recovery is fundamental to a successful HCT. It is imperative that every effort be made to report this data.

Question 9: First date of 3 consecutive labs:

Enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 0.5 × 10^9/L. For an example of tracking ANC recovery, see Example 2.

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

Question 10: Date of last assessment:

If ANC of ≥ 0.5 × 10^9/L was not achieved for three or more consecutive days, enter the date of the last laboratory report.

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

Question 11: Did graft failure occur?

Graft failure includes persistent neutropenia, < 5% donor chimerism, and ANC < 0.5 × 10^9/L for three or more consecutive laboratory values. Graft failure often requires an additional infusion of donor cells. Graft failure may result from the use of specific drugs, infection (especially CMV), GVHD, and other etiologies.

If the recipient meets the criteria of graft failure, check “yes.”

Q12-14: Initial Platelet Recovery

> **Transfusions**
> Currently there is an error on the Form 2450 regarding the date of platelet recovery. The form should read: “date platelet greater than or equal to (≥) 20 × 10^9/L.”

The following questions refer to **initial** platelet recovery following the HCT for which this form is being completed. All dates should reflect **no platelet transfusions administered for seven consecutive days.**

Report the date of the first of three consecutive laboratory values ≥ 20 × 10^9/L obtained on different days, as shown in 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 blood cell counts. When the data is later used for analysis, it is important to be able to distinguish between a recipient whose own body was creating the cells and a recipient who required transfusions to support the counts.

The following example illustrates the procedure to follow for reporting platelet recovery.

> **Example:** 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 × 10^9/L

Question 12: Initial platelet recovery

Indicate whether or not there was evidence of initial platelet recovery following this HCT.

Check only one response:

- If “yes,” continue with question 13.
- If “no,” continue with question 14.
- Check “never below,” if the recipient’s platelets never dropped below 20 × 10^9/L at any time post-HCT and a platelet transfusion was never required. If the recipient’s platelet count drops below 20 × 10^9/L and/or the recipient received a platelet transfusion even once, do not use this option.
- Check “previously reported” if this is the six-month or annual follow-up, and initial platelet recovery has already been reported on a previous form.
- Check “unknown” if there is no documentation of platelet recovery and/or laboratory reports cannot be obtained.

Question 13: Date platelet ≥ 20 × 10^9/L

Enter the first date of three consecutive laboratory values obtained on different days where the platelet count was ≥ 20 × 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 × 10^9/L is demonstrated, follow the examples below when determining an estimated date.

Example 1 The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is ≥ 20 × 10^9/L on January 2, January 3, and 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 × 10^9/L. Report January 8 (day seven post-platelet transfusion) for the date of platelet recovery.

Example 2 The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is ≥ 20 × 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.

Question 14: Date of last assessment

If a platelet count of ≥ 20 × 10^9/L was not achieved; enter the date of the last laboratory report.

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

Q15-18: Graft versus Host Disease (Allogeneic Only)

> **Autologous and Syngeneic Transplants**
> If this was an autologous or syngeneic HCT, continue with the New Malignancy section at question 19.

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 HCT, leave questions 15-18 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.

Question 15: Maximum 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 histologic 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 the table below.

Table 1: GVHD Grading and Staging

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/m^2/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/m^2/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/m^2/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	Stages 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 histologic evidence of GVHD in the stomach or duodenum.

[5] Criteria for grading given as minimum degree of organ involvement required to confer that grade.

[6] Grade IV may also include lesser organ involvement with an extreme decrease in performance status

* **Pediatric Recipients**
Diarrhea in pediatric recipients is assessed in mL/m^2 rather than mL/kg since the recipient’s weight may fluctuate due to cardiac failure, renal failure, or severe diarrhea.

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%

Indicate the maximum grade of acute GVHD present during this reporting period [including acute GVHD that persists from a previous HCT or donor cellular infusion (DCI)].

If acute GVHD was present, but the maximum grade was not documented nor is it able to be determined from the grading and staging table, check “present (but) grade unknown.”

Example 1: 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.

Example 2: A recipient developed acute liver GVHD with elevated LFTs with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in Table 1; “present, grade unknown” would be the best option to report.

If the recipient did not develop acute GVHD, check “0.”

* **Reporting Chronic GVHD, Date of Diagnosis, and Continuation From Last Report (Questions 16, 17, & 18)**
Question 16 is intended to capture the maximum extent of chronic GVHD during the *reporting period*.
Question 17 is intended to capture the date of onset of chronic GVHD or flare of chronic GHVD if the previous episode has resolved for at least 30 days.
Question 18 is intended to capture if the *chronic* GVHD episode has continued from the last post-TED form (Form 2450).

Question 16: Maximum extent of Chronic GVHD during this period

Chronic GVHD can occur following acute GVHD or without prior evidence of acute GVHD (*de novo*). Chronic GVHD affects 25-50% of long-term survivors of allogeneic transplants and usually develops after day 100. 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. The staging system for chronic GVHD is divided into two categories: limited and extensive.

* **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.

Indicate the maximum grade of chronic GVHD present during this reporting period. If the recipient did not develop chronic GVHD, check “none” and continue with question 19.

Report “limited” if chronic GVHD includes only localized skin involvement and/or liver dysfunction. Continue with question 17.

Report “extensive” if **any** of the following symptoms are attributed to chronic GVHD:

- Generalized skin involvement and/or liver dysfunction
- Liver histology showing chronic aggressive hepatitis, bridging necrosis, or cirrhosis
- Involvement of the eye
- Involvement of the salivary glands or oral mucous membranes
- Involvement of any other target organ

Continue with question 17.

