Instructions for Post-TED (2450) Form

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Post-TED Form.

Post-TED

Transplant centers participating in the CIBMTR must submit a Post-TED (2450) 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 but 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 SCTOD Requirements.

For more information, including information on the TED and Comprehensive Report Form Selection Algorithm, see the Data Management Guide.

The Post-TED (2450) Form must be completed at the following time points: 100 days, six months, and annually post-infusion. 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 infusion.

Reporting Data for Each Reporting Period

If the Post-TED (2450) Form is being completed for the Day 100 reporting period, answers to all questions should reflect Day +1 until the reported Day 100 contact date. For the six-month or annual evaluation, the answers to all questions should reflect since

the contact date for the prior reporting period until the reported contact date for the current reporting period.

Subsequent Infusions
If the recipient received a subsequent infusion (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 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 the CIBMTR Customer Service Center if the subsequent Pre-TED does not come due automatically.

Non-Malignant Diseases

If the HCT being reported was given to treat a non-malignant disease (as reported on the Pre-TED Disease Classification (2402) Form), do not complete the following sections of the Post-TED (2450) Form:

- Q41 – 66: Disease Assessment at the Time of Best Response to Infusion
- Q67 – 73: First Relapse or Progression Post-Infusion
- Q77 – 84: Post-Infusion Intervention for Disease
- Q85 – 91: Post-Infusion Treatment Given to Prevent Relapse or Progression
- Q92 – 95: Fecal Microbiota Transplant (FMT)
- Q96 – 98: Current Disease Status

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 no documentation exists and several unsuccessful attempts have been made to contact the recipient, they are considered lost to follow-up and the form may be marked as such using the Lost to Follow-Up tool in FormsNet3^{SM} for each reporting period in which no contact exists.

Links to Sections of Form:
Q1 – 2: Survival
Q3: Subsequent Transplant
Q4 – 6: Initial ANC Recovery
Q7 – 8: Initial Platelet Recovery
Q9 – 33: Graft-Versus-Host Disease
Q34 – 36: Liver Toxicity Prophylaxis
Q37 – 38: Veno-occlusive disease (VOD) / Sinusoidal obstruction syndrome (SOS)
Q39: New Malignancy, Lymphoproliferative or Myeloproliferative Disorder
Q40: Chimerism Studies (Cord Blood Units and Non-Malignant Diseases)
Q41 – 66: Disease Assessment at the Time of Best Response to Infusion
Q67 – 73: First Relapse or Progression Post-Infusion
Q74 – 76: Recurrence of Non-Malignant Disease
Q77 – 84: Post-Infusion Intervention for Disease
Q85 – 91: Post-Infusion Treatment Given to Prevent Relapse or Progression
Q92 – 95: Fecal Microbiota Transplant (FMT)
Q96 – 98: Current Disease Status

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

To reference the historical Manual Change History for this form, please reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
7/25/2025	Post-TED: 2450	Add	Version 8 of the 2450: Post-TED section of the Forms Instructions Manual released. Version 8 corresponds to revision 9 of the Form 2450.

Q1 – 2: Survival

The date of actual contact with the recipient to determine medical status for this follow-up report is based on a medical evaluation conducted by a clinician with responsibility for the recipient's care. Report the date of the medical evaluation performed closest to the designated time period of the form (e.g., Day+100, 6 months, or annual follow-up visit). Time windows are provided to guide selection of dates for reporting purposes.

Recipients are not always seen within the time windows used for reporting follow-up dates, and some discretion is therefore required when determining which date to report. If the recipient is not seen within the time windows, report the date closest to the date of contact within reason.

If the Post-TED Form reports a subsequent infusion (transplant or genetically modified cellular therapy), report the date of latest follow-up as the day prior to the start of the preparative regimen / systemic therapy. If no preparative regimen or conditioning / systemic therapy was given, report the day prior to infusion as the date of contact.

No Documentation of Contact Date
The contact date data field cannot be left blank and is required to be reported. In cases where the recipient passed away and there is no documentation to report the date of death, the guidelines for reporting estimated dates must be used.

Reporting Latest Follow-Up
When reporting the date of latest follow-up prior to a subsequent infusion (HCT or cellular therapy), report the date specified above regardless of whether there is actual patient contact on the date. This is an exception to the standard date of follow-up reporting to ensure all dates are captured within the sequence of forms**.**

Reporting the 1-Year Date of Contact
If this form is being completed for the 1-year reporting period, ensure the reported contact date is > Day 365. Review the 1-Year Date of Contact instructions below for additional information.

Reporting Contact Dates Reporting Instruction Overview
Review the Contact Dates Reporting Instruction Overview for additional information on reporting contact dates for recipient death, subsequent infusions, and various contact date reporting examples.

Question 1: Date of actual contact with the recipient to determine medical status for this follow-up report

Report 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. Please capture a physician evaluation that falls within the appropriate range, if possible, rather than other types of patient contact that may be closer to the actual time point. 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, complete the Survival Tool referenced in the CIBMTR Data Management Guide.

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:

Time Point	Approximate Range
100 days	+/- 15 days (Day 85-115)
6 months	+/- 30 days (Day 150-210)
1 year	+ 60 days (Day 366 – 425)
Annual reporting 2+ years	+/- 30 days (Months 23-25, 35-37, etc.)

Date of Contact and Death

In the case of recipient death, the date of death should be reported as the date of contact regardless of the time until the ideal date of contact. The date of death should be reported no matter where the death took place (inpatient at the transplant facility, at an outside hospital, in a hospice setting, or within the recipient's home).

If the death occurred at an outside location and records of death are not available, the dictated date of death within a physician note may be reported. If the progress notes detailing the circumstances of death are available, request these records. These records are useful for completing required follow-up data fields and the cause of death data fields on this form. If the exact date of death is not known, use the processed described for reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Date of Contact and Subsequent Infusion

If the recipient has a subsequent infusion (HCT or cellular therapy), the date of contact will depend on the type of subsequent infusion. If the subsequent infusion is an HCT or genetically modified cellular therapy (e.g. CAR-T), report the date of contact as the day before the preparative regimen / lymphodepleting therapy begins for the subsequent infusion. If no preparative regimen / lymphodepleting therapy is given, report the date of contact as the day before the subsequent infusion. 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 / lymphodepleting therapy) should be reported. This allows every day to be covered by a reporting period but prevents overlap between

infusion events. If the subsequent infusion is a non-genetically modified (e.g. DLI) cellular therapy infusion, report the date of contact as appropriate to the reporting period.

Review the Contact Dates Reporting Instruction Overview for additional information on reporting contact dates for recipient death, subsequent infusions, and various contact date reporting examples.

Specify the Survival Status
If the survival status is reported as **Dead**, the Recipient Death Data (2900) Form will come due. It is encouraged to complete Recipient Death Data (2900) Form along with the Post-TED (2450) Form, when applicable.

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.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q3: Subsequent Infusion

Question 3: Did the recipient receive a subsequent infusion?

Indicate if the recipient received a subsequent infusion during the reporting period. Subsequent infusions include transplant, cellular therapy, gene therapy, DLI, and 'boost' (autologous or allogeneic).

If **Yes**, complete the Indication for CIBMTR Data Reporting (2814) Form.

For more information on infusion types, review Appendix D: How to Distinguish Infusion Types.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q4 – 6: Initial ANC Recovery

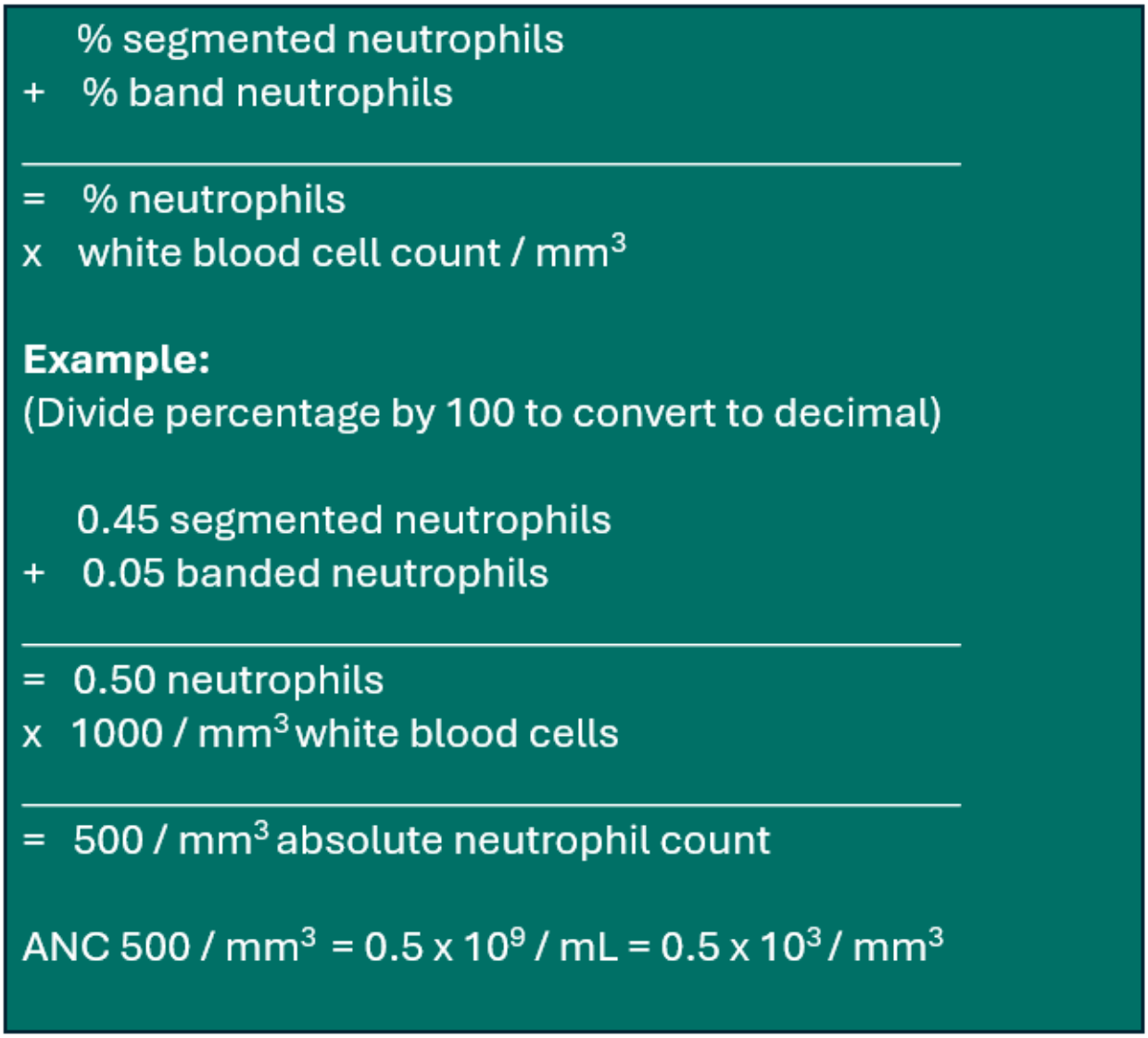
Initial ANC Recovery
The Initial ANC Recovery questions can only be completed on the 100-day, 6-month, 1-year, and 2-year follow-up forms. These questions will be skipped for all subsequent reporting periods. *Did late graft failure occur* must be answered on all follow-up forms.

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.

Combined Follow-Up
In scenarios where a cellular therapy was given after an HCT and this form is now being completed based on the subsequent cellular therapy date, these questions do not apply and are disabled.

ANC recovery is defined as an absolute neutrophil count (ANC) of ≥ 0.5 × 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 × 10^9/L. At some institutions, the laboratory reports display the ANC value once there are sufficient white blood cells to perform a differential count. At other institutions, the laboratory reports do not display the ANC, and it must be calculated from the white blood cell count (WBC) and the percent of segmented and band neutrophils (if the differential was performed on a machine, the percent neutrophils will include both segmented and band neutrophils). If the laboratory report displays an automated ANC value of exactly 0.5, the actual ANC value should be calculated from the manual differential if available. The calculated value from the manual differential will determine ANC recovery. If your institution's laboratory reports do not display the ANC value, use the following calculation to determine the ANC:

Calculating Absolute Neutrophil Count (ANC)[1]



[1] 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.

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	

Not Applicable and Previously Reported
When **Not applicable** is reported for 100-day reporting period, for all future reporting periods, select **Previously reported**.

Question 4: 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** if ANC ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L) achieved and sustained for 3 laboratory values.
- If **No** if ANC ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L) was not achieved.
- Check **Not applicable** if the recipient's ANC never dropped below 0.5 × 10^9/L at any time post-HCT. This option is only applicable in the 100-day reporting period.
- Check **Previously reported** if this is the 6-month or annual follow-up, and the initial ANC recovery has already been reported.

Question 5: Date ANC ≥ 500/mm^3 (first of 3 lab values)

Enter the first date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L). For an example of tracking ANC recovery, see the Tracking ANC Recovery example above.

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

Question 6: Did secondary graft failure occur?

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. Secondary graft failure is more often associated with allogeneic HCT than with autologous HCT. Some possible causes for late graft failure include graft rejection related to residual host immunity, persistent or progressive disease, low donor cell yield, medication side-effect, infection or GvHD.[2]

If the recipient meets the criteria of graft failure, check **Yes**.

[2] Appelbaum, F. R., & Thomas, E. D. (2009). Thomas' Hematopoietic Cell Transplantation: Stem Cell Transplantation (4th ed.). Chichester, UK: Wiley-Blackwell.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q7 – 8: Initial Platelet Recovery

Initial Platelet Recovery
The Initial Platelet Recovery section can only be completed on the 100-day, 6-month, 1-year, and 2-year follow-up forms. These questions will be skipped for all subsequent reporting periods.

Combined Follow-Up
In scenarios where a cellular therapy was given after an HCT and this form is now being completed based on the subsequent cellular therapy date, these questions do not apply and are disabled.

The following questions refer to **initial** platelet recovery following the HCT for which this form is being completed. All dates should reflect **no platelet transfusions administered for seven consecutive days.** Report the date of the first of three consecutive laboratory values ≥ 20 × 10^9/L obtained on different days, as shown in the Reporting Platelet Recovery example below. Note that platelet recovery may take place well after the recipient has returned to the referring physician for care. It is essential that information and laboratory values be obtained from the referring physician.

Transfusions temporarily increase blood cell counts. When the data is later used for analysis, it is important to be able to distinguish between a recipient whose own body was creating the cells and a recipient who required transfusions to support the counts. The following example illustrates the procedure to follow for reporting platelet recovery.

