4100: Cellular Therapy Essential Data Follow-Up

This form must be completed for all recipients of cellular therapy (non-HCT), including post-HCT DCI infusions. For recipients of hematopoietic cellular transplants, complete the appropriate HCT follow-up form. For recipients of Donor Lymphocyte Infusions (DLI), complete the Donor Lymphocyte Infusion (2199) form.

The Post-Cellular Therapy Essential Data (Post-CTED) follow-up form focuses on key follow-up information for each reporting period, including the survival status of the recipient, additional cellular infusions performed, best response to the cellular therapy, development of new malignancies, development and severity of toxicities (e.g. cytokine release syndrome, neurotoxicity), infection and fertility information. The structure of the Post-CTED is such that each form should fit on a timeline with distinct start and stop dates that do not overlap any other forms.

The Post-CTED Form schedule is determined by the center's cell therapy reporting preference and in the infusion details. Each cell therapy infusion will randomize separately. This form will be paired with the Post-Cellular Therapy Follow-Up (4101) form if the infusion is selected for the CRF reporting level. For more information, click here.

Combined follow up
In scenarios where both HCT and cellular therapy forms are being completed, there are two scenarios where the Cellular Therapy Essential Data Follow-Up (4100) form is completed:

Example 1. Cellular therapy after HCT: completion of this form should be based on the time period in relation to the CT infusion date (i.e., 100 days after the CT infusion date). The visit ID and date of contact should match between the corresponding Post-HSCT Data (2100) or Post-Transplant Essential Data (2450).

Example 2. HCT after cellular therapy: completion of this form should be based on the time period in relation to the HCT infusion date (i.e., 100 days after the HCT infusion date). The visit ID and date of contact should match between the corresponding Post-HSCT Data (2100) or Post-Transplant Essential Data (2450).

Duplicate questions between HCT and cellular therapy forms may be disabled on the Post-CTED. A full list of enabled/disabled fields can be found on the Combined Follow Up section of the Data Management Guide. Illustrations of the combined follow up scenarios can also be found the Guide.

Links to sections of form:

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

Date	Manual Section	Add/ Remove/ Modify	Description
10/ 24/ 2025	4100: Cellular Therapy Essential Data Follow-Up	Add	Q82 -83 updated: *Check all that apply from the list of drug(s) given to treat neurotoxicity in this reporting period. Pulse dose of corticosteroids are intravenous (IV) high doses given intermittently over a short time period. Specify if **Other therapy** is selected. Supportive care treatments should not be reported as treatment for neurotoxicity. Examples of what not to report as other therapy include, but are not limited to, antibiotics (e.g., amoxicillin, cefepime, ciprofloxacin, piperacillin), antipsychotics (e.g., Risperdal) narcotics/opioids, or other pain killers. If a drug was started as planned prophylaxis but the recipient develops neurotoxicity and the drug is continued, this is considered a change in intent from prophylaxis to treatment and the drug should also be reported as therapy for neurotoxicity.*
10/ 24/ 2025	4100: Cellular Therapy Essential Data Follow-Up	Add	Q50 – 52 updated: *If **Tocilizumab** was given to treat the CRS, report the number of doses given. This information is important in the grading of the CRS event. If a drug was started as planned prophylaxis but the recipient develops CRS and the drug is continued, this is considered a change in intent from prophylaxis to treatment and the drug should also be reported as therapy for CRS.*
10/ 24/ 2025	4100: Cellular Therapy Essential Data Follow-Up	Modify	GVHD treatment CR criteria updated in table 1 in Q12: ~~*Improvement but not resolution of symptoms, or remains on immune suppression*~~ *Resolution of symptoms and off immune suppression*
10/ 24/ 2025	4100: Cellular Therapy Essential Data	Add	Table 2 added in Q13

	Follow-Up		
4/30/2025	4100: Cellular Therapy Essential Data Follow-Up	Add	Added new warning box above question 47: Effective April 30th, 2025, report only toxicities (e.g. CRS, neurotoxicity, etc.) that are **directly** attributed to the CAR-T product / infusion. It is no longer required to report any toxicity regardless of causality. Treatment given post-infusion may have the effect of re-activating the product and inducing toxicities (e.g. CRS), these toxicities should **NOT** be captured in this section of the form. Contact CIBMTR Center Support with questions.
4/30/2025	4100: Cellular Therapy Essential Data Follow-Up	Remove	Removed the blue note box above question 47: ~~Report any observed toxicity or infection that occurs post-infusion in this reporting period, regardless of causality and whether or not treatment was administered. The intent is to capture all toxicities diagnosed after the cellular therapy infusion. Although treatment given post-infusion may have the effect of re-activating the product and inducing toxicities (e.g. CRS), these toxicities should still be captured in this section of the form.~~
4/19/25	Q12-14: Best Response to Cellular Therapy	Add	Added blue box above question 13: If a subsequent cellular therapy was given for disease relapse / progression and the F4000 was made NRQ, the best response prior to the relapse/ progression should be reported.
10/25/2024	4100: Cellular Therapy Essential Data Follow-Up	Modify	Correct “CRS” to “MAS / HLH-like toxicities”: Check all that apply from the list of the drug(s) given to treat ~~CRS~~ MAS / HLH-like toxicities in this reporting period.
10/25/2024	4100: Cellular Therapy Essential Data Follow-Up	Add	Added red warning box: **Pregnancy Questions** Pregnancy questions will only be answered for recipients between the ages of 10 and 60.
10/25/2024	4100: Cellular Therapy Essential Data Follow-Up	Modify	Removed “IVIG” from 138, 140 Examples 1, 2, 3, 4, 5 and added “immunoglobulin replacement therapy (includes, but not limited to, IVIG or SCIG)” in 138
10/25/	4100: Cellular	Modify	Removed Disabled for TED reporting level

2024	Therapy Essential Data Follow-Up		
10/25/2024	4100: Cellular Therapy Essential Data Follow-Up	Modify	Updated the definition for MAS/HLH-like toxicity onset date: ~~Report the date (YYYY-MM-DD) when the first symptom of MAS/HLH was documented by either the date of the pathological confirmation of MAS/HLH (bone marrow or other organ biopsy) or the first date of a ferritin level > 100,000 ng/mL among patients without pathologic confirmation but with high clinical suspicion (persistent high fevers, ongoing cytopenias, high triglyceride levels, low fibrinogen levels or organomegaly).~~ Report the date (YYYY-MM-DD) when the first symptom of MAS / HLH-like toxicities was documented by a physician or other health care provider in the progress note or chart.
10/25/2024	4100: Cellular Therapy Essential Data Follow-Up	Modify	Added bold text below question header: Questions 142-147: Tumor lysis syndrome **Disabled for TED reporting level**
7/26/2024	4100: Cellular Therapy Essential Data Follow-Up	Add	Instructions added to Q4
7/26/2024	4100: Cellular Therapy Essential Data Follow-Up	Add	Subsequent HCT and Cellular Therapy red warning box added above Q5
6/11/2024	4100: Cellular Therapy Essential Data Follow-Up	Modify	Normal limits of IgG concentration in the blood vary with age. For adults, levels lower than 600 mg/dL of circulating IgG are considered to be hypogammaglobulinemia. Children ages 4 to ~~10~~ 18, levels lower than 500 mg/dL are considered hypogammaglobulinemia.
5/22/2024	4100: Cellular Therapy Essential	Add	Added new note regarding combined follow up for question 148: In scenarios where an HCT was given after a cellular therapy and this form is now being completed based on the subsequent HCT date, these questions do not apply and are disabled.