If chronic GVHD was present, but the maximum extent was not documented, check “unknown” and continue with question 19.

Example 1. A recipient developed stage 1 acute skin GVHD in the 100 day reporting period that persisted into the 6 month reporting period. During the 6 month reporting period, the acute skin GVHD progressed into limited chronic skin GVHD. The chronic skin GVHD was in remission by the end of the 6 month reporting period, and there was no subsequent episode of chronic GVHD in the 1 year reporting period.

Reporting Period	Maximum Extent (Question 16)	Date of Diagnosis (Question 17)	Continued From Last Report (Question 18)
100 day	None	—	—
6 month	Limited	*Date acute progressed to chronic GVHD*	—
1 year	None	—	—

Example 2. A recipient developed *de novo* chronic oral GHVD in the 100 day reporting period, which persisted into the 6 month reporting period. There was no subsequent chronic GVHD through the 1 year reporting period.

Reporting Period	Maximum Extent (Question 16)	Date of Diagnosis (Question 17)	Continued From Last Report (Question 18)
100 day	Extensive	*Date of clinical diagnosis*	—
6 month	Extensive	*Leave blank*	Yes

1 year	None	—	—

Example 3. A recipient developed stage 1 acute skin GVHD in the 100 day reporting period which was in remission by the date of contact for the 100 day form. Towards the end of the 6 month reporting period, the recipient developed limited, chronic GVHD of the skin, which persisted into the 1 year reporting period.

Reporting Period	Maximum Extent (Question 16)	Date of Diagnosis (Question 17)	Continued From Last Report (Question 18)
100 day	None	—	—
6 month	Limited	*Date of clinical diagnosis*	No
1 year	Limited	*Leave blank*	Yes

Example 4. A recipient developed *de novo* extensive gastrointestinal (GI) chronic GVHD in the 6 month reporting period. The chronic GI GVHD is in remission on the date of contact for the 6 month reporting period. Two months into the 1 year reporting period, the recipient developed a flare of the extensive GI GVHD.

Reporting Period	Maximum Extent (Question 16)	Date of Diagnosis (Question 17)	Continued From Last Report (Question 18)
100 day	None	—	—
6 month	Extensive	*Date of clinical diagnosis in the 6-month reporting period*	No
1 year	Extensive	*Date of clinical diagnosis in the 1-year reporting period*	Yes

Example 5. A recipient developed stage 2 acute GVHD of the skin in the 100 day reporting period, which persisted into the 6 month reporting period; and subsequently progressed into limited, chronic GVHD of the skin. Limited chronic GVHD of the skin persisted through the 6 month reporting period and into the 1 year reporting period. The chronic GVHD of the skin cleared for the last two months in the 1 year reporting period. However, the recipient developed extensive chronic oral GVHD near the end of the 1 year reporting period.

Reporting Period	Maximum Extent (Question 16)	Date of Diagnosis (Question 17)	Continued From Last Report (Question 18)
100 day	None	—	—
6 month	Limited	*Date of progression from acute to chronic*	No
1 year	Extensive	*Date of oral GVHD onset*	Yes

Question 17: Date of diagnosis of chronic GVHD

Report the date of clinical diagnosis of chronic GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began. If the clinical diagnosis date is not documented, then report the date of histologic confirmation.

If this form is being completed for the six-month or annual follow-up time point, and the recipient had a previous onset of chronic GVHD that subsequently resolved for at least 30 days and then reactivated ("flare"), report the flare as a new episode and list the new date of diagnosis.

If chronic GVHD progressed directly from acute GVHD, the date of onset should be reported as the date the recipient's symptoms progressed from acute to chronic.

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

Question 18: Continued from last report (answer is only valid on > day 100 evaluation)

Indicate whether the chronic GVHD episode has continued from the last Post-TED form. This question is not intended to capture when acute GVHD progresses to chronic GVHD.

Q19-61: New Malignancy, Lymphoproliferative or Myeloproliferative Disorder

Question 19: Did a new malignancy, lymphoproliferative or myeloproliferative disorder occur?

Indicate whether a new or secondary malignancy, lymphoproliferative disorder, or myeloproliferative disorder has developed. Do not report recurrence, progression, or transformation of the recipient's primary disease (disease for which the transplant was performed), or relapse of a prior malignancy.

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

- Skin cancers (basal, squamous, melanoma)
- New leukemia
- New myelodysplasia
- Solid tumors
- PTLD (post-transplant lymphoproliferative disorder) (report as lymphoma or lymphoproliferative disease)

The following should **not** be reported as new malignancy:

- Recurrence of primary disease (report as relapse or disease progression)
- Relapse of malignancy from recipient's pre-HCT medical history
- Breast cancer found in other (i.e., opposite) breast (report as relapse)
- Post-HCT cytogenetic abnormalities associated with the pre-HCT diagnosis (report as relapse)
- Transformation of MDS to AML post-HCT (report as disease progression)

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 discrete episode. For example, a recipient had a basal cell skin cancer diagnosed on the neck four months post-HCT and six months later had another basal cell located on the nose. The lesion on the nose is not considered a metastasis from the neck, but a new discrete lesion.
These discrete episodes should be reported in the "Other skin malignancy" questions on the Post-TED forms (questions 47-49).

If a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder has occurred following the HCT, check "yes" and continue with question 20. If not, check "no" and continue with question 62.

New Malignancy, Lymphoproliferative or Myeloproliferative Disorder
Paper submission of new malignancy: if more than one new malignancy occurred in a single reporting period and each malignancy had a different diagnosis date, copy the page and report each malignancy separately, labeling them 1st, 2nd, 3rd, etc. If multiple malignancies occurred with the same diagnosis date, report all malignancies from that diagnosis date on the same page.