Reporting Platelet Recovery

	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

Not Applicable and Previously Reported
Not applicable and Previously reported options: When **Not applicable** is reported for 100-day reporting period, for all future reporting periods, select **Previously reported**.

Question 7: Was an initial platelet count ≥ 20 × 10^9/L achieved?

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

Check only one response:

- Select **Yes** if platelet count ≥ 20 × 10^9/ L was achieved and sustained for 3 consecutive laboratory values, obtained on different days without platelet transfusions administered in the previous 7 days
- Select **No** if platelet count was not ≥ 20 × 10^9 / L or if platelet transfusions were administered in the previous 7 days.
- Check **Not applicable**, if the recipient's platelets never dropped below 20 × 10^9/L at any time post-HCT and a platelet transfusion was never required. If the recipient's platelet count drops below 20 × 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.
- 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.

Reporting Estimated Dates
If a recipient is not seen within a month after their last platelet transfusion, an estimated date may be reported. In this case, the date seven days after the last platelet transfusion may be reported (see example A below). However, if the recipient is seen within a month of the last platelet transfusion, an estimated date should not be reported.

Question 8: 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 the Reporting Platelet Recovery example above, when determining the recovery date.

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

Reporting Scenarios

- Example 1: The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is 22 × 10^9/L on January 2, 24 × 10^9/L on January 3, and 28 × 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 × 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 an estimated date of recovery using the guidelines available in General Instructions, General Guidelines for Completing Forms.

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

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q9 – 33: Graft versus Host Disease (Allogeneic Only)

Autologous Infusions
If this was an autologous infusion, continue with the Liver Toxicity Prophylaxis section of the form. The graft-versus-host disease section should only be completed for allogeneic infusions.

GVHD Reporting Instruction Overview
Review the GVHD Reporting Instruction Overview for detailed GVHD reporting instructions and various GVHD reporting scenarios.

Question 9: Did acute GVHD develop?

Indicate whether acute GVHD developed in the reporting period.

The **Unknown** option should only be used when there is no information about the recipient’s GVHD status for the *entire* reporting period. This option should be used sparingly and only when no judgement can be made about the presence or absence of GVHD in the reporting period.

For detailed instructions regarding whether a new development of acute GVHD should be captured, review the GVHD Reporting Instruction Overview.

Question 10: Date of acute GVHD diagnosis

Report the date of clinical diagnosis of acute GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed a rash

one week prior to the physician clinically diagnosing acute skin GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of acute GVHD in the same reporting period, report the diagnosis date of the first episode of acute GVHD.

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

Persistent GVHD and Day 100 Reporting Period
Previously, reporting **Yes** for *Did acute GVHD persist since the date of last report* was not an applicable option for the Day 100 reporting period. However, if there was a prior infusion, the recipient developed acute GVHD in the last reporting period of the previous infusion *and* acute GVHD persisted into the Day 100 reporting period of the current infusion, report **Yes**, acute GVHD persisted since the date of last report.

Question 11: Did acute GVHD persist?

Indicate if acute GVHD was clinically diagnosed in the previous reporting period and persisted, with active symptoms, into the current reporting period.

The **Unknown** option should only be used when there is no information about the recipient's GVHD status for the *entire* reporting period. This option should be used sparingly and only when no judgement can be made about the presence or absence of GVHD in the reporting period.

Review the GVHD Reporting Instruction Overview for various GVHD reporting examples.

GVHD Grading and Staging Criteria
The CIBMTR will continue to collect overall grade of acute GVHD data based on the Przepiorka et al. criteria. New methods of grading acute GVHD, such as the MAGIC consortium criteria[7], can be used internally at sites; however, all data reported to the CIBMTR should be consistent with the Przepiorka et al. criteria.

[7] Harris AC, Young R, Devine S, et al. International, Multicenter Standardization of Acute Graft-versus-Host Disease Clinical Data Collection: A Report from the Mount Sinai Acute GVHD International Consortium. Biol Blood Marrow Transplant. 2015;22(1):4–10. doi:10.1016/j.bbmt.2015.09.001

Questions 12 – 18: Overall grade and organ staging of acute GVHD at diagnosis

These questions are intended to capture each organ stage and the overall grade at the time of acute GVHD diagnosis. For reporting purposes, "at diagnosis" is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic). The acute GVHD grading scale is based on **clinical**

evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on *clinical* severity, not histological severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, **overall grading remains clinical** and is based on the criteria published by Przepiorka et al., *Bone Marrow Transplant* 1995; 15(6):825-8, see the GVHD Grading and Staging table below.

Report the overall grade and organ staging at the diagnosis of acute GVHD. Review the GVHD Reporting Instruction Overview for additional information and on the criteria for each organ staging and grading.

Questions 19 – 26: Maximum overall grade of acute GVHD and maximum organ stage of acute GVHD

These questions are intended to capture the maximum organ stage of each organ involved in acute GVHD as well as the overall maximum grade of acute GVHD within the reporting period. For detailed reporting instructions about reporting the maximum grade and organ staging of acute GVHD, review the GVHD Reporting Instruction Overview.

Question 27: Did chronic GVHD develop?

Indicate whether a new clinical diagnosis of chronic GVHD was documented during the reporting period.

The **Unknown** option should only be used when there is no information about the recipient's GVHD status for the *entire* reporting period. This option should be used sparingly and only when no judgement can be made about the presence or absence of GVHD in the reporting period.

For detailed instructions on whether a new development of chronic GVHD should be captured, review the GVHD Reporting Instruction Overview.

Question 28: 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 (i.e., the recipient developed shortness of breath one month prior to the clinical diagnosis of pulmonary chronic GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of chronic GVHD in the same reporting period, report the diagnosis date of the first episode of chronic GVHD.

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

Persistent GVHD and Day 100 Reporting Period
Previously, reporting **Yes** for *Did chronic GVHD persist* was not an applicable option for the Day 100 reporting period. However, if there was a prior infusion, the recipient developed chronic GVHD in the last reporting period of the previous infusion *and* chronic GVHD persisted into the Day 100 reporting period of the current infusion, report **Yes**, chronic GVHD persisted since the date of last report.

Question 29: Did chronic GVHD persist?

Indicate if chronic GVHD was clinically diagnosed in the previous reporting period and persisted, with active symptoms, into the current reporting period. Do not report quiescent or inactive chronic GVHD, or a prior history of GVHD. See instructions above on reporting a chronic GVHD flare.

The **Unknown** option should only be used when there is no information about the recipient's GVHD status for the *entire* reporting period. This option should be used sparingly and only when no judgement can be made about the presence or absence of GVHD in the reporting period.

Review the GVHD Reporting Instruction Overview for various GVHD reporting examples.

Question 30: Maximum grade of Chronic GVHD *(according to best clinical judgement)*

Report the maximum chronic GVHD involvement, based on the opinion of the clinician (i.e., clinical grade), since the date of the last report. The intent of this question is to capture the maximum grade based on the best clinical judgment. If both the global severity score and the score based on the clinician's opinion is documented, report the clinician score. If the maximum clinical grade is not documented, request documentation from the recipient's primary care provider.

Additional guidelines on reporting the maximum grade of chronic GVHD are outlined in the GVHD Reporting Instruction Overview.

Question 31: Date of maximum grade of chronic GVHD

Report the date of maximum chronic GVHD involvement, based on clinical grade, during the current reporting period. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date.

Review the GVHD Reporting Instruction Overview for various GVHD reporting examples.

Question 32 – 33: GVHD treatment

These questions are intended to capture if the recipient was still receiving systemic steroids (steroid dose ≤ 10 mg / day for adults, < 0.1 mg / kg / day for children, excluding steroids for adrenal insufficiency) and non-steroid immunosuppressive agents for GVHD on the contact date. Review the GVHD Reporting Instruction Overview for reporting instructions to these questions.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q34 – 36: Liver Toxicity Prophylaxis

Liver Toxicity Prophylaxis
Liver Toxicity Prophylaxis section can only be completed on the 100 day and 6-month follow-up forms. These questions will be skipped for all subsequent reporting periods.

Question 34: Was specific therapy used to prevent liver toxicity?

Liver toxicities in transplant patients may be related to drugs / treatments, infection, GVHD, iron overload, cirrhosis, or sinusoidal obstructive syndrome (SOS) / veno-occlusive disease (VOD). Agents such as ursodiol may be given as prophylaxis against one or more of these transplant-related liver injuries. Agents given to prevent liver toxicity will generally be started prior to or during the conditioning regimen and may be continued well after transplant.

Indicate whether the recipient received any therapy intended to prevent liver toxicity during the current reporting period. For the Day 100 reporting period, this includes any 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.

Indicate if liver toxicity prophylaxis was given in the reporting period.

Questions 35 – 36: Specify therapy *(check all that apply)*

Select the agent(s) given during the reporting period to prevent liver toxicity, including therapy given during the conditioning regimen. Only report agents given to prevent liver toxicities, not those given to treat a diagnosed liver injury or toxicity. If **Other** therapy is reported, specify agent(s).

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q37 – 38: Veno-Occlusive Disease (VOD) / Sinusoidal Obstruction Syndrome (SOS)

VOD / SOS
VOD / SOS section can only be completed on the 100 day and 6-month follow-up forms. These questions will be skipped for all subsequent reporting periods.

Veno-occlusive disease (VOD) / Sinusoidal obstruction syndrome (SOS) occurs following injury to the hepatic venous endothelium, resulting in hepatic venous outflow obstruction due to occlusion of the hepatic venules and sinusoids. This typically results in a distinctive triad of clinical signs including hepatomegaly with right upper quadrant tenderness, third space fluid retention (e.g., ascites), and jaundice with a cholestatic picture. For more information on VOD / SOS including diagnostic criteria, refer to the VOD / SOS .

Questions 37 – 38: Did veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS) develop since the date of last report?

Indicate whether VOD / SOS was diagnosed during the reporting period. If **Yes**, report the date of diagnosis.

If VOD/SOS was reported on the Post-TED (2450) Form, the Veno-occlusive Disease (VOD) / Sinusoidal Obstruction Syndrome (SOS) (2553) Form must also be completed.

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

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q39: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder

Combined Follow-Up
In scenarios where a cellular therapy was given after an HCT and this form is now being completed based on the subsequent cellular therapy date, these questions do not apply and are disabled.

Question 39. Did a new malignancy, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the HCT or cellular therapy was performed? (include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders)

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

New malignancies, lymphoproliferative disorders, or myeloproliferative disorders include but are not limited to:

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

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-infusion medical history
- Breast cancer found in other (i.e., opposite) breast (report as relapse)

- Post-infusion cytogenetic abnormalities associated with the pre-infusion diagnosis (report as relapse)
- Transformation of MDS to AML post-infusion (report as disease progression)

Post-Transplant Lymphoproliferative Disorder (PTLD)
PTLD should be reported as a new malignancy if it was confirmed via a biopsy (treatment not required) or suspected to be PTLD and treated.

Recurrent Skin Cancers
For most malignancies, do not report recurrence, progression or transformation of the recipient's primary disease (disease for which the infusion was performed) or relapse of a prior malignancy in the "New Malignancy" section.
For example, a recipient was diagnosed with basal cell skin cancer on the neck four months post-infusion 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 as a 'new malignancy' on the Post-TED (2450) Forms.

If a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was diagnosed during the reporting period, report **Yes** and complete the Subsequent Neoplasms (3500) Form, which will come due.

The **Previously reported** option should only be used if the same malignancy has already been reported on a Subsequent Neoplasms (3500) Form that was made do on demand. See examples below. If it is unclear when to use this option, contact CIBMTR Center Support if there are questions.

- Example 1: A recipient developed a new malignancy at Day +68 and is reported at the time the Day 100 Post-TED (2450) Form is completed. In this scenario, report Yes, the recipient developed a new malignancy, and a Subsequent Neoplasms (3500) form will be completed to report the new malignancy information. For all future reporting periods, select **No**.
- Example 2: A recipient developed a new malignancy during the seven-year reporting period and the transplant center decided to create the Subsequent Neoplasms (3500) form as an unscheduled form in FormsNet3^{SM} to report the new malignancy information immediately since a Post-TED (2450) Form for seven-year reporting period will not come due. When the eight-year Post-TED (2450) Form is completed, **Previously reported**, will be reported since a prior Subsequent Neoplasms (3500) form has already been submitted for the new malignancy.
- Example 3: A recipient was diagnosed with basal cell skin cancer on the neck in the one-year reporting period and two months later, within the same reporting period, there was a diagnosis of basal cell located on the nose. The lesion on the nose is not considered a metastasis from the neck, but a new discreet lesion. Report **Yes**, there was a new malignancy on the Post-TED (2450) Form, and a

single Subsequent Neoplasms (3500) Form will come due to report one of the basal cell malignancies. Create a second Subsequent Neoplasms (3500) form to report the other basal cell malignancy as these are discreet episodes.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q40: Chimerism Studies (Corb Blood Units and Non-Malignant Diseases)

Chimerism Studies
This section relates to chimerism studies from allogeneic infusions using cord blood units, or for allogeneic infusion recipients whose primary disease is any non-malignant disease. If this was an autologous infusion or an allogeneic infusion using a bone marrow or PBSC product, and / or an allogeneic infusion whose primary disease for infusion is a malignant disease continue to the disease assessment section.

Questions 40: Were chimerism studies performed?

Indicate whether chimerism studies were performed within the reporting period. If **Yes**, a Chimerism Essential Data (2451) Form will come due.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q41 – 66 - Disease Assessment at the Time of Best Response to Infusion

Malignant Diseases Only
Only complete Disease Assessment at the Time of Best Response to Infusion questions if the infusion being reported was given to treat a malignant disease. If the infusion being reported was given to treat a non-malignant disease, leave these questions blank. FormsNet3^{SM} should enable / disable this section based on the primary disease reported on the Disease Classification (2402) Form. Contact CIBMTR Customer Support if it is believed FormsNet3^{SM} is incorrectly enabling / disabling these fields.

Combined Follow-Up
In scenarios where both HCT and cellular therapy forms are being completed and a disease specific form is being completed for the cellular therapy, disease assessment at time of best response is not reported on this form and these questions are disabled. It will be captured on the corresponding disease form.

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 and does not include response to treatment given for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease.

If the recipient receives therapy for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease, the response to that additional therapy should not be reported in this section. The best response prior to the therapy should be reported. For subsequent reporting periods where the best response prior to the start of unplanned therapy was reported, if a CR was achieved prior to relapse / progression, the date of best response will be reported as **Previously reported**. If a CR was not achieved prior to the administration of therapy, the best response will be reported as **Not evaluated**. Refer to the best response to infusion questions below for more information.