	Data Follow-Up		
4/26/2024	4100: Cellular Therapy Essential Data Follow-Up	Modify	Correction of required to received: **Questions 138-139: Did the recipient ~~require~~ receive immunoglobulin replacement therapy?** Replacement therapy is given to prevent infections. If the recipient ~~required~~ received immunoglobulin replacement therapy (IVIG) regardless of hypogammaglobulinemia that developed post-infusion, select Yes and indicate if the recipient is still ~~requiring~~ receiving the therapy on the contact date for this reporting period. If the last immunoglobulin replacement therapy (IVIG) was given less than 6 months from the date of contact, report Yes unless it's clearly stated in the medical record that no more immunoglobulin replacement therapy is required.
4/23/2024	4100: Cellular Therapy Essential Data Follow-Up	Modify	Updated blue box above question 24: The disease relapse or progression questions are ~~applicate~~ applicable for malignant diseases ~~that do not generate~~ when ~~a~~ disease specific form s ~~(e.g., AML, CML, MDS, MPN)~~ are not present or ~~and for~~ the following products are reported in question 1: Letetresgene autoleucel, Other product, or No product name.
1/19/2024	4100: Cellular Therapy Essential Data Follow-Up	Add	Added text in red to the first blue box above question 12: If the primary disease reported is Acute Lymphoblastic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), Hodgkin Lymphoma (HL), Non-Hodgkin Lymphoma (NHL), or Multiple Myeloma (MM) and there is a corresponding disease form, best response is not reported on this form.
1/16/2024	4100: Cellular Therapy Essential Data Follow-Up	Add	Added the following text to question 85: Lower scores are associated with a higher level of encephalopathy. Report the lowest score of any evaluation from the reporting period. **Unable to complete assessment** should be selected when an assessment was started and couldn't be finish for any reason or the recipient couldn't perform the evaluation. This should be used rarely since evaluations may be given multiple times a day.
1/15/2024	4100: Cellular Therapy Essential Data Follow-Up	Modify	Added the text in red: Disease relapse or progression can be documented by a variety of methods including molecular, flow cytometry, cytogenetic/fluorescent in situ hybridization (FISH), radiographic or hematological/clinical. The intent is to captures any new relapse or progression event that occurred in the reporting period, not just the initial relapse or progression. Report Yes if any new disease relapse or progression was detected by any one of the methods in the current reporting period and report the first date (YYYY-MM-DD) of the relapse or progression detected.
12/19/2023	4100: Cellular Therapy	Modify	Time frame for reporting the 1Y contact date updated in the Contact Date table in Q2: _F4100 , 1 Year, + 60 days (Day 36 ~~5~~ 6 – 425)

	Essential Data Follow-Up		
12/12/2023	4100: Cellular Therapy Essential Data Follow-Up	Modify	Select **Not applicable** when: The recipient never got immunoglobulin replacement therapy due to never having a decreased IgG level Or There was no decline in IgG levels in this reporting period Or IgG levels were never tested in this reporting period
11/21/2023	4100: Cellular Therapy Essential Data Follow-Up	Modify	DO report an infection in the following scenarios: A recipient has a positive COVID-19 diagnostic result (PCR or antigen) ~~or if treatment was given or if the recipient was asymptomatic.~~ regardless of if treatment was given or if the recipient was asymptomatic.
9/7/2023	4100: Cellular Therapy Essential Data Follow-Up	Modify	Select **Not applicable** when: The recipient never got immunoglobulin replacement therapy due to never having a decreased IgG level Or There was no decline in IgG levels in this reporting period
8/25/2023	4100: Cellular Therapy Essential Data Follow-Up	Modify	Diagnosis of COVID-19 after the start of the lymphodepleting therapy: Any COVID-19 infections diagnosed after the start of the lymphodepleting therapy should be reported in the following questions on the Cellular Therapy Essential Data Follow-Up (4100) form. ~~An associated Respiratory Virus Post-Infusion Data (2149) form will be generated.~~ Effective August 25, 2023, the Respiratory Virus Post-Infusion Data (2149) form for infusions on the cellular therapy track will no longer be required. Additionally, an unscheduled Respiratory Virus Post-Infusion Data (2149) form cannot be created for these recipients.
8/24/2023	4100: Cellular Therapy Essential Data Follow-Up	Add	If the recipient never got immunoglobulin replacement therapy and their immunoglobulin levels were never decreased, select **Not applicable**.
8/22/2023	4100: Cellular Therapy Essential Data Follow-Up	Modify	Clarified the intention of the question: Indicate if the recipient received pre-exposure drugs for COVID-19 in this reporting period.

7/28/2023	4100: Cellular Therapy Essential Data Follow-Up	Add	Version 9 of the 4100: Post- Cellular Therapy Follow-Up section of the Forms Instruction Manual released. Version 9 corresponds to revision 9 of the form 4100.

Last modified: Oct 31, 2025

Q1: Product

Question 1: Name of Product: (for most recent cell therapy infusion)

The name of the product reported will be auto populated with the value reported on the Pre-Cellular Therapy Essential Data (4000) form. If the cellular therapy product infused is a commercially available or pre-commercial product, this question is used to enable questions related to toxicities and disable questions that do not apply.

Combined follow up
In scenarios where both HCT and cellular therapy forms are being completed, and the recipient has received the HCT after the cellular therapy, the product name should be for the prior cellular therapy product.

Section Updates:

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

Last modified: Jul 29, 2023

Q2-3: 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-CTED 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 whether there is actual patient contact on the date. This is an exception to standard date of follow-up reporting to ensure all dates are captured within the sequence of forms.

Question 2: Date of actual contact with the recipient to determine medical status for this follow-up report:

Enter the date of actual contact with recipient to determine medical status for this follow-up report. Acceptable evaluations include those from the transplant center, referring physician, or other physician currently assuming responsibility for the recipient's care. 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, found here.

In general, the date of contact should be reported as close to the 100-day, 6 month, or annual anniversary to transplant as possible. Report the date of actual contact with the recipient to evaluate medical status for the reporting period. In the absence of contact with a clinician, other types of contact may include a documented phone call with the recipient, a laboratory evaluation, or any other documented recipient

interaction on the date reported. If there was no contact on the exact time point, choose the date of contact closest to the actual time point. Below, the guidelines show an ideal approximate range for reporting each post-transplant time point:

Form	Time Point	Approximate Range
F4100	100 Days	+/- 15 days (Day 85 – 115)
F4100	6 Months	+/- 30 days (Day 150 – 210)
F4100	1 Year	+ 60 days (Day 366 – 425)
F4100	Annual reporting 2+ Years	+/- 30 days (Months 23-25, 35-37, etc.)

Recipients are not always seen within the approximate ranges and some discretion is required when determining the date of contact to report. In that case, report the date closest to the date of contact within reason. The examples below assume that efforts were undertaken to retrieve outside medical records from the primary care provider, but source documentation was not available.