Question 20: For all new malignancies except "other skin malignancy (basal cell, squamous)," was testing performed to determine the cell of origin?

Indicate if testing was performed to determine the cell of origin of the new malignancy. If testing was performed, check "yes" and continue with question 21. If not, check "no" and continue with question 23.

Question 21: Specify the cell origin of the new malignancy

Indicate the cell origin of the new malignancy.

Question 22: Is a copy of the cell origin evaluation (VNTR, cytogenetics, FISH) attached?

Attaching a copy of the evaluation for the cell origin of the new malignancy reduces the need for later data queries.

If "yes," complete the Log of Appended Documents Form (Form 2800) and attach the pathology report. Do not attach the pathology report to the 2450. For more information regarding the Form 2800, see the Log of Appended Documents manual section.

> * **Questions 23-60**
> **FormsNet3℠ application:** Check either "yes" or "no" for each option listed, and enter the "date of diagnosis," if applicable.
> **Paper form submission:** Check all that apply.

Question 23-60: Specify which new disease(s) occurred

Indicate the disease classification(s) at diagnosis.

Question 27: Other leukemia (including ALL) – Specify

If the disorder is "other leukemia," specify the type. Do not report AML/ANLL in this category.

Question 44: Is the tumor EBV positive?

If the disorder is lymphoma or lymphoproliferative disease, indicate if the tumor is EBV positive.

Question 60: Other malignancy – Specify

If the disorder does not fit one of the categories listed, specify the type.

Question 61: Is a pathology/autopsy report or other documentation attached?

Attaching a copy of the diagnostic pathology report for the new malignancy assists in disease confirmation and **reduces the need for later data queries.**

If "yes," complete the Log of Appended Documents Form (Form 2800) and attach the pathology report. Do not attach the pathology report to the 2450. For more information regarding the Form 2800, see the Log of Appended Documents manual section.

Q62-74: Survival

The latest follow-up date is based on a medical evaluation conducted by a transplant center physician, referring physician, or other physician currently assuming responsibility for the recipient's care. Report the date of the medical evaluation performed closed to the designated time period of the form (e.g., day 100, six-month, or annual follow-up visit). Recipients are not always seen within the time windows used for reporting follow-up dates and some discretion is required when determining which date to report. In that case, report the date closest to the date of contact within reason. If this Post-TED Form is being completed for the day 100 time period, the answers to all questions should reflect the clinical status of the recipient between the HCT infusion date and the latest follow-up date. If this Post-TED Form is being completed for the six-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 physician but the survival status is known, submit the Post-TED reporting only the survival status.

If this form reports a subsequent stem cell infusion, report the date of contact as the day before the preparative regimen began for the subsequent HCT. If no preparative regimen is given, report the date of contact as the day before the subsequent HCT.

Paper submission of Post-TED: For survival status, include the date of latest follow-up, date of death, or last known date alive in the "latest follow-up" space.

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

Question 62: Survival status at latest follow-up

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 63. If the recipient has died, continue with question 64.

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 before the date of a subsequent HCT. 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).

Questions 63-64: Latest follow-up

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 six 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 physician 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, six 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. Preferred evaluations include those from the transplant center physician, referring physician, or other physician currently assuming responsibility for the recipient’s care. In the absence of contact with a physician, other types of contact may include a documented phone call with the recipient, a laboratory evaluation, or any other documented recipient interaction on the date reported. If there was no contact on the exact time point, choose the date of contact closest to the actual time point. Below, the guidelines show an ideal approximate range for reporting each post-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: Indicate the recipient is lost to follow-up in FormsNet
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).

Example 3. The recipient has died before their six month anniversary.
The recipient is transplanted on 1/1/13, was seen regularly through the first 100 days. They had restaging exams on 4/4/13 and was seen on 4/8/13, and then died on 5/13/13 in the hospital emergency room.

What to report:
100 Day Date of Contact: 4/8/13 (note the latest disease assessment would likely be reported as 4/4/13)
6 Month Date of Contact: 5/13/13 (though the death does not occur within the ideal approximate range for 6 months)

Example 4. The recipient has died after their six month anniversary.
The recipient is transplanted on 1/1/13, was seen regularly through the first 100 days. They had restaging exams on 4/22/13 and was seen on 4/23/13. Based on findings in the restaging exam, the recipient was admitted for additional treatment. The disease was found to be refractory on a 6/25/13 restaging exam, and the recipient was discharged to hospice on 7/8/13. The hospital was notified via telephone that the recipient died on 7/16/13.

What to report:
100 Day Date of Contact: 4/23/13 (note the latest disease assessment would likely be reported as 4/22/13)
6 Month Date of Contact: 7/16/13 (note the latest disease assessment would likely be reported as 6/25/13)

Date of Contact & Subsequent Transplant

If the recipient has a subsequent HCT, report the date of contact as the day before the preparative regimen begins for the subsequent HCT. If no preparative regimen is given, report the date of contact as the day before the subsequent HCT. In these cases, actual contact on that day is not required, and the day prior to the initiation of the preparative regimen (or infusion, if no preparative regimen) should be reported. This allows every day to be covered by a reporting period, but prevents overlap between transplant events.

Example 5. The recipient had a 2nd transplant with a preparative regimen.
The recipient has their first transplant on 1/1/13 and a planned second transplant on 2/1/13. The recipient was admitted on and received their first dose of chemotherapy for the preparative regimen for HCT #2 on 1/28/13.