Reporting Complete Remission (CR) Post-HCT
Complete remission (CR) criteria vary by disease and are outlined in the CIBMTR Forms Instructions Manual. Please refer to the appropriate disease response criteria section of the Forms Instructions Manual and review the criteria to report CR.

Tandem Transplants
For recipients receiving a tandem transplant, the best response to the prior infusion (i.e., HCT #1 of the tandem) depends on the pre-infusion disease status.

- If the recipient was in complete remission at the time of HCT #1, report the best response to transplant as **Continued complete remission (CCR).**

- If the recipient was not in complete remission at the time of HCT #1, and ***no*** disease assessments (including labs and / or physician's exams) occurred in the reporting period, between HCT #1 and HCT #2 of their tandem transplant, report **Not evaluated**. However, ensure the best response to infusion and the current disease status are reported consistently
- If the recipient was not in complete remission at the time of HCT #1, and achieved complete remission prior to HCT #2 of their tandem transplant, report **Complete remission**, the date which complete remission was achieved
- If the recipient was not in complete remission at the time of HCT #1 and did not achieve complete remission in response to HCT #1 and prior to HCT #2 of their tandem transplant, report **Not in complete remission (NCR)**

Review the example below for additional information:

- Example 1: A recipient with neuroblastoma is not in complete remission prior to transplant, in the 100-day reporting period the recipient receives a tandem transplant. Between HCT 1 and HCT 2 the only disease assessment performed was a clinical evaluation. In this case either option would be appropriate to answer for the best response: **Not evaluated** or **Not in complete remission (NCR)** and **No disease detected but incomplete evaluation to establish CR.**

Continued Complete Remission (CCR)

Continued Complete Remission (CCR) should be reported for all recipients who were already in CR at the start of the preparative regimen.

Question 41: Compared to the disease status prior to the preparative regimen, what was the best response to infusion? *(Include response to any therapy given for post-infusion maintenance or consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease)*

Report the best response to infusion, using the following guidelines:

- **Continued complete remission (CCR)**: The recipient was already in CR at the start of the preparative regimen.
- **Complete remission (CR)**: The recipient achieved CR post-infusion, excluding unplanned therapy (i.e., therapy given for relapsed, persistent, progressive, measurable residual disease, or decreased / loss of chimerism).
- **Not in complete remission**: The recipient has not achieved a post-infusion CR.
- **Not evaluated**: The not evaluated option should be used in two scenarios:
    - The recipient's disease was not evaluated post-infusion
        - This should be rare as this would indicate no tests, radiological, laboratory, or clinical assessment, was not performed at *any time* in the reporting period.

- The recipient never achieved a post-infusion CR and started unplanned therapy (including treatment given for decreased / loss of chimerism or measurable residual disease), in a previous reporting period).

Question 42: 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, using the guidelines below:

- **No disease detected but incomplete evaluation to establish CR**: The most recent assessments have shown resolution of disease, not all assessments required to report complete remission have been completed or the recipient has not previously achieved a post-infusion **Complete remission** but does not have any disease assessments performed within the reporting period.
- **Disease detected**: The most recent radiological or clinical / hematological assessment detects disease
  - Persistence of abnormalities by molecular, cytogenetic, or flow cytometry assessments does not constitute 'disease detected' and should not be reported as disease detected for this question.

Review the examples below for additional information:

- Example 2: A recipient with multiple myeloma goes to transplant in VGPR, without a bone marrow showing < 5% plasma cells completed prior to transplant. Post-transplant serum and urine electrophoreses and immunofixations are negative. However, no bone marrow biopsy is performed within the 100-day reporting period. In this case, **Not in complete remission** should be selected for the best response, and **No disease detected but incomplete evaluation to evaluation to establish CR** for specifying the disease status if not in complete remission data field.
- Example 3: A recipient with AML goes to transplant in **Primary induction failure**. Post-transplant, they recover their blood counts, but had circulating blasts noted on peripheral blood differential. They expire due to persistent disease with their last CBC performed on their date of death showing circulating blasts. In this case, **Not in complete remission** should be selected for the best response to HCT, and **Disease detected** for specifying the disease status if not in complete remission data field.
- Example 4**:** 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 0.5×10^9/L with no blasts detected on their differential. A bone marrow biopsy was not performed between transplant and the date of death. In this case, **Not in complete remission** should be selected for the best response to HCT, and **No disease detected by incomplete evaluation to establish CR** for specifying the disease status if not in complete remission data field.

Question 43: Was the date of best response previously reported?

Indicate whether complete remission was reported in a previous reporting period. This question does not apply if the best response is **Not in complete remission**.

Question 44: Date of best response

Report the date complete remission was achieved. This date should fall after the infusion date 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 the clinical / hematologic complete remission criteria for the recipient's primary disease for infusion.

Disease Assessment at Time of Best Response

The disease assessment questions (i.e., molecular, flow cytometry, cytogenetic, radiologic and clinical / hematologic assessments) refer to disease assessments performed at the time of best response (*Date assessed*). The following guidelines should be used to determine whether testing was performed at the time of best response:

- If the recipient's best response is **Not in Complete Remission**, report the latest assessment performed during the reporting period. If the recipient never achieved a CR and started treatment for decreased / loss of chimerism, measurable residual disease, persistent disease, relapse, or progression, report the most recent assessments prior to the start of therapy. Review examples 9 and 10 below.
- If the recipient's best response is **Complete Remission**, report testing performed closest to the date of best response (*Date assessed*) and within the time windows in the Disease Assessment Time Windows table.

Disease Assessment Time Windows

Follow-Up Form	Approximate Range
100 Day	+/- 15 days of date of best response (*Date assessed*)
6 Month	+/- 15 days of date of best response (*Date assessed*)
Annual	+/- 30 days of date of best response (*Date assessed*)

Disease Assessment Reporting Scenarios

- Example 5: A recipient receives a transplant on 1/1/2015 for multiple myeloma in Partial remission. Prior to infusion, FISH testing detects an IGH rearrangement associated with the recipient's primary disease. During the 100-day reporting

period, the recipient achieves a Very good partial remission. FISH testing is only performed on 2/1/2015, which is positive for the previously detected IGH rearrangement. The 100-day date of contact is 4/15/2015. In this case, report the recipient was **Not in complete remission** on the 100 Day Post-TED (2450) Form and report FISH testing was performed on 2/1/2015. When the best response is **Not in complete remission** report the most recent testing performed during the reporting period (assuming treatment was not started for decreased / loss of chimerism, measurable residual disease, persistent disease, progressive / relapsed, disease during the reporting period – see example 6).

- Example 6: A recipient receives a transplant on 1/1/2015 for multiple myeloma in Partial remission. Prior to infusion, FISH testing detects an IGH rearrangement associated with the recipient's primary disease. During the 100-day reporting period, the recipient has disease progression and starts treatment on 3/1/2015. FISH testing is performed on 2/1/2015 and 3/15/2015. Both tests are positive for the previously detected IGH rearrangement. The 100-day date of contact is 4/15/2015. In this case, report the recipient was **Not in complete remission** on the 100 Day Post-TED (2450) Form and report FISH testing was performed on 2/1/2015. When the best response is **Not in complete remission** report the most recent testing performed during the reporting period and prior to any unplanned therapy.
    - *Note***:** For all subsequent reporting periods, report **Not evaluated** for the best response to infusion. If unplanned treatment was started in a prior reporting period, the recipient's best response to the infusion can no longer be assessed.
- Example 7: A recipient receives a transplant on 1/1/2015 for AML in Primary induction failure. Prior to infusion, molecular testing confirms the recipient's disease is FLT3 positive. On 2/1/2015, the recipient achieves a morphologic remission, but FLT3 is not tested at that time. Later, on 2/10/2015, molecular testing is performed and confirms the recipient is FLT3 negative. In this case, the report the recipient achieved a **Complete remission** on 2/1/2015 on the 100 Day Post-TED (2450) Form and report molecular testing was performed at the time of best response as testing was done within 15 days of 2/1/2015.
- Example 8: A recipient receives a transplant on 1/1/2015 for AML in Primary induction failure. Prior to infusion, molecular testing confirms the recipient's disease is FLT3 positive. On 2/1/2015, the recipient achieves a hematologic remission, but FLT3 is not tested at that time. Later, on 3/1/2015, molecular testing is performed and confirms the recipient is FLT3 negative. In this case, the report the recipient achieved a **Complete remission** on 2/1/2015 on the 100 Day Post-TED (2450) Form and report no molecular testing was performed at the time of best response as testing was not done within 15 days of 2/1/2015.
- Example 9: A recipient receives a transplant on 1/1/2015 for NHL in Stable disease. During the 100 Day reporting period, a PET / CT was performed on Day 60, confirming stable disease but then on Day 95, another PET / CT was performed and showed progression. As a result, therapy for progression began on Day 100. The best response to infusion for the Day 100 reporting period

would be reported as **Not in complete remission – disease detected** and report **Yes**, radiologic assessments were performed with the Day 60 PET / CT, as this is the most recent scan prior to disease progression.

- Example 10: A recipient receives a transplant on 1/1/2020 for IgA Kappa Multiple Myeloma in Stable disease. During the 100 Day reporting period, the first set of myeloma labs on Day 29, 1/30/2020, show Progressive disease. Myeloma labs repeated on Day 60 and Day 100 also showed disease progression. As a result, therapy is planned to be given, starting in the 6-month reporting period, on Day 110. The best response to infusion for the Day 100 reporting period would be reported as **Not in complete remission – disease detected** and report **Yes**, clinical / hematologic assessments were performed with the Day 100 myeloma labs, as this is the most recent testing in the reporting period. In cases where the first assessment post-infusion shows progression, report the last assessment prior to the start of treatment. If treatment doesn't start until the next reporting period, report the last assessment in the current reporting period.

Molecular Testing
The molecular testing questions are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH, may identify molecular marker results but should **not** be reported in the molecular section of the Post-TED (2450) Form. Abnormalities identified by karyotyping, FISH, or microarray should only be reported in the cytogenetic section of the Post-TED (2450) Form.

Question 45: Was the disease status assessed via molecular markers? (e.g. PCR, NGS)

Molecular assessment involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection and can indicate known genetic abnormalities associated with the disease for which the HCT was performed. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD). Molecular marker results identified by FISH or chromosomal microarray assessments should not be reported as molecular testing.

- If the recipient's best response is **Not in Complete Remission**, report **Yes** if assessments were performed, prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. Report **No** if assessments were not performed prior to any unplanned therapy.
- If the recipient's best response is **Complete Remission**, report **Yes** if disease assessments were performed within the time windows listed in the *Disease*

Assessments Time Windows table above. If testing was not performed within the applicable time window, report **No**.

Question 46: Date assessed

If the best response is **Complete remission**, report the date of testing performed nearest to the date of best response (within the time windows listed in the *Disease Assessments Time Windows* table above) and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease, if applicable.

If the best response is **Not in complete remission**, report the date of the most recent testing performed during the reporting period and prior to progression or treatment for persistent disease, if applicable.

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 47: Was disease detected?

Report whether the recipient's primary disease was detected via assessment by molecular marker. This question may be reported as **Yes** even when **Not in complete remission – no disease detected but incomplete evaluation to establish CR** is reported as the best response. In order to be considered positive for disease, the assay must detect a number of copies of the molecular marker exceeding the threshold for sensitivity of the assay, for a quantitative study. However, do note that presence of only a single marker among numerous tested is sufficient to indicate disease detected.

Question 48: Was the disease status assessed via ClonoSEQ®?

ClonoSEQ® assessments measure minimal residual disease (MRD) at the molecular level through proprietary bioinformatics and advancements in next-generation sequencing (NGS). These assessments can be used to identify a recipint's tumor-associated DNA sequences, predict long term outcomes, assess treatment response, detect early relapse, inform changes to treatment, and monitor a recipient's disease burden over time.

If the recipient's best response is **Not in Complete Remission**, report **Yes** if assessments were performed, prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. Report **No** if assessments were not performed prior to any unplanned therapy.

If the recipient's best response is **Complete Remission**, report **Yes** if disease assessments were performed within the time windows listed in the *Disease*

Assessments Time Windows table above. If testing was not performed within the applicable time window, report **No**.

Question 49: Date assessed

If the best response is **Complete remission**, report the date of testing performed nearest to the date of best response (within the time windows listed in the *Disease Assessments Time Windows* table above) and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

If the best response is **Not in complete remission**, report the date of the most recent testing performed during the reporting period and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

Report the date of specimen collection for ClonoSEQ® 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 50: Was disease detected?

Report whether the recipient's primary disease was detected by ClonoSEQ® on the date reported. This question may be reported as **Yes** even when **Not in complete remission – no disease detected but incomplete evaluation to establish CR** is reported as the best response.

Question 51: Was the disease status assessed via flow cytometry?

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. This allows for the detection of abnormal cell populations for some diseases.

If the recipient's best response is **Not in Complete Remission**, report **Yes** if assessments were performed, prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. Report **No** if assessments were not performed prior to any unplanned therapy.

If the recipient's best response is **Complete Remission**, report **Yes** if disease assessments were performed within the time windows listed in the *Disease Assessments Time Windows* table above. If testing was not performed within the applicable time window, report **No**.

Question 52: Date assessed

If the best response is **Complete remission**, report the date of testing performed nearest to the date of best response (within the time windows listed in the *Disease Assessments Time Windows* table above) and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

If the best response is **Not in complete remission**, report the date of the most recent testing performed during the reporting period and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

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 53: Was disease detected?

Report whether the recipient's primary disease was detected by flow cytometry. Report **Yes** if an abnormal cell population associated with the recipient's primary 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. This question may be reported **Yes** even when **Not in complete remission – no disease detected but incomplete evaluation to establish CR** is reported as the best response.

Question 54: 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.

If the recipient's best response is **Not in Complete Remission**, report **Yes** if assessments were performed, prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. Report **No** if assessments were not performed prior to any unplanned therapy.

If the recipient's best response is **Complete Remission**, report Yes if disease assessments were performed within the time windows listed in the *Disease*

Assessments Time Windows table above. If testing was not performed within the applicable time window, report **No**.

Question 55: 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. Chromosomal microarrays / chromosomal genomic arrays should be reported as FISH assessments.

If the recipient's best response is **Not in Complete Remission**, report **Yes** if assessments were performed, prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. Report **No** if assessments were not performed prior to any unplanned therapy.

If the recipient's best response is **Complete Remission**, report **Yes** if disease assessments were performed within the time windows listed in the *Disease Assessments Time Windows* table above. If testing was not performed within the applicable time window, report **No**.