Example 1. *The 100 day date of contact doesn't fall within the ideal approximate range*.
The recipient had an infusion on 1/1/18 and is seen regularly until 3/1/18. After that, the recipient was referred home and not seen again until 7/1/18 for a restaging exam and 7/5/18 for a meeting to discuss the results.

What to report:
100 Day Date of Contact: 3/1/18 (Since there was no contact closer to the ideal date of 4/11/18, this date is acceptable)
6 Month Date of Contact: 7/5/18 (note the latest disease assessment would likely be reported as 7/1/18)

Example 2. *The 100 day date of contact doesn't fall within the ideal approximate range and the recipient wasn't seen again until 1 year post-cellular therapy*.

The recipient had an infusion on 1/1/18 and is seen regularly until 3/1/18. After that, the recipient was referred home and not seen again until 1/1/19 for a restaging exam and 1/4/19 for a meeting to discuss the results.

What to report:
100 Day Date of Contact: 3/1/18 (Since there was no contact closer to the ideal date of 4/11/18, this date is acceptable)
6 Month form: Indicate the recipient is lost to follow-up in FormsNet3^{SM}
1 Year Date of Contact: 1/4/19 (note the latest disease assessment would likely be reported as 1/1/19)

Additional information:

- A date of contact should never be used multiple times for the same recipient's forms.
    - For example, 6/1/18 should not be reported for both the 6 month and 1 year. Instead, determine

the best possible date of contact for each reporting period; if there is not a suitable date of contact for a reporting period, this may indicate that the recipient was lost to follow-up.

- If the recipient has a disease evaluation just after the ideal date of contact, capturing that data on the form may be beneficial.
    - For example, if the recipient's 90 day restaging exam was delayed until day 115 and the physician had contact with the recipient on day 117, the restaging exams can be reported as the latest disease assessment and day 117 would be the ideal date of contact, even though it is just slightly after the ideal approximate range for the date of contact.

Date of Contact & 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 unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Example 3. *The recipient has died before their six month reporting period.*
The recipient had an infusion on 1/1/18 and was seen regularly through the first 100 days. They had restaging exams on 4/4/18 and were seen on 4/8/18, and then died on 5/13/18 in the hospital emergency room.

What to report:
100 Day Date of Contact: 4/8/18 (note the latest disease assessment would likely be reported as 4/4/18)
6 Month Date of Contact: 5/13/18 (though the death does not occur within the ideal approximate range for 6 months)

Example 4. *The recipient has died after their six month time point.*
The recipient had an infusion on 1/1/18 and was seen regularly through the first 100 days. The recipient had restaging exams on 4/22/18 and was seen on 4/23/18. Based on findings in the restaging exam, the recipient was admitted for additional treatment. The disease was found to be refractory on a 6/25/18 restaging exam, and the recipient was discharged to hospice on 7/8/18. The hospital was notified via telephone that the recipient died on 7/16/18.

What to report:
100 Day Date of Contact: 4/23/18 (note the latest disease assessment would likely be reported as 4/22/18)
6 Month Date of Contact: 7/16/18 (note the latest disease assessment would likely be reported as 6/25/18)

Date of Contact & 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 / systemic therapy begins for the subsequent infusion. If no preparative regimen / systemic 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 / systemic (or infusion, if no preparative regimen / systemic 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. DCI) cellular therapy infusion, report the date of contact as **appropriate** to the reporting period.

Example 5. *The recipient receives a subsequent HCT with a preparative regimen*
The recipient had a cellular therapy on 1/1/18 and was seen regularly through the first 100 days. The recipient was admitted on and received their first dose of chemotherapy for the preparative regimen for HCT #2 on 1/28/18

What to report:
100 Day Date of Contact: 1/27/22 (regardless of actual contact on that date)

The cell therapy was a CAR-T or other genetically modified cell therapy: Both HCT and cellular therapy forms will be completed simultaneously, but all applicable cellular therapy follow-up forms will be reset to the new event date (i.e., Forms 2450+4100 or Forms 2100+4100). The forms will then have the same event date and due date. See Subsequent Infusions – Updates to Follow-Up Reporting in the Data Management Manual for more information on combined follow up.

The cell therapy was a non-genetically modified: *Reporting on the cellular therapy event will end*.

Combined follow up
In scenarios where both HCT and cellular therapy forms are being completed, the contact date must match between the Form 2100+4100 or Form 2450+4100.

Example 6. *The recipient receives a subsequent HCT without a preparative regimen.*
Following their first cellular therapy infusion on 1/1/22, a recipient with solid tumor required a subsequent allogeneic transplant. The recipient has remained inpatient following the first infusion. The physician planned the subsequent transplant for 5/31/22, and proceeded without a preparative regimen.

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

The cell therapy is CAR-T or other genetically modified cell therapy: HCT and cellular therapy forms

will be completed simultaneously, but all applicable cellular therapy follow-up forms will be reset to the new event date (i.e., Forms 2450+4100 or Forms 2100+4100). The forms will then have the same event date and due date. See Combined Follow Up section in the Data Management Manual for more information on combined follow up.

The cell therapy is non-genetically modified: *Reporting on the cellular therapy event will end*.

Example 7. *The recipient had a subsequent genetically modified cellular therapy with lymphodepleting therapy administered prior to infusion.*
The recipient has their first cell therapy infusion on 2/1/22 and a genetically modified (e.g. CAR-T) cellular therapy infusion on 3/1/22. The recipient was admitted on and received their first dose of lymphodepleting therapy 2/28/22.

What to report:
100 Day Date of Contact: 2/27/22 (regardless of actual contact on that date). Reporting on the first cellular therapy event will end

Example 8. The recipient had a subsequent non-genetically modified cellular therapy.
The recipient has their first cell therapy infusion on 1/21/15 and a non-genetically modified (e.g. DCI) cellular therapy infusion on 2/15/15. There was no lymphodepleting therapy administered.

What to report:
100 Day Date of Contact: The date of contact reported will be appropriate to the reporting period. Combined follow up will not be applied, a single F4100 is required, then HCT reporting continues.

p.(banner tip). **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-CTED (4100) form, when applicable.

Question 3: Specify the recipient's survival status at the date of last contact:

Indicate the clinical status of the recipient on the date of actual contact for follow-up evaluation. If the recipient has died, answers to subsequent questions should reflect the recipient's clinical status between the date of last report and their death. The center must also complete a Recipient Death Data (2900) form.

Combined follow up
In scenarios where both HCT and cellular therapy forms are being completed, the death must be reported on both the HCT and cellular therapy forms. If there are Comprehensive Report forms for the HCT, two Recipient Death Data (2900) forms will come due. You only need to complete one form. Contact CIBMTR Center Support to remove the duplicate.

Section Updates:

Question	Date of	Add/	Description	Reasoning (If

Number	Change	Remove/ Modify		applicable)
Q2	12/19/ 2023	Modify	Time frame for reporting the 1Y contact date updated in the Contact Date table: _F4100 , 1 Year, + 60 days (Day 36 ~~5~~ 6 – 425)	Updated to be consistent with reporting 1Y contact date for HCT

Last modified: Apr 23, 2024

Q4-11: Subsequent Cellular Infusions

Combined follow up

In scenarios where both HCT and cellular therapy forms are being completed, duplicate questions will exist between the Cellular Therapy Essential Data Follow-Up (4100) form and the Post-HCT Data (2100) or Post-Transplant Essential Data (2450) form. To reduce the reporting burden, duplicate questions, including subsequent infusions, on the Cellular Therapy Essential Data (4100) form are disabled and will be answered on the Post-HCT Data (2100) or Post-Transplant Essential Data (2450) form.