What to report:
100 Day Date of Contact: 1/27/13 (regardless of actual contact on that date)

Example 6. The recipient had a subsequent transplant without a preparative regimen.
Following their first transplant on 1/1/13, a recipient with SCID required a subsequent allogeneic transplant due to poor graft function. The recipient has remained inpatient following the first transplant. The physician planned the second transplant for 5/31/13, and proceeded without a preparative regimen.

What to report:
100 Day Date of Contact: 4/11/13 (+/- 15 days)
6 Month Date of Contact: 5/30/13

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

Question 65: Main cause of death

Cause of death is considered the main disease, complication, or injury that leads to death. Do not report the mode of death (e.g., cardiopulmonary arrest). Only one primary cause of death may be specified; however, under "HSCT-related causes," multiple contributing causes may be listed if relevant.

Primary cause of death is separated into three main categories: relapse or recurrence of disease for which the HCT occurred, HCT-related causes, and new malignancies (not transformation or progression). Typically, one of these three categories applies, but if not, the "other" option may be used. Report the recipient's primary cause of death as **one** of the following:

- **Relapse / Progression / Persistent disease:** Primary cause of death is attributed to persistence or recurrence of the underlying disease for which the HCT was performed. Post-HCT disease evaluation must reflect the presence of disease. If this option is chosen, questions 96-106 should also reflect the disease relapse/recurrence.

> * **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.

- **HCT-related causes:** See the detailed instructions for questions 66-73 below. If the recipient's primary cause of death is HCT-related, questions 66-73 must be completed.
- **New malignancy:** Primary cause of death is attributed to the onset of a new malignancy after HCT. If the malignancy was diagnosed prior to this HCT, report the disease as "other" and specify the disease in question 72. The new malignancy must differ from the disease for which the HCT was performed.

Examples include de novo leukemia, and AML diagnosed many years after a transplant for ALL. If the recipient received an HCT for MDS, and post-transplant MDS transformed into AML, this would be considered progression of disease, not a new malignancy.

- **Other:** See the detailed instructions for question 74 below.
- **Unknown:** This option should be used only when there is no documentation of the recipient's cause of death and all methods to try to obtain documentation have been utilized.

Questions 66-73
FormsNet3℠ application: Check either "yes" or "no" for each option listed
Paper form submission: Check all that apply
Include all complications, including those only detected at autopsy.

Question 66: GVHD

Check "yes" if a cause of death is attributed to acute and/or chronic GVHD. If "yes" is answered for this question, there must also be data reported in the GVHD section of the form (questions 15-18).

Question 67: Cardiac toxicity

Check "yes" if cardiac toxicity was a cause of death. Examples of cardiac toxicity include: heart failure, congestive heart failure, non-infectious pericarditis, and/ or cardiac tamponade.

Question 68: Infection

Check "yes" if a fungal, bacterial, and/or viral infection (documented or suspected) was a cause of death. Examples of infection include: viral pneumonia and viral infection of other organs.

Interstitial pneumonia (in the absence of viral infection or pneumocystis) should be reported as "pulmonary toxicity."

Question 69: Pulmonary toxicity

Check "yes" if a pulmonary toxicity was a cause of death. An example of pulmonary toxicity is non-infectious lung failure, which can include ARDS, pulmonary hemorrhage, radiation pneumonia, etc. If bronchiolitis obliterans is a part of chronic GVHD, it can also be reported here.

Question 70: Rejection/Poor graft function

Check “yes” if rejection/poor graft function was a cause of death. This may also be recorded as bone marrow failure or aplasia. Rejection/poor graft function should be reported if one of the following conditions is met and the recipient has not relapsed.

- ANC < 0.5 × 10^9/L after day 28 post-HCT and bone marrow biopsy with < 5% cellularity.
- ANC sustained > 0.5 × 10^9/L for three or more consecutive days with subsequent decrease to < 0.5 × 10^9/L and bone marrow examination with < 5% cellularity.

Question 71: Veno-Occlusive Disease (Hepatic)

Check “yes” if Veno-Occlusive Disease (**VOD**) was a cause of death. VOD is often caused by chemotherapy and/or radiation therapy. VOD is characterized by endothelial damage, micro-thrombosis of the hepatic venules, and sinusoidal fibrosis. VOD is more common in allogeneic than in autologous HCT and typically occurs within 3 weeks of transplant. In the absence of a histological diagnosis, recipients must fulfill the criteria below for a diagnosis of VOD.

Clinical Criteria for Veno-Occlusive Disease Of Liver[12]:
Recipients reported as having VOD based only on clinical signs and symptoms must have two or more of the following, and no other identifiable cause for liver disease:

- Jaundice (bilirubin ≥ 2 mg/dL or > 34 µmol/L)
- Hepatomegaly with right upper quadrant pain
- Ascites and/or weight gain (> 5% over baseline, as generally accepted)

[1] McDonald GB, et al., *Hepatology* 1984;4:116-122.

[2] Jones RJ, et al., *Transplantation* 1987;778-783.

Questions 72-73: Other, specify (HCT-related)

Check “yes” if the cause of death is not one of the listed HCT-related options. Examples of other causes of death include but are limited to multi-organ failure, stroke, and hemorrhage.

Question 74: Other, specify (primary cause of death)

This option should only be used if the primary cause of death does not fit one of the categories listed (e.g., suicide, sudden death, etc.).

Q75-77: Post-HCT Therapy

> * **Post-HCT Therapy**
> This section collects data on specific therapies for current CIBMTR studies. It is not intended to collect every type of possible post-HCT therapy.