Question 56: Date assessed

If the best response is **Complete remission**, report the date of testing performed nearest the date of best response (within the time windows listed in the *Disease Assessments Time Windows* table above) and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

If the best response is **Not in complete remission**, report the date of the most recent testing performed during the reporting period and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

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 57: Was disease detected?

Report whether the recipient's primary disease was detected by FISH testing on the date reported. This question may be reported as **Yes** even when **Not in complete remission – no disease detected but incomplete evaluation to establish CR** is reported as the best response.

Question 58: Was the disease status assessed via karyotyping?

Report **No** if karyotyping studies were not performed during the current reporting period.

If the recipient's best response is **Not in Complete Remission**, report **Yes** if assessments were performed, prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. Report **No** if assessments were not performed prior to any unplanned therapy.

If the recipient' best response is **Complete Remission**, report **Yes** if disease assessments were performed within the time windows in the Disease Assessments Time Windows table above. If testing was not performed within the applicable time window, report **No**.

Question 59: Date assessed

If the best response is **Complete remission**, report the date of testing performed nearest the date of best response (within the time windows listed in the *Disease Assessments Time Windows* table above) and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

If the best response is **Not in complete remission**, report the date of the most recent testing performed during the reporting period and prior to progression or treatment for persistent disease, if applicable.

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 60: Was disease detected

Report whether the recipient's primary disease was detected by karyotyping on the date reported. 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. This question may be reported as **Yes** even when **Not in complete remission – no disease detected but incomplete evaluation to establish CR** is reported as the best response.

Question 61: 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.

If the recipient's best response is **Not in Complete Remission**, report **Yes** if assessments were performed, prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. Report **No** if assessments were not performed prior to any unplanned therapy.

If the recipient's best response is **Complete Remission**, report **Yes** if disease assessments were performed within the time windows listed in the *Disease Assessments Time Windows* table above. If testing was not performed within the applicable time window, report **No**.

Question 62: Date assessed

If the best response is **Complete remission**, report the date of the assessment performed nearest the date of best response (within the time windows listed in the *Disease Assessments Time Windows* table above) and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

This date may match the date CR was achieved reported in *Date assessed* for the best response for recipients with lymphomas, solid tumors, or other diseases with imaging criteria for reporting CR.

If the best response is **Not in complete remission – no disease detected but incomplete evaluation to establish CR**, report the last assessment performed in the reporting period and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

If the best response is **Not in complete remission – disease detected**, report the most recent radiological testing performed in the reporting period that detects disease and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease, if applicable. If disease was not detected by this method report the date of the most recent radiological testing performed **and** prior to any unplanned therapy.

If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms for information about reporting partial or unknown dates.

Question 63: Was disease detected?

Report whether the recipient's primary disease was detected by radiologic assessment on the reported date.

Reporting 'No' for Clinical / Hematologic Assessments
The **No** option should rarely be used as this would indicate *no* clinical / hematologic

assessments (including labs and physician's exams) were not performed at the time of best response.

Question 64: Was the disease status assessed by clinical / hematologic assessment?

Clinical / hematologic disease assessments are 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 answering this question.

If the recipient's best response is **Not in Complete Remission**, report **Yes** If assessments were performed prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. Report **No** If assessments were not performed prior to any unplanned therapy.

If the recipient' best response is **Complete Remission**, report **Yes** if disease assessments were performed within the time windows in the *Disease Assessment Time Windows* table above. If testing was not performed within the applicable time window, report **No**.

Question 65: Date assessed

If the best response is **Complete remission**, report the date of the assessment performed nearest the date of best response (within the time windows listed in the *Disease Assessments Time Windows* table above) and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease. This will likely match the date CR reported in Date assessed for the best response, since complete remission criteria generally require clinical or hematologic assessment to confirm.

If the best response is **Not in complete remission – no disease detected but incomplete evaluation to establish CR**, report the last assessment performed in the reporting period and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease.

If the best response is **Not in complete remission – disease detected**, report the most recent assessment performed in the reporting period that detects disease and prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease, if applicable. If disease was not detected by this method report the date of the most recent assessment performed **and** prior to any treatment for decreased / loss of chimerism, measurable residual disease, persistent, progressive, or relapsed disease, if applicable.

If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms for information about reporting partial or unknown dates.

Question 66: Was disease detected?

Report whether the primary disease was detected by clinical / hematologic assessments. In general, if the clinical / hematologic assessment date is the same as the reported *Date assessed* for the best response, for recipients achieving complete remission in the reporting period, the answer to this question should be **No**.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q67 – 73: First Relapse or Progression Post-Infusion

Malignant Diseases Only
Only complete the relapse or progression post-infusion questions if the infusion being reported was given to treat a malignant disease. If the infusion being reported was given to treat a non-malignant disease, leave these questions blank. Intervention for relapsed, persistent, or progressive disease questions must be completed regardless of disease type. FormsNet3^{SM} should enable / disable this section based on the primary disease reported on the Disease Classification (2402) Form. Contact CIBMTR Center Support if it is believed FormsNet3^{SM} is incorrectly enabling / disabling these fields.

Combined Follow-Up
In scenarios where both HCT and cellular therapy forms are being completed and a disease specific form is being completed for the cellular therapy, relapse or progression post-infusion is not reported on this form and these questions are disabled. It will be captured on the corresponding disease form.

Question 67 – 68: Did the recipient experience a relapse or progression by any method(s) of assessment post-infusion?

Report if the recipient has experienced a first relapse or progression by *any* method (molecular, flow cytometry, cytogenetic, radiological, or clinical / hematologic) post-

infusion. If **Yes**, select all methods of relapse and / or progression detection in the reporting period

If the *first* relapse or progression (by *any* method) occurred in a previous reporting period, select **Previously reported**.

See below for definitions and examples of each method of detection:

- **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. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers, Sanger sequencing, and next generation sequencing. This option should also be selected if the recipient relapsed / progressed by ClonoSEQ®.
- **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.
- **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.
- **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.
- **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.

Questions 69 – 73: First date of relapse or progression

For each method of assessment that detected a relapse or progression in the reporting period, report the assessment date. If relapse / progression was detected multiple times

by the assessment in the reporting period, report the first assessment detecting relapse / progression.

If the exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q74 – 76: Recurrent of Non-Malignant Disease

Non-Malignant Diseases Only
Only complete the recurrent of non-malignant disease section if the HCT being reported was given to treat a non-malignant disease. If the HCT being reported was given to treat a malignant disease, these questions will be skipped. FormsNet3^{SM} should enable / disable this section based on the primary disease reported on the Pre-TED Disease Classification (2402) Form. Contact the CIBMTR Center Support if you believe FormsNet3^{SM} is incorrectly enabling / disabling these fields.

Combined Follow-Up
In scenarios where both HCT and cellular therapy forms are being completed and a disease specific form is being completed for the cellular therapy, recurrent of non-malignant disease is not reported on this form and these questions are disabled. It will be captured on the corresponding disease form.

Question 74: Was there recurrence of the primary non-malignant disease post-infusion?

Indicate if the recipient had recurrence of the non-malignant disease the reporting period. The determination of recurrent disease is based on the treating physician's clinical judgment.

Question 75 – 76: Was the date of recurrence previously reported?

This question is intended to capture the first instance of disease recurrence. Specify if the date of recurrent was previously reported.

If the first recurrence date was reported in a prior reporting period, select **Yes**. If the first instance of recurrence is within the current reporting period, select **No** and report the date of the assessment that first showed recurrent disease.

If the exact date is not known, refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q77 – 84: Post-Infusion Intervention for Disease

Combined Follow-Up
In scenarios where both HCT and cellular therapy forms are being completed and a disease specific form is being completed for the cellular therapy, intervention is not reported on this form and these questions are disabled. It will be captured on the corresponding disease form.

Question 77: Was intervention given for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease? *(Do NOT include any maintenance and consolidation therapy)*

Indicate whether therapy was given during the reporting period for decrease / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease. Do not include therapy given for maintenance or post-infusion consolidation. Any post-infusion therapy included as part of the initial transplant protocol is reported in a subsequent section below.

Relapse / progression treatment given in the same reporting period where the first relapse / progression occurred is only reported. If treatment for relapse / progression started after the reporting period in which relapse / progression was first reported in, this section is disabled.

See the *Intervention reporting scenarios* provided below for further clarification.

Question 78: Specify reason for which intervention was given *(check all that apply)*

Report the reason why therapy for decreased / loss of chimerism, measurable residual disease, persistent disease, progressive disease, or relapsed disease was given in the reporting period. Select all the indications. See below for definitions of each indication. If the intent of the therapy is unclear, seek physician clarification.

- **Decreased / loss of chimerism:** Chimerism is the percentage of donor immune cells in a recipient compared to the percentage of recipient immune system cells. Treatment may be given for decreasing chimerism to prevent relapsed disease.
- **Measurable Residual Disease:** Recipient is in hematologic CR but has evidence of disease by more sensitive assessments including molecular, flow cytometry or cytogenetic methods.
- **Persistent Disease:** The recipient was in primary induction failure or relapse at the time of infusion and has not achieved a hematologic CR post-infusion.
- **Progressive Disease:** The recipient has not achieved a complete remission and has worsening disease burden.
- **Relapsed Disease:** The recipient was in CR at the time of infusion, or the recipient achieved a CR post-infusion. In either case, treatment is administered for a relapse which occurred post-infusion.

See the *Intervention reporting scenarios* provided below for further clarification.

Question 79: Specify the method(s) of detection for which intervention was given *(check all that apply)*

Indicate the methods detecting the reason for which therapy for decreased / loss of chimerism, measurable residual disease, persistent disease, progressive disease, or relapsed disease was administered (as reported above). Indicate all methods of detection; given that the assessment was performed prior to the start of the intervention(s) and was consistent with the rationale reported above. There may be scenarios 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 this case, the method of disease assessment should be reported.

If multiple therapies were given during the reporting period for different reasons (i.e., the recipient initially receives treatment for persistent disease and subsequently receives different treatment for progressive disease during the same reporting period), select any methods of detection confirming the reason above. See the *Intervention reporting scenarios* provided below for further clarification.

If assessment by that method was not performed or was performed and not consistent with the reason for which intervention was given reported above, do not report the disease assessment.

Question 80: Date intervention started

Report the date therapy was started for the reason specified above; if multiple instances, cycles, or lines of therapy are administered, report the date of the first treatment. If treatment was started in a prior reporting period and continues into the current reporting period, report the original therapy start date (prior to the start of the current reporting period) and override the validation error in FormsNet3^{SM} using the code "verified correct." If therapy was stopped in a prior reporting period and restarted (or a new therapy was started) during the current reporting period, report the earliest date treatment was administered during the current reporting period. See the *Intervention reporting scenarios* provided below for further clarification.

Intervention Reporting Scenarios

- Example 1: A recipient with NHL in CR at the time of infusion has a relapse during the 100 day reporting period. Relapse was detected by a PET scan and a lymph node biopsy. Following these assessments, Rituximab was started on 5/1/2016. The disease did not respond to this therapy prompting a switch to Brentuximab on 6/1/2016. The 100 Day date of contact is 6/15/2016.
    - 100 Day Post-TED Form
        - *Was intervention given for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease*: Report **Yes** to indicate therapy was given for relapsed disease during this reporting period.
        - *Specify reason for which intervention was given*: Report **Relapsed disease**.
        - *Specify the method(s) of detection for which intervention was given*: Check the boxes to indicate that disease was detected by both **Clinical / hematologic** (lymph node biopsy) and **Radiological** (PET scan) assessments.
        - *Date intervention started*: Report **5/1/2016** to reflect the date of the first treatment given for relapsed disease.
        - *Specify systemic therapy*: Report both **Rituximab** and **Brentuximab** as treatments for relapsed disease given during the reporting period.
- Example 2: A recipient with multiple myeloma in VGPR at the time of infusion was started on maintenance Lenalidomide during the six-month reporting period. Later in the reporting period, progression was detected by serum protein electrophoresis on 9/15/2014 and so the recipient stopped lenalidomide and started bortezomib as well as dexamethasone on 9/20/2014. The recipient continued bortezomib and dexamethasone treatment into the one-year reporting period.
    - Six Month Post-TED Form
        - *Was intervention given for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease*: Report **Yes** to indicate therapy was given for progressive disease during this reporting period.

        - *Specify reason for which intervention was given*: Report **Progressive disease**.
        - *Specify the method(s) of detection for which intervention was given*: Check the box to indicate that disease was detected by **Clinical / hematologic** (serum protein electrophoresis) assessment.
        - *Date intervention started*: Report **9/20/2014** to reflect the date of the first treatment given for progressive disease.
        - *Specify systemic therapy*: Report **Bortezomib** as treatment for progressive disease given during the reporting period. Dexamethasone is no longer captured on the Post-TED (2450) Form. The lenalidomide therapy should not be reported in this section of the form. This medication was given as maintenance therapy and will therefore be reported under *Post-Infusion Treatment Given to Prevent Relapse or Progression*
    - One Year Post-TED Form
        - *Was intervention given for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease* questions: These questions will be disabled in FormsNet3^{SM}. Starting with Revision 5 of the Post-TED (2450) Form, therapy given for relapsed or progressive disease will only be captured in the reporting period in which treatment first started.
- Example 3: A recipient with multiple myeloma in PR at the time of infusion was started on lenalidomide during 100-day reporting period (started 3/15/2012) due to persistent disease (detected by serum electrophoresis testing). This treatment was not planned and was given due to an unsatisfactory disease response to HCT. Thirty days after lenalidomide started, a karyotype assessment confirmed persistent cytogenetic abnormalities present in a bone marrow sample. Lenalidomide was continued into the six-month reporting period, during which, there was disease progression (detected by serum electrophoresis). Lenalidomide was stopped and carfilzomib was started on 5/30/2012. By the end of the six-month reporting period, the recipient achieved complete remission in response to carfilzomib and was switched to a lower maintenance dose of carfilzomib which was continued into the one-year reporting period.
    - 100 Day Post-TED Form
        - *Was intervention given for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease*: Report **Yes** to indicate therapy was given for persistent disease during this reporting period.
        - *Specify reason for which intervention was given*: Report **Persistent disease**.
        - *Specify the method(s) of detection for which intervention was given*: Check the box to indicate that disease was detected by **Clinical / hematologic** (serum protein electrophoresis) assessment. he karyotype test would not be reported as a method of detection

since it was performed after treatment was started and, therefore, did not inform the decision to start lenalidomide.
    - *Date intervention started*: Report **3/15/2012** to reflect the date of the first treatment for persistent disease.
    - *Specify systemic therapy*: Report **Lenalidomide** as the only treatment given during the reporting period.
- Six Month Post-TED Form
    - *Was intervention given for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease*: Report **Yes** to indicate therapy was given for persistent and progressive disease during this reporting period.
    - *Specify reason for which intervention was given*: Report **Progressive disease**. If therapy continued from a prior reporting period and a new therapy was started for a different reason during the current reporting period, report the reason the new therapy was started.
    - *Specify the method(s) of detection for which intervention was given*: Check the box to indicate that disease was detected by **Clinical / hematologic** (serum protein electrophoresis) assessment.
    - *Date intervention started*: Report **5/30/2012** to reflect the date of the first treatment for progressive disease.
    - *Specify systemic therapy*: Report the **Lenalidomide** and **Carfilzomib** as treatments received during the reporting period
- One Year Post-TED Form
    - *Was intervention given for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease* questions: These questions will be disabled. Starting with Revision 5 of the Post-TED (2450) Form, therapy given for relapsed or progressive disease will only be captured in the reporting period in which treatment first started. Since the recipient experienced disease progression in the six-month reporting period, only treatment administered in the reporting period in which the first progression occurred will be captured and no treatment will be captured in subsequent reporting periods.