Subsequent Cellular Infusions
All additional cellular therapy infusions of the same product given for the same indication per protocol require a separate Cellular Therapy Infusion (4006) form. However, they will only require a single Cellular Therapy Product (4003) form for this course of cellular therapy. If a cellular therapy was administered for a different indication (i.e., in response to disease progression / no response, another infusion of a commercial product, etc.) a new Pre-Cellular Therapy Essential Data (4000) form must be completed.

Question 4: 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).

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

Subsequent HCT and Cellular Therapy
The following questions are disabled as of July 26, 2024: *Did the recipient receive a subsequent HCT?*, *Has the recipient received a cellular therapy?*, *Was this infusion a donor lymphocyte infusion (DLI)?*, *Number of DLIs in this reporting period*, *Are any of the products, associated with the course of cellular therapy, genetically modified?*, *Date of cellular therapy*; and will be removed with the next revision of this form. All subsequent infusions are reported in the question above *Did the recipient receive a subsequent infusion?*

Question 5: Has the recipient received a new course of cellular therapy (unplanned) since the date of the last report?

Cellular Therapy Infusions Over Multiple Reporting Periods
If a course of cellular therapy carries over a reporting period, and has already been reported on a prior form, do not re-report that course of cellular therapy. For example, if a course of cellular therapy includes three infusions, and the third infusion overlaps from the one year to

two-year reporting period, do not report a new cellular therapy since the date of the last report on the two year follow up form. This would trigger a new Pre-CTED (4000) form which is not required for infusions part of a single course of cellular therapy.

A course of cellular therapy consists of all infusions given for the same indication, using the same donor / product, per protocol. If the recipient started a new course of cellular therapy (unplanned) that is different than the course this follow up form is being completed for, select **Yes**.

If additional infusions were given for the same indication per protocol, do not report those infusions here. Update the Cellular Therapy Product (4003) form for the applicable product with the correct number of infusions given per protocol. Each infusion requires a separate Cellular Therapy Infusion (4006) form.

In cases where a new course of cellular therapy is being given post-HCT, only the first infusion is reported on the appropriate HCT follow up form (either the Post-HCT Data (2100) or Post-Transplant Essential Data (2450) form). Remaining infusions of a single course of cellular therapy (e.g., multiple DCIs) are not reported as subsequent infusions. They are captured on a single Cellular Therapy Product (4003) Form as the number of planned infusions.

Example 1. The new course of cellular therapy (post-HCT) consisting of multiple infusions started at the end of the 6- month HCT reporting period and continued into the beginning of the 1-year HCT reporting period.

How to report: The new course of cellular therapy should be reported only on the 6-month HCT follow-up form (either the Post-HSCT Data (2100) or Post-Transplant Essential Data (2450) form) and not on the Cellular Therapy Essential Data Follow-Up (4100) form.

- Reporting an infusion on the Cellular Therapy Essential Data Follow-Up (4100) form as a subsequent infusion will generate a new Pre-Cellular Therapy Essential Data (4000) form. If you need help removing a Pre-Cellular Therapy Essential Data (4000) form, please make sure the field is corrected and contact CIBMTR Center Support to remove the form.

Example 2. Two non-genetically modified courses of post-HCT cell therapy (e.g., DCI/DLI and MSCs) are given within 100 days of each other in the same reporting period.

How to report: Report the first course as a subsequent cellular therapy on either the Post-HSCT Data (2100) or Post-Transplant Essential Data (2450) form. This will make a new Pre-Cellular Therapy Essential Data (4000) form due. When it is completed, report the second course of cellular therapy on the 100-day Cellular Therapy Essential Data Follow-Up (4100) form to generate the second Pre-Cellular Therapy Essential Data (4000) form.

Example 3. Two non-genetically modified courses of post-HCT (e.g., DCI/DLI and MSCs) are given greater than 100 days apart, but still within the same reporting period.

How to report: Report the first course as a subsequent cellular therapy on the Post-HSCT Data (2100) or

Post-Transplant Essential Data (2450) form. Then create a new indication form to report the second course, which will make a second Pre-Cellular Therapy Essential Data (4000) form come due.

Example 4. Two genetically modified courses of post-HCT (e.g., Kymriah® and Yescarta®) are given in the same reporting period.

How to report: Report the first course as a subsequent cellular therapy on the Post-HSCT Data (2100) or Post-Transplant Essential Data (2450) form. This will make a new Pre-Cellular Therapy Essential Data (4000) form due. When it is completed, combined follow up rules will apply and both HCT and cellular therapy forms will be completed. Report the second course of cellular therapy on the 100-day Cellular Therapy Essential Data Follow-Up (4100) form to generate the second Pre-Cellular Therapy Essential Data (4000) form.

Question 6: Was this infusion a Donor Lymphocyte Infusion?

Donor lymphocyte infusions (DLI) are considered a type of cellular therapy. These infusions are not intended to promote hematopoiesis. If the recipient received additional cells due to engraftment issues, or if they received an infusion of unmanipulated CD34+ cellular product (stimulated peripheral blood stem cells, bone marrow, or cord blood), report as a subsequent HCT rather than a cellular therapy. For more information on how to distinguish infusion types (example: HCT versus DCI), see Appendix D.

Indicate if the infusion was a donor lymphocyte infusion (DLI). An infusion is donor lymphocyte infusion when all the following criteria are met:

- The intent of the infusion is something other than to restore hematopoiesis
- The infusion must be post-Allogenic HCT, often by the same donor as the HCT
- The product must be a lymphocyte-only product
- The product cannot be genetically modified

If the infusion meets the above definition of DLI, select **Yes** and complete the Donor Lymphocyte Infusion (2199) form instead of the Cellular Therapy Essential Data Pre-Infusion (4000) form.

If the infusion does not meet CIBMTR DLI criteria, select **No**.

Question 7: Number of DLIs in this reporting period:

Report the number of Donor Lymphocyte Infusions (DLI) the recipient received in the reporting period. This question is used to make the correct number of Donor Lymphocyte Infusion (2199) Forms come due.

Question 8: Are any of the products, associated with this course of cellular therapy, genetically modified?

Genetically modified products include any product that was manipulated to alter its gene expression through the insertion of different genes or editing of genes. An example of a genetically modified product is the manipulation of T-lymphocytes to express Chimeric Antigen Receptors (CAR T-cells) directed towards specific tumor targets (antigens). Donor Lymphocyte infusions are typically not genetically modified.

Report **Yes** if the product associated with the course of cell therapy being reported in this instance is genetically modified. This question is used to determine the follow up schedule of the cellular therapy.

Question 9: Date of cellular therapy:

Report the date (YYYY-MM-DD) of the new course of cellular therapy (unplanned). If the new course of cellular therapy includes multiple infusions, the date of the first infusion should be reported here. This will require completion of a new Pre-Cellular Therapy Essential Data (4000) form.

Questions 10 – 11: Did the recipient receive an HCT since the date of last report?