Questions 75-77 are optional for non-US centers.

Questions 75-77: FGF (velafermin), Imatinib mesylate (Gleevec, Glivec), KGF (palifermin, Kepivance)?

Check “yes” if FGF (velafermin), Imatinib mesylate (Gleevec, Glivec), and/or KGF (palifermin, Kepivance) were given as post-HCT therapy.

Check “masked trial” if the recipient is part of a study where the agent the recipient received is not known (e.g., placebo, drug, or other agent). **Use the error correction process to update the data field once the trial is over and the drug the recipient was given is known.**

Check “no” if the recipient was not given FGF (velafermin), Imatinib mesylate (Gleevec, Glivec), and/or KGF (palifermin, Kepivance) as post-HCT therapy.

Check “unknown” if there is no documentation to indicate whether the recipient did, or did not receive FGF (velafermin), Imatinib mesylate (Gleevec, Glivec), and/or KGF (palifermin, Kepivance) as post-HCT therapy, and all methods to try to obtain documentation have been utilized.

Q78: HCT for Non-Malignant Disease Only

> ! **HCT for Non-Malignant Diseases**
> This section should only be completed if the primary disease for this HCT is a non-malignant disease. Disease evaluation is not collected for non-malignant diseases, as there are no standard criteria for measuring non-malignant disease response.

Non-malignant diseases can be identified by the CIBMTR database code number shown in brackets { } on the Pre-TED, and are numbered 300 and above, with the exception of “Paroxysmal Nocturnal Hemoglobinuria (PNH) (56)” and “other disease (900)” (where the disease can be either malignant or non-malignant).

* **FormsNet3SM application:** Form 2450, question 78 currently contains an error. If "yes," questions 107-109 and 110-146 should be completed. If "no," questions 107-109 should be completed and the form submitted.
Paper form submission: Form 2450, question 78 currently contains an error. If "yes," questions 107-109 and 110-146 should be completed. If "no," questions 107-109 should be completed and pages one and two will be submitted.

Question 78: DCI given in this period?

A Donor Cellular Infusion (DCI) is a cellular therapy that uses cells obtained from the original HCT donor. The types of cells used for a DCI include, but are not limited to: lymphocytes, unstimulated peripheral blood, mononuclear cells, dendritic cells, or mesenchymal cells. For more information regarding DCI, see question 110.

If the recipient received a DCI in this reporting period, check "yes" and continue with question 107 and complete the DCI section. If the recipient did not receive a DCI in this reporting period, check "no," continue with questions 107-109, and submit form.

Q79-81: Malignant Disease Evaluation for this HCT

! **This section should only be completed if the primary disease for which this HCT is being completed is a malignant disease.**

Malignant diseases can be identified by the CIBMTR database code number shown in brackets on Pre-TED { }, and are numbered 299 and below, with the exception of with the exception of "Paroxysmal Nocturnal Hemoglobinuria (PNH) (56)" and "other disease (900)" (where the disease can be either malignant or non-malignant).

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 does not include 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. If the recipient was in complete remission (CR) at the start of the preparative regimen, the best response is "not applicable," as CR has already been attained.

* **Reporting Complete Remission (CR) Post-HCT**
The disease criteria of the Pre-TED (2400) Manual should be used when determining the recipient's CR status.

* CR undetermined (CRU) is the complete disappearance of all known sites of disease with the exception of persistent scan abnormalities of unknown significance. CRU should be reported as "complete remission."

Question 79: Was a CR ever achieved in response to HCT (including any therapy as of Day 0, excluding any change in therapy in response to disease assessment)?

If the recipient was already in CR at the start of the preparative regimen, check "Recipient already in CR at start of preparative regimen" and continue with question 82.

If the recipient achieved CR post-HCT (excluding unplanned therapy), check "yes" and continue with question 80.

If the recipient never achieved CR post-HCT, check "no" and continue with question 81.

If the recipient's disease status was not evaluated post-HCT, check "not evaluated" and continue with question 82. 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 80: Date (Yes, post-HCT CR was achieved)

Indicate the date CR was achieved. If CR was reported on a previous Post-TED, check "First CR date reported previously." This option should only be chosen for > 100 day Post-TED (i.e., six-month or annual evaluation).

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

Question 81: Date assessed (No, never in CR from HCT)

If the recipient never achieved CR post-HCT, indicate the date of latest disease assessment. If the recipient received unplanned therapy, indicate the date of the latest disease assessment prior to receiving the therapy.

If the recipient never achieved CR post-HCT and unplanned therapy was reported on a previous Post-TED, check “best response was previously reported.” This option should only be chosen for > 100 day Post-TED (i.e., six-month or annual evaluation).

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

Q82-91: First Relapse or Progression after HCT (in this period, any type, not persistent disease)

Question 82: First relapse or progression after HCT

The three methods used to evaluate disease status are: molecular, cytogenetic/fluorescent *in situ* hybridization (FISH)/flow cytometry, and clinical/ hematological. Any of these three methods can record relapse or progression, but only the **first** instance for each method should be reported.

If question 82 is answered “yes,” questions 83, 86, and 89 should be answered.

If question 82 was answered “yes” on a previous Post-TED and there are no new methods which detect relapse or progression, check “no” and continue to 92.

Molecular

Question 83: Relapse/progression detected by molecular method

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 BCR/ABL.

If molecular markers for relapse/progressive disease were found, check “yes” and continue with question 84.

If molecular markers for relapse/progressive disease were not found, check “no” and continue with question 85.

If disease was detected and reported on a previous Post-TED follow-up, check “previously reported” and continue with question 86. This option should only be chosen for > 100 day Post-TED.