Question 81: Specify intervention *(check all that apply)*

Indicate which therapies were given in the current reporting period for decreased / loss of chimerism, measurable residual disease, persistent disease, or progressive / relapsed disease.

- **Accelerated withdrawal of immunosuppression in response to disease assessment:** Immunosuppressive medications may be tapered or entirely withdrawn in order to promote a graft vs leukemia effect in the setting of relapsed, progressive, or persistent disease. For reporting purposes, accelerated

withdrawal is defined as any decrease in immunosuppression to promote graft versus leukemia effect.

- **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.
- **Intrathecal therapy:** Intrathecal therapy is chemotherapy administered to the CNS via a lumbar puncture. It may be given to treat or prevent leukemic blasts in the cerebrospinal fluid or other CNS tissues.
- **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.
- **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.
- **Other intervention**: Indicate whether the recipient received additional therapy for decreased / loss of chimerism, measurable residual disease, persistent disease, progressive / relapsed disease which does not fit into the previous categories (i.e. surgery). Specify the other intervention given. Do not report a subsequent infusion (i.e. DLI, cellular therapy, subsequent HCT) in this field if one was given. All subsequent infusions will be captured at the top of this form and do not need to be re-reported.

Steroids Administered Post-Infusion
Previously, steroids given for relapsed, persistent, or progressive disease were reported as **Other systemic therapy**. Steroids (e.g. dexamethasone) are no longer captured on the Post-TED (2450) Form and they *should not* be reported.

Questions 82 – 84: Specify systemic therapy *(check all that apply)*

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.

Indicate which systemic therapy agents were administered during the current reporting period for relapse, persistent, or progressive disease. If the recipient received a chemotherapy agent that is not listed (i.e., cyclophosphamide), **Chemotherapy** should be selected. If the recipient received a therapeutic agent, other than chemotherapy, that is not listed, select **Other systemic therapy** and specify the systemic therapy.

Do not report a subsequent infusion (i.e. DLI, cellular therapy, subsequent HCT) if one was given. All subsequent infusions will be captured at the top of this form and do not need to be re-reported.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q85 – 91: Post-Infusion Treatment Given to Prevent Relapse or Progression

Malignant Diseases Only
Only complete the *Post-Infusion Treatment Given to Prevent Relapse or Progression* if the infusion being reported was given to treat a malignant disease. If the infusion being reported was given to treat a non-malignant disease, leave the *Post-Infusion Treatment Given to Prevent Relapse or Progression* questions blank. FormsNet3^{SM} should enable / disable this section based on the primary disease reported on the Pre-TED Disease Classification Form (2402) Form. Contact the CIBMTR Customer Service Center if it is believed FormsNet3^{SM} is incorrectly enabling / disabling these fields.

Prior Relapse / Progression
If the recipient has had a prior relapse or progression that was reported in a previous reporting period, any therapy given to prevent further relapse / progression (such as maintenance or consolidation therapy) does not need to be captured and this section of the form can be skipped. If the relapse / progression occurred in the current reporting period for which the form is being completed, then this section of the form will need to be completed and will be skipped in subsequent reporting periods.

Combined Follow-Up
In scenarios where both HCT and cellular therapy forms are being completed and a disease specific form is being completed for the cellular therapy, post-infusion therapy is not reported on this form and these questions are disabled. It will be captured on the corresponding disease form.

Report therapy given to prevent relapse or progressive disease, which may include maintenance and consolidation therapy. Any therapy given for decreased / loss of chimerism, minimal residual disease, persistent disease, or progressive / relapsed disease should *not* be reported in this section and is reported above in the *Post-Infusion Intervention for Disease* section.

Question 85: Was therapy given to prevent relapse or progressive disease? *(Include maintenance and consolidation therapy)*

Indicate whether therapy was given to prevent relapse or progressive disease (i.e., maintenance or consolidation) during the reporting period; this therapy may have been specifically planned as part of the original transplant protocol or determined after transplant. Do not include therapy given for decreased / loss of chimerism, minimal residual disease, persistent disease, or progressive / relapsed disease. Any post-infusion therapy included as part of the initial transplant protocol should be reported in this area of the form.

Question 86: Specify therapy *(check all that apply)*

Indicate which therapies were given to prevent relapse or progressive disease in the current reporting period.

- **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.
- **Intrathecal therapy**: Intrathecal therapy is chemotherapy administered to the CNS via a lumbar puncture. It may be given to treat or prevent leukemic blasts in the cerebrospinal fluid or other CNS tissues.
- **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.
- **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.
- **Other therapy**: Indicate whether the recipient received additional therapy for reasons other than decreased / loss of chimerism, minimal residual disease, persistent disease, or progressive / relapsed disease which does not fit into the previous categories. Examples may include surgery. Do not report a subsequent infusion (i.e. DLI, cellular therapy, subsequent HCT) in this field if one was given. All subsequent infusions will be captured at the top of this form and do not need to be re-reported.

Steroids Administered Post-Infusion

Previously, steroids given for relapsed, persistent, or progressive disease were reported

as **Other systemic therapy**. Steroids (e.g. dexamethasone) are no longer captured on the Post-TED (2450) Form and they *should not* be reported.

Questions 87 – 89: Specify systemic therapy *(check all that apply)*

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.

Indicate which systemic therapy agents were administered during the current reporting period for reasons other than relapse, persistent, or progressive disease. If the recipient received a therapeutic agent that is not listed, select **Other systemic therapy** and specify the therapy.

Do not report a subsequent infusion (i.e. DLI, cellular therapy, subsequent HCT) in this field if one was given. All subsequent infusions will be captured at the top of this form and do not need to be re-reported.

Question 90 - 91: Was the initial therapy date previously reported?

Indicate if therapy given to prevent relapse or progressive disease was reported in a previous reporting period. If **No**, report the initial therapy start date.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q92 – 95: Fecal Microbiota Transplant

Questions 92 – 93: Did a fecal microbiota transplant (FMT) occur?

Fecal microbiota transplant (FMT) is a procedure where fecal matter is collected from a pre-screened donor and transferred to a recipient by the oral or rectal route (i.e., by nasogastric tube or enema) in order to restore intestinal microbial flora.

Specify if the recipient received a FMT in the current reporting period. If **Yes**, report the date of the FMT. If multiple FMTs occurred during the reporting period, report the date of the first procedure.

If exact date is not known, refer to General Instructions, General Guidelines for Completing Forms for information about reporting partial or unknown dates.

If a FMT did not occur or it is not known if one occurred during the current reporting period, select **No**.

Questions 94 – 95: Specify indication for the FMT

Specify the indication for the FMT. If the indication is not listed, select **Other** and specify.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q96 – 98: Current Disease Status

Malignant Diseases Only
Only complete the *Current Disease Status* section if the infusion being reported was given to treat a malignant disease. If the infusion being reported was given to treat a non-malignant disease, leave these questions blank. FormsNet3^{SM} should enable / disable this section based on the primary disease reported on the Disease Classification (2402) Form. Contact the CIBMTR Center Support if it is believed FormsNet3^{SM} is incorrectly enabling / disabling these fields.

Combined Follow-Up
In scenarios where both HCT and cellular therapy forms are being completed and a disease specific form is being completed for the cellular therapy, current disease status is not reported on this form and these questions are disabled. It will be captured on the corresponding disease form.

Tandem Transplants
For recipients receiving a tandem transplant, the current disease status prior to HCT #2 of the tandem depends on the pre-transplant disease status and the best response to the prior transplant (i.e., HCT #1 of the tandem).

- If the recipient was in complete remission at the time of HCT #1 or achieved complete remission prior to HCT #2 of their tandem transplant, the current disease status should be reported as **Complete remission (CR)** (given there is no evidence of relapse / progression disease based on labs / clinical assessments between the tandem HCTs).

- If the recipient was not in complete remission or did not achieve complete remission in response to HCT #1 prior to HCT #2 of their tandem transplant, either **Not in complete remission (NCR)** or **Not evaluated** would be appropriate options; however, ensure the best response to infusion and the current diseases status are answered consistently

Question 96: 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.

Use the following guidelines when reporting the current disease status:

- **Complete remission (CR):** The recipient achieves CR or continues in CR at the time of last evaluation in the reporting period,
- **Not in complete remission**: 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
- **Not evaluated**: The recipient's disease status was not evaluated post-infusion. This option is *not* commonly used, as this would indicate that no tests (radiological, laboratory, or clinical assessment) were performed to assess the CR status at *any time* during the reporting period.

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

- Example 1: A recipient with neuroblastoma is not in complete remission prior to transplant, in the 100-day reporting period the recipient receives a tandem transplant. Between HCT 1 and HCT 2 the only disease assessment performed was a clinical evaluation. In this case either option would be appropriate to answer for the current disease status: **Not evaluated** or **Not in complete remission (NCR)** and **No disease detected but incomplete evaluation to establish CR**. However, ensure the best response and the current disease status are consistent.
- Example 2: A recipient with neuroblastoma is in complete remission prior to transplant, in the 100-day reporting period the recipient receives a tandem transplant. Between HCT 1 and HCT 2 the only disease assessment performed was a clinical evaluation in which the clinician did not mention progressive or relapsed disease. In this case **Complete remission (CR)** should be reported for the current disease status.

Question 97: 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. Review the guidelines below:

- **No disease detected but incomplete evaluation to establish CR**: All assessments have shown resolution of disease, but not all assessments required to report complete remission have been completed. This option is also appropriate for scenarios in which the recipient has not previously achieved a post-infusion CR and the only assessment completed in the reporting period was a physician's evaluation.
- **Disease detected**: Disease persists by radiological or clinical / hematologic assessments. Persistence of abnormalities by molecular, cytogenetic, or flow cytometry assessments does not constitute "disease detected."

Review the examples below for additional information:

- Example 3: A recipient with multiple myeloma goes to transplant in VGPR, without a bone marrow showing < 5% blasts completed prior to transplant. Post-infusion serum and urine electrophoreses and immunofixations are negative. However, no bone marrow biopsy is performed within the 100-day reporting period. Report the status as **Not in complete remission – No disease detected but incomplete evaluation to establish CR**.
- Example 4: A recipient with AML goes to transplant in primary induction failure. Post-infusion, the recipient's counts recover, but had circulating blasts noted on differential. The recipient expired due to persistent disease with their last CBC performed on their date of death showing circulating blasts. Report the status as **Not in complete remission – Disease Detected**.
- Example 5: Similar to example 4, a recipient with AML goes to transplant in primary induction failure. The recipient expired on D+11 due to infection and had not engrafted as of that date. Their last CBC showed a WBC of 0.5 × 109/L with no blasts detected on their differential. A bone marrow biopsy was not performed between transplant and the date of death. Report the status as N**ot in complete remission - No disease detected by incomplete evaluation to establish CR**.

Question 98: Date of assessment of current disease status

Report the date of latest clinical / hematologic assessment for the current disease status using the guidelines below:

Report the date of the clinical / hematologic assessment using the guidelines below:

- If the current disease status is **Complete remission**, report the date of the most disease specific clinical / hematologic or radiologic assessment performed within approximately 30 days of the contact date.
- If the current disease status is **Not in complete remission – disease detected**, report the most recent clinical / hematologic or radiologic assessment performed in the reporting period that detects disease.
- If the current disease status is **Not in complete remission – no disease detected but incomplete evaluation to establish CR**, report the last clinical / hematologic or radiologic assessment performed in the reporting period.
- If there are no disease-specific assessments within the reporting period, report the latest assessment in which the recipient was clinically assessed by a physician or midlevel clinician. In this scenario, this date does not need to be consistent with the disease status reported current disease status.

Refer to General Instructions, General Guidelines for Completing Forms, for information about reporting partial or unknown dates.

- Example 6**:** The current disease status for a recipient with non-Hodgkin's lymphoma is **Complete remission.** A PET scan was performed 3 months prior to the contact date showing no evidence of disease and a physician's exam was performed on the contact date. In this case, the physician's exam performed on the contact date should be reported as the current disease assessment date since this is the most disease specific clinical / hematologic assessment performed within 30 days of the contact date.
- Example 7: For a recipient with neuroblastoma, the current disease status is **Not in complete remission – disease detected** since disease was still present on the last PET scan. The PET scan was performed 7 months prior to the contact date and a physician's exam was performed on the contact date – disease cannot be detected by the physician's exam. The date of the PET scan should be reported as the current disease assessment date since this is the most disease specific clinical / hematologic assessment showing evidence of disease.
- Example 8: The bone marrow biopsy performed for a recipient with AML still showed > 5% blasts in the bone marrow and therefore, the current disease status is reported as **Not in complete remission – disease detected**. The bone marrow biopsy was performed 6 months prior to the contact date and a CBC was performed 2 weeks prior to the contact date – the CBC showed > 5% blasts in the blood. In this scenario, the current disease assessment date should be reported as the date of the CBC as this is the most recent disease specific clinical / hematologic assessment showing evidence of disease.
- Example 9: A recipient with multiple myeloma had a bone marrow biopsy performed two weeks prior to the contact date which showed < 5% plasma cells; however, the last set of myeloma labs performed in the prior reporting period still

showed evidence of disease; these labs were not repeated in the current reporting period. On the contact date, a physician's exam was performed. The current disease status is **Not in CR – no disease detected but incomplete evaluation to establish CR** and the current disease assessment date should be reported as the date of the physician's exam as this is the last clinical / hematologic assessment performed in the reporting period.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Instructions for Chimerism Essential Data (2451)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Chimerism Essential Data.