If the recipient received an HCT since the date of the last report, select **Yes** and report the date (YYYY-MM-DD) of the HCT; also complete the Pre-Transplant Essential Data (2400) form.

Combined follow up
Regulatory requirements specify at least 15 years of follow-up data be collected on recipients of genetically modified cellular therapy products, reporting on the cellular therapy event will continue. Both HCT and cellular therapy forms will be completed.

If the recipient did not receive an HCT since the date of the last report, report **No**.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q4	7/26/ 2024	Add	Instructions added to Q4	Questions is now enabled due to the new infusion reporting process released with the Summer 2024 Quarterly Release
Q5	7/26/ 2024	Add	Subsequent HCT and Cellular Therapy red warning box added above Q5	Questions now disabled due to the new infusion reporting process released with the Summer 2024 Quarterly Release

Last modified: Jul 29, 2024

Q12-14: Best Response to Cellular Therapy

This section may not fit perfectly to all possible indications for cellular therapy. Please select the response that is most applicable to the indication for treatment.

> ✻ If the primary disease reported is Acute Lymphoblastic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), Hodgkin Lymphoma (HL), Non-Hodgkin Lymphoma (NHL), or Multiple Myeloma (MM) **and** *there is a corresponding disease form*, best response is not reported on this form. It will be captured on the corresponding disease form. The question should be left blank and override the error with the override code "Verified Correct (VC)" at this time.

> ✻ If the indication for this course of cellular therapy does not require the completion of disease-specific forms, please refer to the disease-specific manuals to locate the response criteria that should be used when reporting best response.

Question 12: What was the best response to the cellular therapy?

This section collects the data known as "best response to cellular therapy". **The purpose of this section is to report the recipient's best response to the planned course of cellular therapy**. This section applies to both malignant and non-malignant diseases and disorders. If the recipient received a prior HCT, do not report the response to the HCT, a separate evaluation to establish best response after the cellular therapy is required.

Combined follow up
If the recipient receives a subsequent HCT, do not report the best response to the HCT here. The reported best response to the cellular therapy was previously reported and can no longer be evaluated once a recipient has a subsequent HCT. Continue to report best response achieved from the cellular therapy.

For malignant diseases (including solid tumors), appropriate responses are:

- Continued complete response
- Complete response
- Partial response
- No response
- Disease progression

For non-malignant disorders and cardiovascular, musculoskeletal, neurologic, ocular or pulmonary disease, appropriate responses are:

- Normalization of organ function
- Partial normalization of organ function

- No response
- Worsening of organ function

If the indication is infection, the appropriate responses are:

- Complete response
- Partial response
- No response

Table 1. Examples of best response to cellular therapy.

Indication	Applicable response options	Partial Response	Complete Response
Cardiovascular Disease, Musculoskeletal Disorder, Neurologic Disease, Ocular Disease, Pulmonary Disease	Do not answer best response	-	-
GVHD prophylaxis (with HCT)	Do not answer best response	-	-
GVHD treatment (post-HCT)	Complete Response, Partial Response, or No Response	Improvement but not resolution of symptoms, Remains on immune suppression	Resolution of symptoms and off immune suppression
Immune Reconstitution (post-HCT)	Complete Response or No Response	-	CD3 >200/mm^3
Infection prophylaxis	Do not answer best response	-	-
Infection treatment	Complete Response, Partial Response, or No Response	Decrease in infectious burden without resolution	Undetectable infection
Malignant Hematologic Disorder	Continued complete response, Complete Response, Partial Response, Progression, or No Response	Refer to the response criteria as published in the disease specific manual and Table 2 below	Refer to the response criteria as published in the disease specific manual and Table 2 below
Non-Malignant Disorder	Normalization of organ function, Partial normalization of organ function, No response, Worsening of organ function	Persistent Disease	Resolution of Disease Process

Other	Do not answer best response	-	-
Prevent disease relapse	Do not answer best response	-	-
Solid Tumor	Continued complete response, Complete Response, Partial Response, No Response, or Disease Progression	Improvement in disease burden, but with persistent disease	No evidence of disease
Suboptimal donor chimerism (post-HCT)	Complete Response, Partial Response, or No Response	Increase in chimerism but not 100% donor	100% donor chimerism

If the recipient relapses / progresses post-infusion and receives therapy for the disease relapse / progression, the response to that additional therapy should not be reported in this section. The best response prior to the relapse/ progression should be reported.

When reporting best response for myeloma, ALL, or lymphoma, refer to Table 2 to determine the appropriate option to select on the Post-CTED.

Table 2.

PCD Response Criteria	Select this Option	ALL Response Criteria	Select this Option	LYM Response Criteria	Select this Option
sCR	CR	CR	CR	CR	CR
CR	CR	CRi	CR	PR	PR
VGPR	PR	PIF	Disease progression	SD	NR
PR	PR			PD	Disease progression
SD	NR				
PD	Disease progression				

✻ If a subsequent cellular therapy was given for disease relapse / progression and the F4000 was made **NRQ**, the best response prior to the relapse/ progression should be reported.

Question 13-14: Was the date of best response previously reported?

If the best response to cellular therapy was first documented during the current reporting period, report **No**. If the best response was achieved during a previous reporting period (and therefore reported on a previous

post-CTED form), report **Yes**.

Do not report **Yes** if completing this form for the 100 day reporting period.

Combined follow up
If the recipient receives an HCT after a cellular therapy and the best response to the cellular therapy was previously reported, it can no longer be evaluated once a recipient has a subsequent HCT. It is appropriate to report **Yes** for this scenario on the 100 day report.

If the date of best response has not been reported, select **No** and report the date (YYYY-MM-DD). The date of best response should be the first date all criteria were met.

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

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
12	10/24/ 2025	Modify	GVHD treatment CR criteria updated: ~~*Improvement but not resolution of symptoms, or remains on immune suppression*~~ *Resolution of symptoms and off immune suppression*	Incorrect instructions
12	4/19/25	Add	Added blue box above question 13: If a subsequent cellular therapy was given for disease relapse / progression and the F4000 was made NRQ, the best response prior to the relapse/ progression should be reported.	Additional clarification for reporting best response when a subsequent cell therapy is given, but the F4000 is NRQ.
12	1/19/24	Add	Added text in red to the first blue box above question 12: If the primary disease reported is Acute Lymphoblastic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), Hodgkin Lymphoma (HL), Non-Hodgkin Lymphoma (NHL), or Multiple Myeloma (MM) and there is a corresponding disease form, best response is not reported on this form.	Additional clarification for TED level reporting.
13	10/24/ 2025	Add	Table 2 added	Added for clarification

Last modified: Oct 31, 2025

Q15-23: Peripheral Blood Count Recovery

> ! Peripheral Blood Count Recovery questions can only be completed on the 100 day and 6 month follow-up forms. These questions will be disabled for all subsequent reporting periods.