If molecular testing was not done, check “not evaluated” and continue with question 86.

Question 84: Date first seen (molecular method)

Indicate the date relapse/progressive disease was determined by molecular method. Continue with question 86.

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

Question 85: Date of assessment (molecular method)

If molecular markers for relapse/progressive disease were not found, indicate the date of latest assessment. Continue with question 86.

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

Cytogenetic/Fluorescent *in situ* hybridization (FISH)

Question 86: Relapse/progression detected by cytogenetic/FISH method

*

Flow Cytometry
Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in question 86.
An exception to the note above applies to multiple myeloma. If the flow cytometry assessment has < 5% malignant plasma cells, this result should not be reported because the result is not reliable; if no other cytogenetic or FISH assessments were performed, report “no/not evaluated.” However, if the flow cytometry assessment found ≥ 5% malignant plasma cells, this should be reported as evidence of disease.

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient's disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

If cytogenetic/FISH/flow markers for relapse/progressive disease were found, check "yes" and continue with question 87.

If cytogenetic/FISH/flow markers for relapse/progressive disease were not found, check "no" and continue with question 88.

If disease was found and reported on a previous Post-TED follow-up, check "previously reported" and continue with question 89. This option should only be chosen for > 100 day Post-TED.

If cytogenetic/FISH/flow testing was not done, check "not evaluated" and continue with question 89.

Question 87: Date first seen (cytogenetic/FISH method)

Indicate the date relapse/progressive disease was determined by cytogenetic methods (e.g., FISH). Continue with question 89.

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

Question 88: Date of assessment (cytogenetic/FISH method)

If cytogenetic/FISH/flow markers for relapse/progressive disease were not found, indicate the date of latest assessment. Continue with question 89.

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

Clinical/Hematologic

Question 89: Relapse/progression detected by clinical/hematologic method

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, as determined either physically or radiographically. Every recipient who has an evaluation by a physician has a "clinical" assessment.

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, check “yes” and continue with question 90.

If clinical/hematologic evidence of relapse/progressive disease was not found, check “no” and continue with question 91.

If disease was found and reported on a previous post-TED follow-up, check “previously reported” and continue with question 57. This option should only be chosen for > 100 day Post-TED.

If clinical/hematological assessment was not done, check “not evaluated” and continue with question 92.

Question 90: Date first seen (clinical/hematologic method)

Indicate the date relapse/progressive disease was determined by clinical/hematological evaluation. Continue with question 92.

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

Question 91: Date of assessment (clinical/hematologic method)

If clinical/hematological evidence of relapse/progressive disease was not found, indicate the date of latest assessment. Continue with question 92.

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

Q92-95: Additional Treatment

Question 92: Additional treatment

If additional treatment(s) was given to the recipient post-HCT for the primary disease for transplant, check “yes” and continue with question 93. Do not report supportive care or treatment for new malignancies or malignancies that were not the primary indication for transplant.

If the recipient did not receive any additional treatment(s) post-HCT for treatment of disease, check “no” and continue with question 96.

Questions 93: Additional treatment – DCI (allo only)

If the recipient received a donor cellular infusion (DCI) following an **allogeneic** HCT, check “yes” and complete the DCI section of the Post-TED (questions 110-121).

If the recipient did not receive a DCI, check “no” and continue with question 94.

If the recipient received an autologous transplant, this question should be left blank.

Question 94: Additional treatment – Planned

If the recipient received additional treatment as planned post-HCT per protocol, check “yes.” Planned treatment is considered part of the treatment plan regardless of the disease status post-HCT. This does **not** include treatment given for relapsed, progressive, or persistent disease that was not planned before the HCT was performed. If post-transplant treatment is given as prophylaxis or maintenance for recipients in CR, or as preemptive therapy for recipients with minimal residual disease, consider this “planned therapy,” even if this was not documented prior to the transplant.

If the recipient did not receive planned additional treatment post-HCT, check “no” and continue with question 95.

Question 95: Additional treatment – Not planned

If the recipient received additional treatment post-HCT, and the treatment was **not planned** per protocol and given for relapsed, progressive, or persistent disease, check “yes.”

If the recipient did not receive unplanned additional treatment post-HCT, check “no” and continue with question 96.

Q96-107: Method of Latest Disease Assessment

METHOD:
This section should be completed for every malignant disease, and should reflect the recipient’s most recent disease assessment. Not all diseases have molecular and/or cytogenetic/FISH abnormalities identified to monitor disease status. If no disease assessments exist, check “not evaluated.” In some circumstances, disease may be detected by molecular or cytogenetic testing, but may not be considered a relapse or progression. Test results should still be reported.

Molecular and cytogenetic assessments are often performed for recipients post-HCT. If the recipient did not have any identified molecular, cytogenetic, or FISH abnormalities at diagnosis or during their pre-transplant course, and post-HCT follow-up assessments continue to identify that no abnormalities are detected, report "No/Not Evaluated" for the molecular and/or cytogenetic/FISH assessment data fields on the Post-TED. However, if routine post-HCT molecular, cytogenetic and/or FISH assessments identify a new abnormality associated with the recipients disease process, begin reporting those assessments.

If the recipient had molecular, cytogenetic, and/or FISH abnormalities prior to transplant, ensure that post-HCT assessments are reported.

DATE:
If more than one test in the same assessment category is done on different days, report the date of the most definitive diagnostic assessment within a reasonable time frame of the date of contact (approximately 30 days).