Chimerism Essential Data

The Chimerism Essential Data (2451) is intended to capture results of chimerism studies completed in the reporting period. This form will come due when it is reported chimerism studies were completed in the reporting period for the following recipients:

- Transplant essential data (TED)
  - Chimerism studies will be collected at the Day 100, Day 180, and Day 365 timepoints for:
    - Recipients who receive an allogeneic transplant using cord blood units
    - Allogeneic recipients whose primary disease for infusion is non-malignant
- Comprehensive report form (CRF) track
  - Chimerism studies will be collected at the Day 100, Day 180, and Day 365 timepoints for:
    - Recipients who receive an allogeneic transplant using cord blood units
    - Allogeneic recipients whose primary disease for infusion is non-malignant
  - Chimerism studies will be collected at the Day 100 and Day 365 timepoints for:
    - Allogeneic recipients whose primary disease for infusion is malignant

Links to Sections of Form:
Q1 – 4: Chimerism Studies

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.

To reference the historical Manual Change History for this form, reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
7/25/2025	2451: Chimerism Essential Data	Add	Version 1 of the 2451: Chimerism Essential Data section of the Forms Instructions Manual released. Version 1 corresponds to revision 3 of the Form 2451.

Q1 – 4: Chimerism Studies

Chimerism studies are performed to determine the percentage of blood or marrow cells post-infusion produced from donor hematopoietic stem cells and the percentage produced from host (recipient) hematopoietic stem cells.

Appendix C: Cytogenetics

Refer to Chimerism and Cytogenetics found in Appendix C: Cytogenetics for additional information.

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 of 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-infusion.

Failed Chimerism Studies

If chimerism studies were attempted, but no evaluable results were obtained, do not report the test.

Multi-Donor Chimerism

When multi-donor chimerism exists and includes a donor (or donors) from a *prior* infusion, report the results as a multi-donor chimerism though there may only be one donor for the current infusion.

Reporting Multiple Chimerism Studies
If multiple chimerism studies were completed on different dates in the reporting period, complete all chimerism questions for each chimerism study by adding an additional instance in the FormsNet3^{SM} application.

Question 1: Date sample collected

Report the date when the sample was collected for the chimerism test. If the exact date is unknown, use the process described in General Instructions, General Guidelines for Completing Forms for reporting estimated dates.

Transplant centers may perform frequent chimerism studies. If there is a need to reduce the number of chimerism study results reported due to volume, ensure that the following are reported at a minimum:

- Studies performed on or at approximately Day 30
- Most recent studies performed prior to or on the date of contact for the Day 100, Day 180, and Day 365 timepoints
- Most recent studies performed prior to and after an intervention (such as a donor cellular infusion)

Questions 2 – 3: Cells tested *(check all that apply)*

For the date of the chimerism study reported above, select all cell types assessed.

- **Unsorted bone marrow**: The specimen is bone marrow but was not sorted for a specific cell line.
- **Unsorted peripheral blood**: The specimen is peripheral blood but was not sorted for a specific cell line.
- **T-cells**: Includes CD3+, CD4+, and / or CD8+ cells.
- **NK cells**: Includes CD56+ cells.
- **Red cells**: Also known as RBCs or erythrocytes. Includes CD71 cells.
- **Other**: If the cell type does not fit in any of the above options, specify the cell type. Includes, but not limited to hematopoietic progenitor cells (includes CD34+ cells), total mononuclear cells (contains only and both lymphocytes and monocytes), granulocytes (also known as polymorphonuclear leukocytes and includes neutrophils, eosinophils, basophils, and CD33+ cells).

Reporting Multiple Chimerism Studies
CIBMTR strongly encourages attaching the chimerism study results.

Donor Identifier
The donor identifier column will auto populate with the donor identifier information.

Question 4: Chimerism study results

For each cell type assessed, specify the donor chimerism result(s) as a percentage. If the chimerism method is karyotyping or FISH (only applicable when the donor and recipient are sex mismatched), convert the results to a percentage.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Instructions for Donor Cellular Infusion (2199)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Donor Cellular Infusion.

Donor Cellular Infusion

This Donor Cellular Infusion is a single abbreviated form with elements of the Pre-CTED (4000), Cell Therapy Product (4003), Cell Therapy Infusion (4006), and Post-CTED (4100), which must be completed for all recipients who receive a donor lymphocyte infusion (DLI).

DCIs are defined as:

- The infusion must be post-allogeneic HCT *and* probably from the same donor*
- Product must be lymphocytes only
- Product cannot be genetically modified

*This is the most common scenario right now, but in the future, DCI products may be obtained from a different donor

For recipients of any other type of cellular therapy, such as CAR T cells, tumor-infiltrating lymphocytes, cytotoxic T cells, or any cellular therapy product that is genetically modified, complete the Pre-CTED (4000).

Multiple donor lymphocyte infusions within the same reporting period require a separate Donor Cellular Infusion (2199) for each infusion. This form will come due for recipients post-HCT when DCI(s) are reported as a subsequent infusion on the

Post-TED (2450), Post-Infusion Follow-Up (2100), and Post-CTED (4100). At the time of completing the Post-TED (2450) / Post-Infusion Follow-Up (2100) / Post-CTED (4100), the total number of DLIs received in the reporting period are reported on the form. The number of DLIs reported will make due the same number of Donor Cellular Infusions (2199). The Post-TED (2450) / Post-Infusion Follow-Up (2100) / Post-CTED (4100)will *not* be completed early to report DLIs given in the reporting period.

HCT or CT reporting will not be interrupted and combined follow up rules do not apply. There will no longer be any Post-CTEDs (4100) for DLIs.

Links to Sections of Form:

- Q1 – 4: Donor Information
- Q5 – 39: Donor Cellular Infusion (DCI)

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.

To reference the historical Manual Change History for this form, reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
7/25/2025	2199: Donor Cellular Infusion	Add	Version 1 of the 2199: Donor Cellular Infusion section of the Forms Instructions Manual released. Version 2 corresponds to revision 2 of the Form 2199.

Q1 – 4: Donor Information

This section is intended to collect specific details about the donor used for the current donor cellular infusion. This section will auto-populate after selecting the appropriate donor from the FormsNet3^{SM} pop-up.

Question 1: Donor ID

Report the donor's ID for the current donor cellular infusion.

Question 2. Donor date of birth

Report the donor's birth date for the current donor cellular infusion.

Question 3: Donor age

Report the donor's age for the current donor cellular infusion.

Question 4: Donor sex

Report the donor's sex. Sex shall refer to an individual's immutable biological classification as either male or female. Sex is not a synonym for and does not include the concept of gender identity. .

Q5 – 39: Donor Cellular Infusion (DCI)

Question 5: Date of this DCI

Report the date when the DCI being reported in this instance was infused. If the product was infused over multiple days, report the first date of infusion.

If the exact date is unknown, review General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Questions 6 – 7: What was the primary indication?

From the list provided, select the primary indication for which the recipient is receiving

the DCI. If the primary indication is unclear, seek clinician clarification.

These indications are given with HCT or post-HCT. No additional consent is required from the recipient per CIBMTR. Please confirm with your local IRB.

If **Other indication** is selected, specify the indication.

Question 8: What therapy to treat disease given prior to the DCI?

This question is intended to capture if the recipient received disease treatment prior to the DCI. Indicate if therapy to treat disease was given prior to the DCI. Do not include preparative regimen or bridging therapy.

If **Yes,** and the recipient is on CRF track for the HCT, ensure all lines of therapy are reported on the disease specific form.

CBC Not Completed Prior to Infusion
In the rare case where the CBC was not assessed at *any time* prior to the DCI, leave *Date complete blood count sample drawn* through *Were platelets transfused ≤ 7 days before the date of the sample was drawn* questions blank and override the FormsNet3^{SM}.

Question 9: Date complete blood sample drawn (CBC)

These questions are intended to determine the clinical status of the recipient prior to the infusion. Report the date of the most recent CBC prior to infusion. Typically, no systemic therapy (therapy not for treatment of disease, but analogous to preparative regimen) is given prior to DLIs. However, if systemic therapy was administered, report the date of the CBC prior to systemic therapy. The CBC from the first day of the systemic therapy may be reported as long as the blood was drawn before any systemic therapy was administered.

Questions 10 – 18: Complete blood count results available (*check all that apply)*

Select all cells assessed on the reported CBC date above.

- **WBC**: The white blood cell count is a value that represents all the white blood cells in the blood. If the count is too high or too low, the ability to fight infection may be impaired. If the WBC was assessed on the reported CBC date, report the value and units of measurement.
- **Neutrophils**: Neutrophils are a subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage or an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. Neutrophils are also known as polymorphonuclear leukocytes (PMNs). If neutrophils were assessed on the reported CBC date, report the percentage.
- **Lymphocytes**: Lymphocytes are another subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage of an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. If lymphocytes were assessed on the reported CBC date, report the percentage.
- **Hemoglobin**: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count value is considered “anemia” and blood transfusions, or growth factors may be required to increase the hemoglobin level. If the hemoglobin was assessed on the reported CBC date, report the value and units of measurement.
- **Hematocrit:** The hematocrit is the percentage (sometimes displayed as a proportion) of red blood cells relative to the total blood volume. Low hematocrit may require red blood cell transfusions or growth factors. Indicate if the recipient received a red blood cell transfusion within 30 days prior to sample draw date. If hematocrit were assessed on the reported CBC date, report the percentage. Additionally, indicate if the recipient received red blood cell transfusion(s) within 30 days prior to the date of the CBC reported above.
- **Platelets:** Platelets are formed elements within the blood that help with coagulation. A low platelet count, called thrombocytopenia, may lead to easy bleeding or bruising. Thrombocytopenia may require platelet transfusions. If platelets were assessed on the reported CBC date, report the value and units of measurement. Additionally, indicate if the recipient received platelet transfusion(s) within seven days prior to the date of the CBC reported above.

Performance Scores
Refer to Appendix L: Karnofsky / Lansky Performance Status for more information on reporting performance scores.

Question 19: What scale was used to determine the recipient’s functional status prior to the donor cellular infusion?

The CIBMTR uses the Karnofsky / Lansky scale to determine the functional status of the recipient immediately prior to the start of lympho-depleting therapy / systemic therapy or infusion. The Karnofsky Scale is designed for recipients aged 16 years and older and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old.

systemic therapy or infusion.

For recipients less than one year old, the *Performance score* questions should be left blank.

Questions 20 – 21: Performance score

Report the recipient's performance status immediately prior to the start of lympho-depleting therapy / systemic therapy or infusion. For the purposes of this manual, the term "immediately prior" represents the pre-infusion work-up phase, or approximately one month prior to the start of the lympho-depleting therapy or systemic therapy.

If a Karnofsky / Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician's clinic note), data management professionals should not assign a performance score based on analysis of available documents. Rather, a physician or mid-level health care provider (NPs and PAs) should provide documentation of the performance score. Documentation from an RN who has been trained and authorized to determine performance scores may also be used.

If only an ECOG is documented, convert the ECGO score to Karnofsky / Lansky. Refer to Appendix L: Karnofsky / Lansky Performance Status and / or the memorandum and worksheet example found in 'Appendix L' of the 'Appendices' section located in the Retired Forms Manuals webpage.

Questions 22 – 23: Date of cell product collection

Indicate if the date of cell product collection is **Known**. If **Known**, report the date. If the cell product is collected over multiple days, report the first date when collection began.

If the exact date is not known, refer to General Instructions, General Guidelines for Completing Forms for more information regarding reporting partial or unknown dates.

Question 24: Was the product previously cryopreserved?

DCI products may be leftover products from a prior HCT. Indicate if the DCI product was previously cryopreserved.

Questions 25 – 26: Tissue Source

Select from the list the tissue source(s) of the cellular product for this infusion. If the source is selected as **Other tissue source**, specify the other source.

The tissue source for non-mobilized peripheral blood, peripheral blood apheresis, and MNCs should be reported as **Peripheral blood**.

DCIs and Genetic Modification
DCIs are not genetically modified by CIBMTR definition. Any product that is genetically modified must be reported on a Pre-CTED (4000) as a cellular therapy, not a DCI, and requires 15 years of follow-up. Contact CIBMTR Center Support if corrections are required.

Question 27: Were the cells in the infused product selected / modified / engineered / manipulated prior to infusion?

Indicate if the cells in DCI were product selected (i.e., selective retention of a population of desired cells through recognition of specified characteristics), modified, engineered and / or manipulated prior to infusion.

Steps in Manipulation
If the manipulation consists of several steps, individual steps do not need to be reported as separate manipulations. For example, T-cell depletion that is part of expansion, does not need to be reported.

Cryopreservation as a Manipulation
Do not report cryopreservation (including plasma removal as part of cryopreservation) as a method of manipulation.

Questions 28 – 29: Specify the method(s) used to manipulate the product (check all that apply)

Specify the method(s) of manipulation. Check all that apply.

- **Cultured (ex-vivo expansion):** cells placed in culture to increase in number (i.e., to expand) allowing for sufficient cells for infusion.
- **Induced cell differentiation:** cells placed in culture to give rise to cellular elements with biological characteristics other than those of the cells being cultured (i.e., mesenchymal stromal cells cultured to make osteoblasts; pluripotent stem cells cultured to make neural cell precursors). Usually, the description of the process would include the term “differentiation of cells X into cells Y”. This scenario can be seen in regenerative medicine indications.
- **Cell selection – positive:** the manipulation of a cellular therapy product such that a specific cell population(s) is enriched. This may be achieved by using an antibody that binds to a specific population of cells (e.g., CD4+ selection).
- **Cell selection – negative:** the manipulation of a cellular therapy product such that a specific cell population(s) is reduced.
- **Cell selection based on affinity to a specific antigen:** the cellular product undergoes selection to isolate the target population based on the ability of the target population to bind or recognize a specific antigen (e.g., a T cell population recognizing viral proteins, or a protein associated with cancer).

Select **Other cell manipulation** if the manipulation is listed above and specify the other manipulation.

Product Analysis
This form captures infusions of lymphocytes only. If this was an infusion of another cell type, it must be reported on a Pre-CTED (4000) as a cellular therapy, not a DLI. Please contact CIBMTR Center Support if corrections are needed.

Product Infusion
The cell type(s) administered should be for a single DCI. If multiple DCIs were given in the reporting period, each DCI should be reported on a separate Donor Cellular Infusion (2199).