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

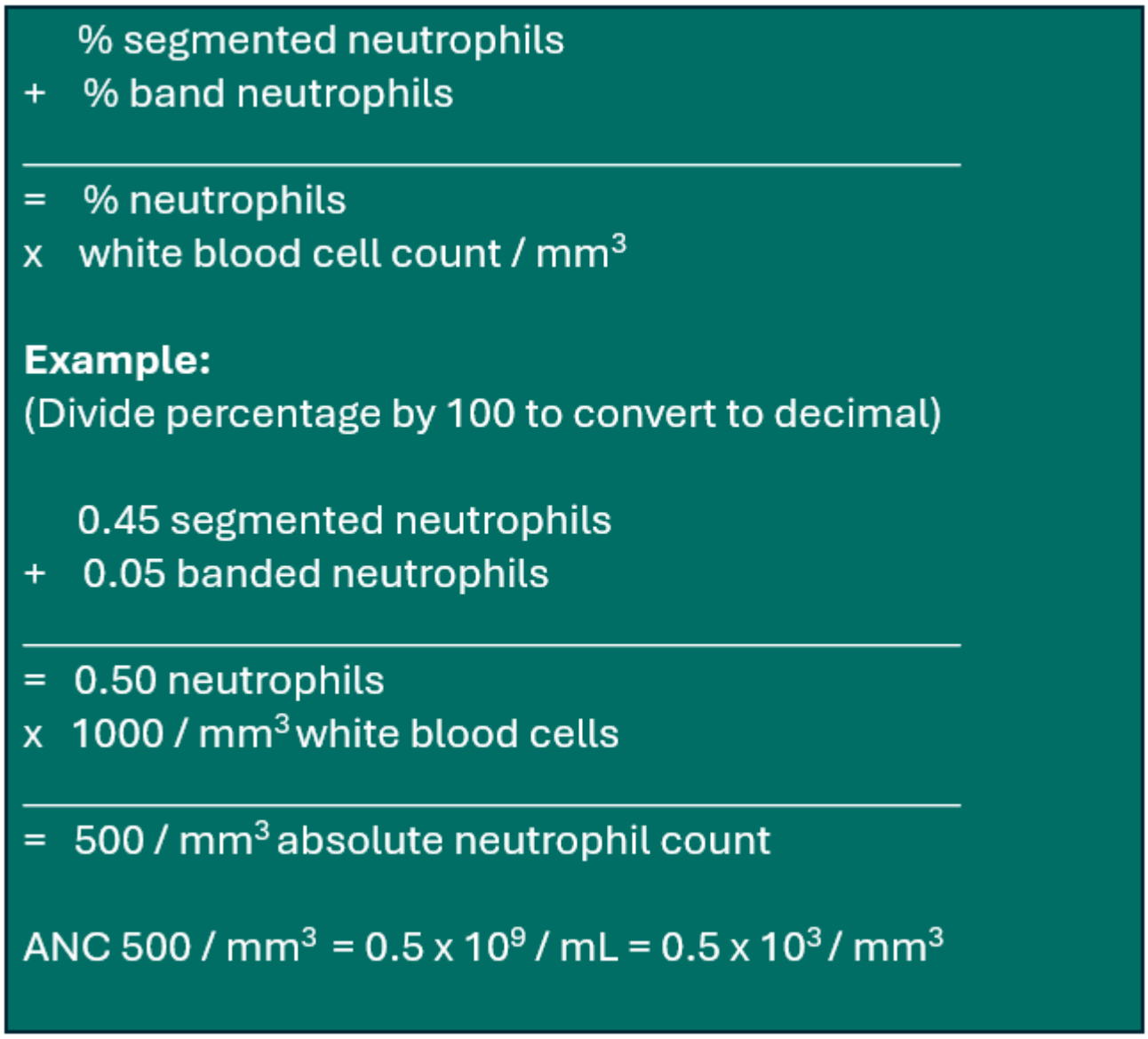
Example 1. Cellular therapy after HCT: completion of this form should be based on the time period in relation to the CT infusion date (i.e., 100 days after the CT infusion date). The visit ID should match between the corresponding Post-HSCT Data (2100) or Post-Transplant Essential Data (2450).

Example 2. HCT after cellular therapy: These questions do not apply and are disabled.

The reporting of peripheral blood count recoveries on the Cellular Therapy Essential Data Follow-Up (4100) form has a different intent than the Post-HSCT Data (2100) or Post-Transplant Essential Data (2450). Systemic therapy (such as lymphodepleting therapy given prior to a CAR-T infusion) may negatively impact ANC and platelet counts. The intent of the questions on the Cellular Therapy Essential Data Follow-Up (4100) form is to determine cell count recovery post systemic therapy, not as a measure of engraftment. These questions are not applicable to all cellular therapies. Not all types of cellular therapies require a course of systemic therapy prior to the infusion.

Absolute neutrophil recovery (ANC) recovery is defined as an ANC of ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L) for three consecutive laboratory values obtained on different days. Date of ANC recovery is the date of the first of three consecutive laboratory values where the ANC is ≥ 500/mm3. 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). The percent neutrophils (if the differential was performed on an instrument, will include both segmented and band neutrophils. If the laboratory report displays an automated ANC value of exactly 500/mm3, the actual ANC value should be calculated from the manual differential if available. The calculated value from the manual differential will determine ANC recovery. If your institution's laboratory reports do not display the ANC value, use the following calculation to determine the ANC:

Example 3: Calculating Absolute Neutrophil Count (ANC)



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

Tracking the date of ANC recovery may not always be straightforward. In some cases, the ANC may fluctuate for a period of time before the recipient fully recovers. In other cases, the ANC may remain above ≥ $500/mm^3$ for several days immediately post-HCT and then fall below ≥ $500/mm^3$. Do not begin counting ANC values of ≥ $500/mm^3$ towards recovery until the ANC has dropped to the lowest level (nadir) post- infusion. See the following example for more information regarding tracking the date of ANC recovery.

To report dates in this question, use the first of 3 consecutive laboratory values obtained on different

days.

Example 4: Tracking ANC Recovery

Transplant Date = May 6
Contact Date = August 15

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 initial recovery: ANC ≥ 500/mm^3 (report this date in question 7)*
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-August 14	—	—	—	ANC ≥ 500/mm^3) for timeframe
August 15 (contact date)	2250	0.43	968	

Example 5: Initial Recovery with Subsequent Decline and Recovery

Transplant Date = May 6
Contact Date = August 15

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 initial recovery: ANC ≥ 500/mm^3 (report this date in question 7)*
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	
May 23	800	0.6	480	*Date of first decline: ANC ≤ 500/mm^3 (report this date in question 9)*
May 24	850	0.41	349	
May 25	720	0.53	382	
May 26	500	0.45	225	
May 27	490	0.3	147	
May 28	650	0.7	455	
May 29	800	0.8	640	*Date of recovery: ANC ≥ 500/mm^3 (report this date in question 12)*
May 30-August 14	—	—	—	ANC ≥ 500/mm^3 for timeframe
August 15 (contact date)	2245	0.72	1616	

Question 15: Was there evidence of initial recovery?

This question is not applicable to all cellular therapies. Some cellular therapies require a course of systemic therapy prior to the infusion, such as in the case of chimeric antigen receptor (CAR) T-cells. One of the described toxicities is the inability for hematologic recovery, either by an added cycle of chemotherapy in a recipient who received many prior lines of chemotherapy or by a direct toxicity from the cellular therapy.

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

Check only **one** response:

- Select **Yes** if ANC ≥ 500/mm3 (or ≥ 0.5 × 109/L) achieved and sustained for 3 laboratory values.
- Select **No** if ANC ≥ 500/mm3 (or ≥ 0.5 × 109/L) was not achieved.
- Select **Not applicable**, if the recipient's ANC never dropped below 500/mm^3 (or ≥ 0.5 × 10^9/L) at any time after the start of lymphodepleting therapy or if the recipient did not receive lymphodepleting therapy. This option is only applicable in the 100 day reporting period.