Example 1 *Leukemia*: Blasts appear in the peripheral blood on a CBC, the next day a bone marrow biopsy is done and reveals relapse of disease. Report the date of the bone marrow biopsy as the date of latest assessment, as this is a more definitive assessment than a CBC.

Example 2 *Lymphoma*: A bone marrow biopsy is performed and reveals relapse of disease. The next day a CT scan is performed, which also reveals relapse of disease. Since both tests reveal the same result, and the tests are of equal diagnostic relevance, either the date of the bone marrow biopsy or the CT scan date may be reported.

Example 3 *Lymphoma*: A PET/CT is done five months prior to the date of contact, which shows no evidence of disease. On the date of contact, the recipient is seen in clinic with no evidence of lymphadenopathy upon physical examination. Report the date of clinic visit as the date of latest assessment.

Example 4 *Multiple Myeloma (IgG Kappa)*: A serum electrophoresis (SPEP), serum immunofixation and bone marrow biopsy are performed one week prior to the date of contact (i.e., the office visit). The SPEP shows no evidence of a monoclonal protein (M-spike); however, the immunofixation is still positive. The bone marrow biopsy shows no evidence of residual disease. Report the date of the SPEP, immunofixation, and bone marrow biopsy as the date of latest assessment. In this case, it should be reported that disease was detected since the immunofixation is positive.

Molecular

Question 96: Molecular

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 BCR/ABL.

In the FormsNet3^{SM} application, check “yes” if a molecular method was used to determine disease status for this follow-up time point and continue with question 97. If a molecular method was not used to determine disease status for this follow-up time point, check “no/not evaluated” and continue with question 100.

This question does not exist on the paper version of the Form.

Question 97: Disease detected? (molecular method)

If molecular markers for disease were found, check “yes” and continue with question 98.

If molecular markers for disease were not found, check “no” and continue with question 99.

Question 98: If yes, was the status considered a disease relapse or progression? (molecular method)

If the physician believes the test results indicate disease relapse or progression, check “yes.” If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression (e.g., a recipient transplanted for CML exhibits a low level of BCR-ABL positivity post-HCT that the physician does not believe is disease), check “no.” Continue with question 100.

Question 99: Date latest assessed (molecular method)

Indicate the date of the latest disease assessment. Continue with question 100.

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

Cytogenetic/Fluorescent *in situ* hybridization (FISH)

Flow Cytometry
Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in question 100.
An exception to the note above applies to multiple myeloma. If the flow cytometry assessment has < 5% malignant plasma cells, this result should not be reported because the result is not reliable; if no other cytogenetic or FISH assessments were performed, report "not evaluated." However, if the flow cytometry assessment found ≥ 5% malignant plasma cells, this should be reported as evidence of disease.

Question 100: Cytogenetic/FISH

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient's disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

In the FormsNet3^{SM} application, check "yes" if a cytogenetic method was used to determine disease status for this follow-up time point and continue with question 101. If a cytogenetic method was **not** used to determine disease status for this follow-up time point, check "no/not evaluated" and continue with question 104.

This question does not exist on the paper version of the Form.

Question 101: Disease detected? (cytogenetic/FISH method)

If cytogenetic/FISH/flow markers for disease were found, check "yes" and continue with question 102.

If cytogenetic/FISH/flow markers for were not found, check "no" and continue with question 103.

Question 102: If yes, was the status considered a disease relapse or progression? (Cytogenetic/FISH method)

If the physician believes the test result indicates disease relapse or progression, check "yes." If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression, check "no." Continue with question 103.

Question 103: Date latest assessed (Cytogenetic/FISH method)

Indicate the date of the latest disease assessment. Continue with question 104.

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

Clinical/Hematologic

Question 104: Clinical/Hematologic:

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, as determined either physically or radiographically. Every recipient who has an evaluation by a physician has a “clinical” assessment.

In the FormsNet3SM application, check “yes” if a clinical/hematologic assessment was used to determine disease status for this follow-up time point and continue with question 105. If a clinical/hematologic assessment was not used to determine disease status for this follow-up time point, check “no/not evaluated” and continue with question 107.

This question does not exist on the paper version of the Form.

Question 105: Disease detected? (clinical/hematologic method)

If clinical/hematologic evidence of disease was found, check “yes.”

If clinical/hematologic evidence of disease was not found, check “no.”

Question 106: Date latest assessed: (clinical/hematologic method)

Indicate the date of the latest disease assessment and continue with question 107.

The date reported should be that of the most disease-specific assessment within a reasonable timeframe of the date of contact (approximately 30 days). Indicate the date the sample was collected for examination for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments, or the date of physical examination.

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

Questions 107-109

Question 107 appears only in the FormsNet3SM version of the Post-TED Form. For the paper version of the Form, if a previous HCT was done for a different malignant disease than this HCT, indicate the status of the original disease and the date determined (see Questions 108-109). If a previous HCT was not done for a different malignant disease, continue to the DCI section or submit the Form. Questions 107-109 only apply to previous HCTs that were performed for another malignant disease.

Question 107: Was a previous HCT performed for a different disease than this HCT?

If prior to this HCT, an HCT was performed for a different disease (**malignant disease only**), check “yes” and continue with question 108.

If this is the recipient’s first HCT, or a prior HCT was not performed for a different disease (malignant disease only), check “no” and continue with question 110.

Question 108: Give status of original disease

Indicate the **current** status of the original malignant disease as either “CR” or “not in CR” and continue with question 109.

Question 109: Date determined

Indicate the date this disease status was determined.

If a DCI was done during this reporting period, continue with the DCI section of the form. If no DCI was done during the reporting period, the form is considered complete and may be submitted to the CIBMTR.