Questions 30 – 37: Specify the cell type(s) administered *(check all that apply)*

Select the cells infused with current DCI. Check all that apply.

- **CD34+ cells**: Also known as hematopoietic stem cells. If administered, report the total number of CD34+ cells infused. Report the absolute number of cells, not cells per kg.
- **Lymphocytes (unselected):** Unselected means a specific lymphocyte sub-population (e.g. CD4+) was not targeted. This includes all types of lymphocytes, those that have not been selected via flow cytometry or other method. If administered, report the total number of unselected lymphocytes infused. Report the absolute number of cells, not cells per kg.
- **CD4+ lymphocytes:** The lab report may display this value as CD3+CD4+. These cells are also known as T-helper cells. If administered, report the total number of CD4+ cells infused. Report the absolute number of cells, not cells per kg.
- **CD8+ lymphocytes:** The lab report may display this value as CD3+CD8+. These cells are also known as cytotoxic T-cells which can destroy virus-infected cells, tumor cells, tissue grafts, etc. If administered, report the total number of CD8+ cells infused. Report the absolute number of cells, not cells per kg.
- **Regulatory T-cells (TREG):** TREG cells express the biomarkers CD4, FOXP3, and CD25. If administered, report the total number of TREG cells infused. Report the absolute number of cells, not cells per kg.

Select **Other cell type** if cell type infused is not listed above, specify the other cell type, and report the total number infused. Report the absolute number of cells, not cells per kg.

Question 38: What was the best response to the donor lymphocyte infusion (DLI)?

This question is intended to collect the recipient's best response to the DCI. If the recipient received a prior HCT, do not report the response to HCT. A separate evaluation to establish the best response after the DCI is required.

Specify the recipient's best response to the DCI. Use Table 1 below to review the applicable response options by indication and the best response definitions.

If an assessment was not completed after the DCI, select **Not assessed**.

Table 1. Best Response Definitions by Indication

Indication	No Response	Disease Progression	Partial response	Complete response	Partial Normalization of Blood Count	Normalization of Blood Count
GVHD prophylaxis	Best response not answered					
GVHD treatment	Does not meet partial response or complete response	-	Improvement but not resolution of symptoms, Remains on immune suppression	Improvement but not resolution of symptoms, or remains on immune suppression	-	-
Immune reconstitution	Does not meet complete response	-	-	CD3 > 200/mm^3	-	-
Infection treatment	Does not meet partial response or complete response	-	Decrease in infectious burden without resolution	Undetectable infection	-	-
Insufficient hematopoietic recovery / graft failure	Does not meet partial normalization of blood count or normalization of blood count	-	-	-	*TBD*	*TBD*
Prevent disease relapse	Best response not answered					
Suboptimal donor chimerism	Does not meet partial response or complete response	-	Increase in chimerism but not 95% donor	95% donor chimerism	-	-
Treatment of disease relapse / progression	Refer to the disease specific manuals for disease criteria				-	-
Treatment of MRD	Does not meet partial response	*TBD*	*TBD*	*TBD*	-	-

	or complete response					
Other indication	Best response not answered					

Question 39: Date response established

Report the date when the best response to the DCI was established. This should be the earliest date when all criteria were met.

For the following indications, report the date the sample was collected for evaluation (i.e., bone marrow biopsy, blood sample, etc.) or the date when imaging took place, if applicable. If no pathologic, radiographic, or laboratory assessments were performed to establish the best response, report the office visit in which the physician clinically evaluated the response.

- Immune reconstitution
- Infection treatment
- Insufficient hematopoietic recovery / graft failure
- Suboptimal donor chimerism
- Treatment of disease relapse / progression
- Treatment of MRD

For the following indication, report the office visit in which the physician clinically evaluated the response:

- GVHD treatment

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Instructions for Recipient Death (2900) Form

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Recipient Death Form.

Recipient Death (2900)

The Recipient Death Data (2900) captures cause of death data fields for all recipients. The leading cause of post-infusion mortality is persistent, recurrent, or relapsed primary disease. Other common causes of death include graft-versus-host disease, infection, and organ failure. As hematopoietic cell transplant and cellular therapy evolves, reporting accurate cause of death data is important to investigating the variables that are associated with post-infusion outcomes.

If **Dead** is reported as the current survival status at the date of last contact on the Post-TED (2450), Post-Infusion Follow-Up (2100) or Cellular Therapy Essential Data Follow-Up (4100) form at the 100-day, six month, and yearly time points, complete the Recipient Death Data (2900) as soon as possible after the recipient has died.

Autologous Recipients with No Consent for Research Database
Do not complete the Recipient Death (2900) Form for Autologous recipients who did not consent to be part of the research database.

Lost to Follow-Up

Occasionally, centers may lose contact with recipients for a variety of reasons, including the recipient's moving, changing physicians, or death. After attempts to contact the recipient or referring physician have failed, the recipient may be declared lost to follow-up. If your center later receives documentation that a recipient is dead, report this on the appropriate follow-up form for the time period in which the recipient died. This may require resetting a form that was previously made Lost to Follow Up (LTF) or Survival (SUR). This may happen when a center becomes aware of the death after it has reported that the recipient is lost to follow-up. To reset the form, click the blue counterclockwise arrow icon.

Links to Sections of Form:
Cause of Death Options
Q1 – 4: Recipient Death

Q5 – 7: Contributing Cause of Death

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.

To review the historical Manual Change History for this form, reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
7/25/2025	Recipient Death (2900)	Add	Version 5 of the 2900: Recipient Death section of the Forms Instructions Manual released. Version 5 corresponds to revision 6 of the Form 2900.

Cause of Death Options

Review the following guidelines when reporting the primary and contributing cause of deaths.

Sepsis and Septic Shock
Sepsis and septic shock should not be reported as **Other cause**, as the true cause of death is an infection. Review the infection section below for additional details.

Post-Transplant Lymphoproliferative Disorder (PTLD)
If PTLD is listed as a cause of death, report the cause of death as a **New malignancy (post-infusion)**.

Recurrence / persistence / progression of disease for which the infusion was performed

- If the cause of death is due to disease, ensure disease detected is reported on the appropriate post-infusion follow-up form.
- If the disease is present at death, but is not the underlying cause of death, this should be reported as a contributing cause of death.
    - Example: The recipient's disease had been stable for months and they died by accidental means, this option should be used as a contributing cause of death (not the primary cause of death).

GVHD

- The determination of acute versus chronic GVHD should rest on clinical features identified by the clinician.
- **Acute GVHD**: If this is reported as a primary or contributing cause of death, acute GVHD should also be reported on the appropriate post-infusion form.
- **Chronic GVHD**: If this is reported as a primary or contributing cause of death, chronic GVHD should also be reported on the appropriate post-infusion form.

Graft failure or poor graft function

- The recipient had no hematopoietic recovery, graft failure following initial hematopoietic recovery, or poor graft function.
- If secondary graft failure is due to GVHD or infection, also report GVHD or infection as causes of death.

Failure to thrive

- A term used to describe a global decline which includes inactivity, weight loss, and decreased appetite.

Hemorrhage

- Recipient died with evidence of hemorrhage. Use the following options to report the hemorrhage location: **Diffuse alveolar hemorrhage (DAH)**, **Gastrointestinal hemorrhage**, **Hemorrhagic cystitis**, **Intracranial hemorrhage**, **Pulmonary hemorrhage**, or **Other hemorrhage**.
- Additional details:
    - **Diffuse alveolar hemorrhage (DAH)**: If this is reported as the primary or contributing cause of death and the recipient is on the CRF track, also report this on the Post-Infusion Follow-Up (2100) Form.
    - **Hemorrhagic cystitis**: If this is reported as the primary or contributing cause of death and the recipient is on the CRF track, also report this on the Post-Infusion Follow-Up (2100) Form.
    - **Intracranial hemorrhage**: Also known as hemorrhagic stroke. If this is reported as the primary or contributing cause of death and the recipient is on the CRF track, also report this on the Post-Infusion Follow-Up (2100) Form.
    - **Pulmonary hemorrhage**: If this is reported as the primary or contributing cause of death and the recipient is on the CRF track, also report this on the Post-Infusion Follow-Up (2100) Form.
    - **Other hemorrhage**: Select this option if the hemorrhage was in an organ system that does not have a cause of death option and report the organ or location of the hemorrhage in the *Specify* data field.

Infection

- Recipient died due to an infection. Use the following options to specify the infection etiology: **Bacterial infection**, **Fungal infection**, **Protozoal infection**, **Viral infection**, or **Other infection**.

- If the organism was not identified, but evidence of infection was present based on clinical opinion, select **Infection, organism not identified**. Also report infections in the "Infection" section on the Post-Infusion Follow-Up (2100) or Cellular Therapy Essential Data Follow-Up (4100) Form.
- Additional details:
    - COVID-19: If the primary or contributing cause of death is COVID-19, select **Viral infection**.
    - Interstitial pneumonitis (IPn): Do not report IPn as an infection cause of death. Report IPn as **Other pulmonary syndrome**.
    - Pneumonia: If the primary or contributing cause of death is 'pneumonia,' report the cause of death as an infection (specify the etiology) or a pulmonary syndrome (specify the syndrome), if applicable. If the only details of the cause of death is 'pneumonia' (i.e., the infection etiology and / or pulmonary syndrome is unknown), select **Infection, organism not identified**.
    - Sepsis / septic shock
        - If the primary cause of death is 'sepsis or septic shock,' report the primary cause of death as an infection (specify the etiology) and the contributing cause of death as **Multiple organ failure**. If the infection etiology is unknown, select **Infection, organism not identified**.
        - If the contributing cause of death is 'sepsis or septic shock,' report the appropriate primary cause of death and specify the contributing cause of death as **Infection** (specify the etiology) *and* **Multiple organ failure**. If the infection etiology is unknown, select **Infection, organism not identified**.

Malignancy

- Recipient died with evidence of a malignancy *other than the primary disease for infusion*. Use the options below to specify the type of malignancy.
- **New malignancy:** If the recipient developed a new malignancy post-infusion, including PTLD, this should also be reported on the appropriate post-infusion form.
- **Prior malignancy**: If there was a history of malignancy prior to infusion (i.e., not the primary disease for infusion) and the recipient died with evidence of recurrence, persistence, or progression of the previous malignancy. This should also be reported on the appropriate pre-infusion form.

Organ failure (not due to GVHD or infection)

- Recipient died with organ failure, not due to GVHD or infection. Use the options below to specify the organ system that failed.
- **Cardiac failure**: If cardiac failure was related to congestive heart failure and / or myocardial infarctions, also report this on the appropriate Post-Infusion Follow-Up (2100) Form.

- **Central nervous system (CNS) failure**: Includes radiation-induced atrophy, brain stem dysfunction, or encephalitis of unknown origin.
    - Do not use this option if the cause of death is a brain infection (i.e., meningitis) – use the infection option.
    - Do not use this option if the cause of death is a hemorrhagic stroke – use the **Intracranial hemorrhage** option.
- **Gastrointestinal (GI) failure (not liver)**: Includes intestinal obstruction or perforation.
    - Do not use this option if the cause of death is a GI hemorrhage – use the **Gastrointestinal hemorrhage** option.
    - Do not use this option if the cause of death is liver failure – use the **Liver failure (not VOD)** option.
    - Do not use this option if the cause of death is GI GVHD – use the **Acute GVHD** or **Chronic GVHD** option.
- **Liver failure (not VOD)**: Excludes veno-occlusive disease/sinusoidal obstruction syndrome (use VOD/SOS) and GVHD (use Acute GVHD or Chronic GVHD). If this is reported as the primary or contributing cause of death, also report this on the appropriate Post-Infusion Follow-Up (2100) Form.
- **Multiple organ failure**: If the cause of death is due to failure of more than one organ, provide additional detail and specify in question. Do not select this option if there is a root cause of the multiple organ failure (i.e., infection).
- **Pulmonary failure**: Includes pulmonary failure from non-infectious causes such as bronchiolitis obliterans (BO) or cryptogenic organizing pneumonia (COP). BO and COP should also be reported on the appropriate Post-Infusion Follow-Up (2100) Form.
- **Renal failure**: Renal failure that was severe enough to warrant dialysis (or the recommendation of dialysis) should also be reported on the appropriate Post-Infusion Follow-Up (2100) Form.
- **Veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS)**: Include pulmonary veno-occlusive disease. Do not report other types of liver failure using this option. Liver VOD / SOS should also be reported on the appropriate post-infusion form.
- **Other organ failure**: If the organ system that failed is not specified, but present at death based on clinical opinion, use **Other organ failure**, and specify the organ involved.

Pulmonary

- **Acute respiratory distress syndrome (ARDS) (other than IPS)**: Also known as adult respiratory distress syndrome. Acute onset, infiltrative respiratory distress. Excludes IPS. ARDS should also be reported on the appropriate Post-Infusion Follow-Up (2100) Form.
- **Diffuse alveolar damage (without hemorrhage)**: Describes histologic changes found in lung disease. This is associated with ARDS and transfusion related acute lung injury (TRALI).

- **Idiopathic pneumonia syndrome (IPS)**: Describes non-infectious lung injuries that occur post-infusion (within 100 – 120 days). IPS should also be reported on the appropriate Post-Infusion Follow-Up (2100) Form.
- **Pneumonitis due to Cytomegalovirus (CMV)**: Pneumonitis can result from infection by cytomegalovirus, adenovirus, respiratory syncytial virus, influenza, or Pneumocystis jirovecii (PCP). Select this option if interstitial pneumonitis resulted from cytomegalovirus. Also report interstitial pneumonitis on the appropriate Post-Infusion Follow-Up (2100) Form.
- **Pneumonitis due to other virus**: Pneumonitis can also result from infection by adenovirus, respiratory syncytial virus, influenza, or Pneumocystis jirovecii (PCP). Select this option if pneumonitis was caused by a virus (other than CMV). Also report interstitial pneumonitis on the appropriate Post-Infusion Follow-Up (2100) Form
- **Other pulmonary syndrome** *(excluding pulmonary hemorrhage)*: Select this option to report any other pulmonary syndrome, excluding pulmonary hemorrhage and specify the syndrome. Additionally, select this option for pneumonitis due to any other organism, specify IPn and the organism. Report interstitial pneumonitis on the appropriate Post-Infusion Follow-Up (2100) Form.
- Additional information:
    - If the primary or contributing cause of death is 'pneumonia,' report the cause of death as an infection (specify the etiology) or a pulmonary syndrome (specify the syndrome), if applicable. Refer to infection section above for more details.