✻ Report Not applicable for DCI infusions where systemic therapy was not given pre-infusion.

- Select **Previously reported** if this is the 6 month or annual follow-up, and ANC initial recovery (including **Not applicable**) has already been reported on a previous form.

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

Combined follow up
If the recipient receives an HCT after a cellular therapy, and both HCT and cellular therapy forms are being completed, select **Previously reported** on all Cellular Therapy Essential Data Follow-Up (4100) forms. Peripheral blood count recoveries will now be captured in the context of engraftment on the Post-HSCT Data (2100) or Post-Transplant Essential Data (2450).

Question 16: Date ANC >500/mm3 (first of 3 lab values):

Enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L). For an example of tracking ANC recovery, see Example 4 above.

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

Question 17: Following the initial recovery, was there subsequent decline in ANC to < 500/mm3 for ≥ 3 days since the date of last report?

Indicate **Yes** or **No** if there was subsequent decline in ANC < 500/mm^3(or < 0.5 × 109/L) (three consecutive laboratory values obtained on different days where the ANC declined to < 500/mm^3.

> **Multiple Recoveries and Declines**
> The form does not allow for multiple recoveries and declines in the same reporting period. If the recipient's ANC initially recovers and then declines, followed by another recovery and another decline, report the date of the first (initial), the first decline, and the last recovery.

Question 18: Date of decline in ANC to < 500/mm3 for ≥ 3 days (first of 3 days that the ANC declined):

Enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC declined to < 500/mm^3 (or < 0.5 × 10^9/L). For an example of tracking a subsequent decline and recovery, see Example 5 above.

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

Question 19: Did recipient recover and maintain ANC ≥ 500/mm3 following the decline?

Indicate **Yes** or **No** whether there was evidence of ANC recovery following the decline (three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm3 (or ≥ 0.5 × 109/L).

Questions 20 – 21: Date of ANC recovery

Report if the date of ANC recovery following the decline is **Known** or **Unknown**. If the date of recovery is **Known**, enter the first date of the three consecutive laboratory values obtained on different days where the ANC recovered to ≥ 500/mm^3 (or ≥ 0.5 × 10^9/L) following the decline. For an example of tracking a subsequent decline and recovery, see Example 5 above.

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

Question 22: Was an initial platelet count > 20 × 10^9/L achieved?

This question does not apply to all cellular therapies. Some cellular therapies require a course of systemic therapy prior to the infusion, such as in the case of chimeric antigen receptor (CAR) T-cells. One of the described toxicities is the inability for hematologic recovery, either by an added cycle of chemotherapy in a recipient who received many prior lines of chemotherapy or by a direct toxicity from the cellular therapy.

The following questions refer to **initial** platelet recovery following the cellular therapy infusion for which this form is being completed. All dates should reflect **no platelet transfusions administered in the previous**

seven days. Report the date of the first of three consecutive laboratory values ≥ 20 × 10^9/L obtained on different days, as shown in Example 6 below. Note that platelet recovery may take place well after the recipient has returned to the referring physician for care. It is essential that information and laboratory values be obtained from the referring physician.

Transfusions temporarily increase platelet counts. When the data is later used for analysis, it is important to be able to distinguish between a recipient whose body was creating the platelets on its own and a recipient who required transfusions to support the counts.

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

Example 6. Reporting Platelet Recovery

	Transfusion ↓										
Day	0	1	2	3	4	5	6	7	8	9	10
Platelet Count	10,000	35,000	30,000	25,000	10,000	15,000	19,000	23,000	25,000	40,000	50,000
Date	1/1/2008	1/2/2008	1/3/2008	1/4/2008	1/5/2008	1/6/2008	1/7/2008	1/8/2008	1/9/2008	1/10/2008	1/11/2008
								↑ 1st of 3			
Report 1/8/08 as date platelet count ≥ 20 x 10^9/L											

Example 7: Reporting Platelet Recovery (≥ 20 × 109/L and ≥ 50 × 109/L)

Date	Day	Platelet Count	
June 13	0	10,000	*Date of last platelet transfusion*
June 14	1	30,000	
June 15	2	25,000	
June 16	3	10,000	
June 17	4	15,000	
June 18	5	19,000	
June 19	6	23,000	

June 20	7	25,000	*1st of 3 consecutive laboratory values ≥ 20 × 10^9/L (report this date in question 15)*
June 21	8	40,000	
June 22	9	50,000	*1st of 3 consecutive laboratory values ≥ 50 × 10^9/L (report this date in question 18)*
June 23	10	56,000	
June 24	11	65,000	
June 25	12	72,000	

This question relates to **initial** platelet recovery. Dates should not reflect transfusions that took place 7 days prior to the date that it listed. To report dates in this question, use the first of 3 consecutive laboratory values obtained on different days.

Indicate whether or not there was evidence of initial platelet recovery following this cellular therapy infusion. Check only one response:

- Select **Yes** if platelet count ≥ 20 × 109 / 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 × 109 / L or if platelet transfusions were administered in the previous 7 days.
- Select **Not applicable**, if the recipient's platelets never dropped below 20 × 10^9/L at any time after the start of lymphodepleting therapy and a platelet transfusion was never required at time post-cellular therapy infusion or if the recipient did not receive lymphodepleting therapy. If the recipient's platelet count drops below 20 × 10^9/L and/or the recipient received a platelet transfusion even once, do not report **Not applicable**. This option is only applicable in the 100-day reporting period.

Report **Not applicable** for DCI infusions where systemic therapy was not given pre-infusion.

- Select **Previously reported** if this is the 6 month or annual follow-up, and initial platelet recovery has already been reported on a previous form.

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

Combined follow up
If the recipient receives an HCT after a cellular therapy, and both HCT and cellular therapy forms are being completed, select **Previously reported** on all Cellular Therapy Essential Data Follow-Up (4100) forms. Peripheral blood count recoveries will now be captured in the context of engraftment on the Post-HSCT Data (2100) or Post-Transplant Essential Data (2450).

Question 23: Date platelets > 20 × 10^9/L:

Enter the **first** date of three consecutive laboratory values obtained on different days where the platelet count was ≥ 20 × 10^9/L. Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in Example 6 above, when determining the recovery date.

p(banner tip).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.

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:

A. 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.

B. 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.

Section Updates:

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

Last modified: Aug 27, 2024

Q24-25: Disease Relapse or Progression

The disease relapse or progression questions are applicable for malignant diseases when disease specific forms are not present or the following products are reported in question 1: **Letetresgene autoleucel**, **Other product**, or **No product name**.

Question 24-25: Was a disease relapse or progression detected since the date of last report?

Disease relapse or progression can be documented by a variety of methods including molecular, flow cytometry, cytogenetic/fluorescent in situ hybridization (FISH), radiographic or hematological/clinical. The intent is to capture any new relapse or progression event that occurred in the reporting period, not just the initial relapse or progression. Report **Yes** if any new disease relapse or progression was detected by any one of the methods in the current reporting period and report the first date (YYYY-MM-DD) of the relapse or progression detected.