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

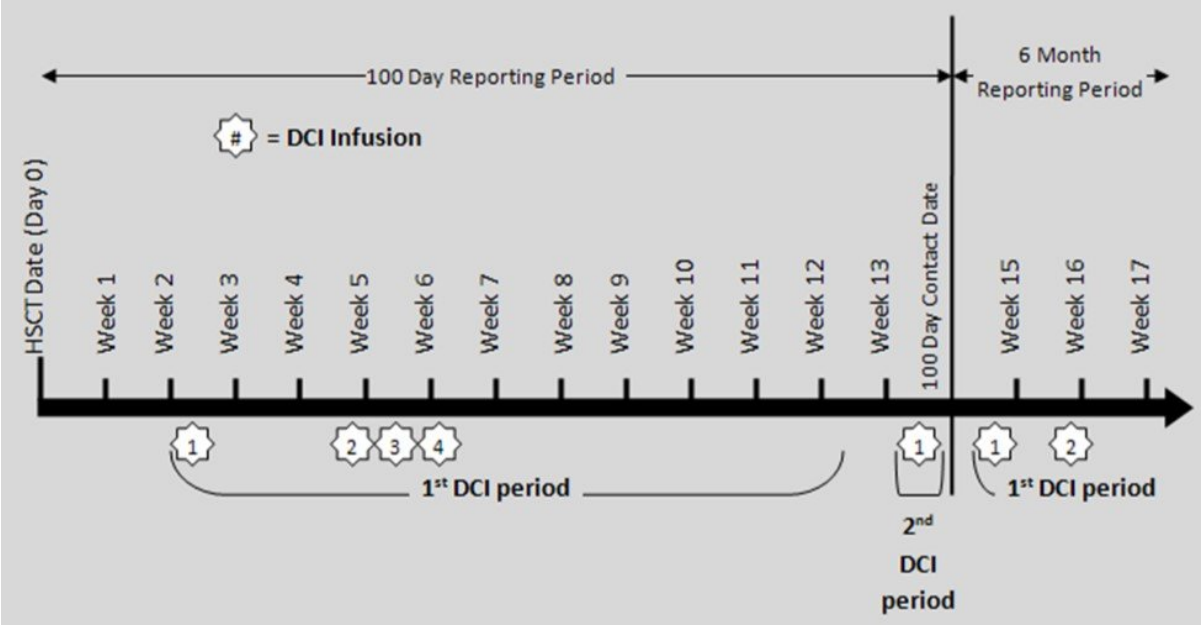
Q110-145: Donor Cellular Infusion (DCI)

The paper version of Post-TED allows the data manager to report up to three Donor Cellular Infusions (DCI) events. If more than three DCIs were performed during the reporting period, copy the page and continue to report the subsequent DCIs. The FormsNet3SM application will allow as many DCI entries as needed.

A DCI is a form of cellular therapy that involves cells from any donor, and is commonly used to create a graft-versus-leukemia (GVL) effect. The recipient does not receive a preparative regimen prior to receiving the donor cells. The types of cells used for a DCI include, but are not limited to: lymphocytes, unstimulated peripheral blood mononuclear cells, dendritic cells, and/or mesenchymal cells.

A DCI should be reported for a recipient who received cells from any donor without a preparative regimen for **any reason** other than those pertaining to the original HCT graft (e.g., no engraftment, partial or poor engraftment, loss of graft, or late graft failure). **If the recipient received an infusion due to the graft, report as a subsequent HCT, not a DCI.**

Recipients may receive a DCI over several days or weeks. A single DCI section should be completed for all infusions given within a 10-week period. See the illustration below for an example of a recipient receiving multiple DCIs:



Question 110: Date of first DCI

Indicate the date of the recipient's first DCI given in this reporting period. Continue with question 111.

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

Question 111: Total # DCI in 10 weeks

Indicate the total number of DCIs given in a 10-week period. (In example above, the total number is four.) Continue with question 112.

> **Questions 112-117: Type of cell(s)**
> **FormsNet3^{SM} application:** Check either "yes" or "no" for each option listed
> **Paper form submission:** Check all that apply

Questions 112-117: Type of cell(s)

From the list provided, indicate the type of cell(s) used for the DCI. The most common type of DCI is the DLI (Donor Lymphocyte Infusion), but there are other types of cellular therapy as indicated. If the type of cell(s) used for the DCI is not listed, choose "other" and specify the cell type used. Continue with question 118.

Questions 118-119: Indication

From the list provided, indicate the reason the cells were infused. If there was more than one reason for the DCI, check all applicable indications.

The "other" option should rarely be used. If the reason the recipient receives an infusion of cells is due to the graft (e.g., no engraftment, partial or poor engraftment, loss of graft, or late graft failure), then the infusion should be reported as a subsequent HCT, not a DCI. Continue with question 120.

Question 120: Maximum Grade of Acute Graft Versus Host Disease (GVHD)

DCI can trigger acute GVHD independent of the HCT. If the recipient develops acute GVHD as a result of the DCI, indicate the maximum grade. See question 15, Table 1 for reporting guidelines.

> **Question 121**
> This question should only be answered if the recipient receives an additional DCI after the initial 10-week period.

Question 121: If another DCI was received in this reporting period, disease status before next DCI

Indicate the recipient's disease status prior to receiving a subsequent DCI as either "CR," "not in CR," or "not assessed."

Questions 122-133: Date of second DCI

See the detailed instructions for questions 110-121.

Questions 135-146: Date of third DCI

See the detailed instructions for questions 110-121.