Toxicity

- **Cytokine release syndrome (CRS)**: Development of constellation of signs and symptoms seen post-infusion of monoclonal antibodies or cellular therapy products.
- **Macrophage activation syndrome (MAS) / hemophagocytic lymphohistiocytosis (HLH) – like toxicities**: Severe systematic inflammatory syndromes caused by excessive activation and expansion of T lymphocytes and macrophagic histocytes.
- **Neurotoxicity (ICANS)**: The development of different neurologic signs and symptoms reported after the infusion of genetically modified lymphocytes.
- **Tumor lysis syndrome**: Disorder characterized by metabolic abnormalities resulting from spontaneous or therapy-related cytolysis of tumor cells.

Vascular

- **Disseminated intravascular coagulation (DIC)**: Results in abnormal blood clotting.
- **Ischemic stroke**: Blood clot in an artery to the brain, preventing blood flow.
- **Thromboembolism**: Includes deep vein thrombosis (DVT) and pulmonary embolism (PE). Report DVT or PE on the appropriate Post-Infusion Follow-Up (2100) Form.

- **Thrombotic microangiopathy (TMA) (Thrombotic thrombocytopenia purpura (TTP) / Hemolytic Uremic Syndrome (HUS)**: A multifactorial condition where intravascular platelet activation, formation of thrombi, and microangiopathic hemolytic anemia occur due to generalized endothelial dysfunction. Report TMA or a similar syndrome on the appropriate Post-Infusion Follow-Up (2100) Form.
- **Other vascular**: Select this option to report any other vascular syndrome and specify.

Other

- **Accidental death**: Recipient death resulted from accidental or unintentional means.
- **Suicide**: 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.
- **Stroke, unspecified**:
- **Other cause**: If the cause of death is not listed above, select **Other cause** and specify. Do not include sepsis / septic shock or pneumonia.

Q1 – 4: Recipient Death

No Documentation of Contact Date
The contact date data field cannot be left blank and is required to be reported. In cases where the recipient passed away and there is no documentation to report the date of death, the guidelines for reporting estimated dates must be used.

Question 1: Date of Death

Report the date the recipient died. Confirm that the date matches the last date of actual contact reported on the Post-TED (2450), Post-Infusion Follow-Up (2100), or Cellular Therapy Essential Data Follow-Up (4100) form.

If the death occurred at an outside location and records of death are not available, the dictated date of death within a physician note may be reported. If the progress notes detailing the circumstances of death are available, request these records. These records are useful for completing required follow-up data fields on the post-infusion forms and the cause of death data fields on this form.

If the exact date of death is not known, select **Date estimated** and use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms

Question 2: Was cause of death confirmed by autopsy?

Indicate if the cause of death was confirmed by autopsy.

If **Autopsy pending**, the form will not go to complete (CMP) status until the autopsy results are reported. The form may be submitted with this question answered as **Autopsy pending**, but the form will remain in saved (SVD) status until it is updated with the results. Once the autopsy results are known, update this question and the **Primary cause of death**, if applicable, to ensure all pertinent causes of death are reported, then resubmit to complete the form.

Autopsy Report
It is strongly encouraged to attach the autopsy report if documentation is available. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the training guide.

Primary and Contributing Cause(s) of Death
Report the primary and contributing cause(s) of death based on the physician's determination. If the cause of death is unclear, seek physician clarification to determine the appropriate cause of death.

Cause of Death Options
Review the Cause of Death Options section for additional information to ensure accurate cause of death reporting.

Questions 3 – 4: Primary cause of death

Report the underlying cause of death. According to the Centers for Disease Control and Prevention, National Center for Health Statistics, the underlying cause of death is "the disease or injury that initiated the chain of events that led directly or inevitably to death."

Report only one primary cause of death. If additional details are required, the *Specify* data field will be answered. Information reported in the *Specify* field must pertain to the option selected (i.e., an infectious cause of death should be specified for **Other infection**).

If the recipient has recurrent / persistent / progressive disease at the time of death, consider if the disease was the primary cause of death or a contributing cause of death. It should not be assumed that the presence of the recipient's primary disease indicates that the disease was the primary cause of death.

If a cause of death has related questions on the comprehensive report form, report the appropriate data in both locations. For example, if a primary cause of death was infection, complete the infection data fields on the comprehensive report form. Review the Cause of Death Options section for additional details.

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

Q5 – 7: Contributing Cause of Death

Primary and Contributing Cause(s) of Death
Report the primary and contributing cause(s) of death based on the physician's determination. If the cause of death is unclear, seek physician clarification to determine the appropriate cause of death.

Cause of Death Options
Review the Cause of Death Options section for additional information to ensure accurate cause of death reporting.

Questions 5 – 6: Contributing cause of death *(check all that apply)*

Report any additional causes of death. All contributing causes of death are important for analysis of transplant outcomes. Select all that apply.

If additional details are required, the *Specify* data field will be answered. Information reported in the *Specify* field must pertain to the option selected (i.e., an infectious cause of death should be specified for **Other infection**).

If a cause of death has related questions on the comprehensive report form, report the appropriate data in both locations. For example, if a contributing cause of death was acute graft-versus-host disease (GVHD), complete the acute GVHD data fields on the comprehensive report form.

Review the examples below on how to report primary and contributing cause of death:

- **Example 1**: In the 1-year reporting period, a recipient transplanted for AML has relapsed disease that leads to multiple organ failure. In this scenario, the primary cause of death should be captured as relapsed disease, and the contributing cause of death should be reported as multiple organ failure.
- **Example 2**: A recipient with acute GVHD on immunosuppression develops a fungal infection and then dies. In this scenario, the primary cause of death should be reported as acute GVHD, and the contributing cause of death would be captured as a fungal infection.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Instructions for Subsequent Neoplasm (3500) Form

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Subsequent Neoplasm (3500) Form.

Subsequent Neoplasm (3500)

The Subsequent Neoplasms (3500) form must be completed when a new malignancy is reported on the Post-TED (2450), Post-Infusion Follow-Up (2100) or Cellular Therapy Essential Data Follow-Up (4100) forms. Reported new malignancies should be different than the disease / disorder for which the infusion or cellular therapy was performed. Do not report relapse, progression, or transformation of the same disease subtype as a new malignancy.

New malignancies, lymphoproliferative disorders, and myeloproliferative disorders include but are not limited to:

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

The following should not be reported as new malignancy:

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

A separate Subsequent Neoplasm (3500) Form must be submitted to report each new malignancy diagnosed in the current reporting period. Reporting a new malignancy / disorder on a Post-TED (2450), Post-Infusion Follow-Up (2100) or Cellular Therapy Essential Data Follow-Up (4100) Form will make one Subsequent Neoplasm (3500) Form come due. This form will also have the option to be created on-demand (on-demand is when a form can be generated at any time). If more than one new malignancy occurs during a reporting period, the Subsequent Neoplasm (3500) Form can be made on demand. Contact CIBMTR Center Support with any questions.

Links to Sections of Form:
Q1 – 11: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder
Q12 – 22: Post-Transplant Lymphoproliferative Disorder

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

To review the historical Manual Change History for this form, reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
7/25/2025	3500: Subsequent Neoplasm	Add	Version 3 of the 3500: Subsequent Neoplasm section of the Forms Instructions Manual released. Version 3 corresponds to revision 3 of the Form 3500.

Q1 – 11: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder

Reporting Multiple New Malignancies
A single Subsequent Neoplasms (3500) form will come due whenever a new malignancy / disorder is reported on the Post-TED (2450), Post-HCT Follow-Up (2100) or Cellular Therapy Essential Data Follow-Up Form (4100) form. However, if there is a diagnosis of more than one malignancy in the reporting period, *excluding non-melanoma skin cancers* (see Recurrent Non-Melanoma Skin Cancers note box below), a separate Subsequent Neoplasms (3500) form must be submitted to report each new malignancy.

Recurrent Non-Melanoma Skin Cancers
For basal cell or squamous cell skin cancer, report the number of skin cancer lesions diagnosed in the current reporting period. If basal cell or squamous cell skin cancer was diagnosed again in a future reporting period, report **Yes**, a new malignancy occurred on the appropriate post-infusion follow-up form and specify the number of skin cancer lesions identified in the reporting period. For example, a recipient was diagnosed with basal cell skin cancer on the neck in the one-year reporting period and two months

later, within the same reporting period, there was a diagnosis of basal cell located on the nose. In the two-year reporting period, another basal cell skin cancer was diagnosed, located on the arm. For the one-year reporting period, report **Yes**, there was a new malignancy on the one-year post-infusion follow-up form and a single Subsequent Neoplasms (3500) form will come due to report both basal cell malignancies detected (report **two** in *Number of non-melanoma skin cancer lesions*). For the two-year reporting period, report **Yes**, there was a new malignancy on the two-year post-infusion follow-up form and a single Subsequent Neoplasms (3500) form will come due to report third basal cell malignancies detected (report **one** in *Number of non-melanoma skin cancer lesions*).

Post-Transplant Lymphoproliferative Disorder (PTLD)
PTLD should be reported as a new malignancy if it was confirmed via a biopsy (treatment not required) *or* suspected to be PTLD and treated.

New Malignancy Documentation
The submission of pathology reports and other supportive documentation for each reported new malignancy is *strongly recommended.*
For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Question 1: Specify the new malignancy

Specify which new malignancy / disorder was diagnosed during the reporting period and any applicable questions.

If the new malignancy / disorder is not found in the list, select **Other new malignancy** and specify. An example of an **Other new malignancy** includes histiocytic sarcoma.

Report myeloid sarcoma as **Acute myeloid leukemia (AML / ANLL)**.

Do not report CNS relapse of lymphoma as a new malignancy for recipients whose primary disease for infusion is lymphoma. This should be reported as relapse. However, in cases where a recipient received an infusion for a disease other than lymphoma and later develops CNS lymphoma, lymphoma should be reported as a new malignancy.

Question 2: Specify type of PTLD

Specify the type of PTLD as **Monomorphic** or **Polymorphic** using the guidelines listed below. The PTLD type should be documented within the pathology report, if available. If the documentation is unclear, seek clinician clarification.

- **Monomorphic:** Fulfills the criteria for one of the B-cell or NK/T-cell lymphomas.

- **Polymorphic:** Characterized by the overproduction of both B-cells and T-cells but fail to meet the criteria for lymphoma.

If the PTLD type is not known, select **Unknown**.

Question 3: Specify type of leukemia / lymphoma

Specify if the type of leukemia or lymphoma is **B-cell** or **T-cell**. If this information is unknown, seek clinician clarification.

Question 4: Specify oropharyngeal cancer

If the new malignancy is **Oropharyngeal cancer**, specify the type. If the type is not listed, select **Other oropharyngeal cancer**, and specify the type. Examples of 'other' include nasopharynx and hypopharynx.

Question 5: Specify gastrointestinal malignancy

If the new malignancy is **Gastrointestinal malignancy**, specify the type. If the type is not listed, select **Other gastrointestinal malignancy**, and specify the type.

Question 6: Specify genitourinary malignancy

If the new malignancy is **Genitourinary malignancy**, specify the type. If the type is not listed, select **Other genitourinary malignancy**, and specify the type. Examples include penis and fallopian tube.

Question 7: Specify CNS malignancy

If the new malignancy is **CNS malignancy**, specify the type. If the type is not listed, select **Other CNS malignancy**, and specify.

Adenocarcinoma
Adenocarcinoma is a general term used to describe a type of cancer that develops in glandular tissue and can occur in many parts of the body. If the new malignancy is an 'adenocarcinoma,' do not report 'adenocarcinoma' in the *Specify other new malignancy* data field. Report this malignancy by further defining the location from one of the options listed above. If the location is not listed an option on the form, report the location in the *Specify other new malignancy* data field.

Question 8: Specify other new malignancy

If the new malignancy is **Other new malignancy**, **Other oropharyngeal cancer**, **Other gastrointestinal malignancy**¸ **Other genitourinary malignancy**, or **Other CNS malignancy**, specify the type.

Question 9: Date of diagnosis

Report the diagnosis date of the new malignancy / disorder, using the pathologic diagnosis date. If the original assessment confirming diagnosis is not available, report the date of diagnosis indicated in the progress notes.

If there are multiple non-melanoma skin cancer lesions detected in the current reporting period, report the diagnosis date as the date when the first lesion was identified.

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

Question 10: Number of non-melanoma skin cancer lesions

Report the number of non-melanoma skin cancer lesions diagnosed in the current reporting period.

Cell Origin Evaluation Documentation
The submission of cell origin evaluation (i.e., VNTR, cytogenetics, FISH) reports and other supportive documentation for each reported new malignancy is *strongly recommended.*
For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Question 11: Was the new malignancy donor / cell product derived?

Indicate whether the new malignancy originated from the donor / cell product. If testing to determine the cell origin of the new malignancy was not completed, select **Not done**.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q12 – 22: Post-Transplant Lymphoproliferative Disorder

Question 12: Was PTLD confirmed by biopsy?

Indicate if PTLD was confirmed by a biopsy.

EBV Testing Documentation
The submission of EBV tumor testing documentation (i.e., pathology report) is *strongly recommended.*
For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Question 13: Was the pathology of the tumor EBV positive?

Using the pathology report, specify if the PTLD tumor was EBV positive.

Question 14: Was there EBV reactivation in the blood?

Specify if there was EBV reactivation in the blood. If EBV reactivation (in the blood) was not assessed, select **Not done**.

Questions 15 – 17: How was EBV reactivation diagnosed?

EBV reactivation may be diagnosed by polymerase chain reaction (PCR) methods (qualitative or quantitative) where a blood sample is taken and manipulated using PCR techniques to determine the presence and classification of an organism by identifying DNA sequences unique to the specific organism.

Indicate how EBV reactivation was diagnosed.

- **Qualitative PCR of blood**: Indicates if EBV was detected (provides "positive" or "negative" results).
- **Quantitative PCR of blood**: Provides the number of copies of EBV detected. If selected, specify the viral load of blood (at diagnosis of EBV) in copies / mL.

If EBV reactivation was diagnosed by a method other than qualitative or quantitative PCR of blood, select **Other method** and specify.

Questions 18 – 19: Was a quantitative PCR of blood performed again after diagnosis?

If EBV reactivation was diagnosed by quantitative PCR of blood, as reported above, specify if a quantitative PCR of blood was performed again after diagnosis. If **Yes**, report the *highest* EBV viral load of blood in the current reporting period.

Questions 20 – 22: Was there lymphomatous involvement? (e.g. a mass)

Indicate if there was lymphomatous involvement of PTLD (i.e., a mass). If **Yes**, specify all sites of involvement. If an involvement site is not listed as an option on the form, select **Other site** and specify.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)