If a disease relapse or progression was not detected in the current reporting period, report **No**.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
24	4/23/ 2024	Modify	Updated blue box above question 24: The disease relapse or progression questions are ~~applicate~~ applicable for malignant diseases ~~that do not generate~~ when ~~a~~ disease specific form s ~~(e.g., AML, CML, MDS, MPN)~~ are not present or ~~and for~~ the following products are reported in question 1: Letetresgene autoleucel, Other product, or No product name.	Questions are also applicable to CT TED track
24	1/15/ 2024	Modify	Added the text in red: Disease relapse or progression can be documented by a variety of methods including molecular, flow cytometry, cytogenetic/fluorescent in situ hybridization (FISH), radiographic or hematological/clinical. The intent is to captures any new relapse or progression event that occurred in the reporting period, not just the initial relapse or progression. Report Yes if any new disease relapse or progression was detected by any one of the methods in the current reporting period and report the first date (YYYY-MM-DD) of the relapse or progression detected.	Clarifying the intent is to capture any relapse/ progression, not just the initial one.

Last modified: Apr 23, 2024

Q26: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder

New Malignancies
Report new malignancies that are different than the disease / disorder for which cellular therapy was performed. Do not include relapse, progression or transformation of the same disease subtype. New malignancy related questions will now be asked on the Subsequent Neoplasm (3500) form.

Combined follow up
In scenarios where an HCT was given after a cellular therapy and this form is now being completed based on the subsequent HCT, new malignancies will always be reported on the Cellular Therapy Essential Data Follow- Up (4100) forms and disabled on the Post-HSCT Data (2100) or Post-Transplant Essential Data (2450).

Question 26: Did a new malignancy, myelodysplastic, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the cellular therapy was performed? (Include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders):

Indicate whether a new or second primary malignancy, including lymphoproliferative disorder, or myeloproliferative disorder, developed in the current reporting period. Do not report recurrence, progression, or transformation of the recipient's primary disease (disease for which the cellular therapy was performed) or relapse of a prior malignancy.

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

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

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

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

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 transplant was performed) or relapse of a prior malignancy in the "New Malignancy" section.
For example, a recipient had a basal cell skin cancer diagnosed on the neck four months post-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 **Basal cell skin malignancy** on the Post-CTED 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 whether or not to use of this option, contact CIBMTR Center Support if there are questions.

Example 1. Recipient develops a new malignancy at day +68. It is reported at the time the 100-day Cellular Therapy Essential Data Follow-Up (4100) 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. Recipient received a commercial CAR-T product and develops a new malignancy at day +68. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The Subsequent Neoplasms (3500) form should be created as an unscheduled form in FormsNet3 and completed in a timely manner. In this example, no other new malignancy develops during the 100-day reporting period. When the 100-day Cellular Therapy Essential Data Follow-Up (4100) 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. Recipient received a commercial CAR-T product and develops a new malignancy at day +68. Per protocol, the new malignancy should be reported at the time of knowledge of the new malignancy. The Subsequent Neoplasms (3500) form should be created as an unscheduled form in FormsNet3^{SM} and completed in a timely manner. Another new malignancy develops at day +100 after the same CAR-T infusion. It is decided to report the 2nd new malignancy on the 100-day Cellular Therapy Essential Data Follow-Up (4100) form since it is due at the same time. Select **Yes** to create a second Subsequent Neoplasms (3500) form.

Section Updates:

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

Last modified: Jul 29, 2023

Q27-46: Graft vs. Host Disease

Autologous Transplants
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.

Graft versus Host Disease (**GVHD**) is an immunological phenomenon resulting from the reaction of donor immune cells against major or minor histocompatibility antigens of the recipient. GVHD is primarily caused by donor-derived T-cells. Very rarely, GVHD may occur due to autologous reactivity (autologous GVHD), third party transfusions, or with identical twin transplantation.

Factors influencing the severity of GVHD are related to three main categories: 1) donor or graft, 2) recipient, and 3) treatment. The most influential donor/graft factor is the degree of genetic disparity between the donor and the recipient (HLA match), but other risk factors include female donor to male recipient, donor parity, older donors, and T-cell dose. The occurrence of acute GVHD becomes a risk factor for the development of chronic GVHD. Recipient age and prior infections are also factors.

In the past, GVHD was classified as acute or chronic based on its time to diagnosis following transplant, and other clinical and histological (biopsy or post-mortem) features. Today, there has been increased recognition that acute and chronic GVHD are not dependent upon time since infusion, so determination of acute or chronic should rest on clinical and histologic features. **However, organ staging and overall grade should only be calculated from the clinical picture, not histology.** Acute GVHD usually begins between 10 and 40 days after infusion but can appear earlier or later. The organs most commonly affected by acute GVHD are the skin, gut, or liver. Other sites, such as the lung, may be involved.

Acute / Chronic GVHD
If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form. Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section.
Report any new or persistent acute GVHD symptoms occurring on or after the onset of chronic GVHD only in the chronic GVHD section. If chronic GVHD was diagnosed in a prior reporting period, report **No** for questions *Did acute GVHD develop* and *Did acute GVHD persist* in each subsequent reporting period. See reporting scenarios included in the *Did acute GVHD develop* question.

Transaminitis
Previously, if the recipient only had transaminitis related to acute GVHD, this would have been reported as “stage 0” liver GVHD with and overall grade of “not applicable.” However, as of July 2021, isolated transaminitis should not be reported as acute GVHD. In this

scenario, report **No**, acute GVHD did not develop or persist. If the recipient has transaminitis and other organs involved (i.e., skin rash), then report **Yes**, acute GVHD developed or persisted but do not report there was liver involvement.

Question 27: Did acute GVHD develop since the date of last report?

Did acute GVHD develop since the date of last report and *Did acute GVHD persist since the date of last report* questions on the Post-TED Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either *Did acute GVHD develop since the date of last report* or *Did acute GVHD persist since the date of last report* must be answered **Yes** unless there has been a prior / concurrent diagnosis of chronic GVHD (see Acute / Chronic GVHD note box above). There will not be a situation where **Yes** is reported for both *Did acute GVHD develop since the date of last report* and *Did acute GVHD persist since the date of last report* questions. If this question is answered **Yes** and a diagnosis date has been reported, the question *Did acute GVHD persist since the date of last report* will be disabled in FormsNet3^{SM}. Centers should report **Yes** for this question to indicate the recipient developed acute GVHD in the following scenarios:

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

If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report **No** for this question and **Yes** for the question, *Did acute GVHD persist since the date of last report*. *Did acute GVHD persist since the date of last report*, is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer *Did acute GVHD develop since the date of last report* and *Did acute GVHD persist since the date of last report* questions.

Report **No** for *Did acute GVHD develop since the date of last report* and *Did acute GVHD persist since the date of last report* if the recipient had no active acute GVHD symptoms during the reporting period **OR** all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see Acute / Chronic GVHD note box above).

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

Acute GVHD Diagnosis Scenarios:

A. A recipient receives an infusion on 1/1/2015 and develops acute GVHD which is clinically diagnosed on 2/1/2015. At least one of their symptoms, attributed to acute GVHD, persists beyond the 100 day date of contact which is 4/5/2015. Treatment continues and symptoms completely resolve on 5/1/2015. Immunosuppression is tapered until a flare of acute GVHD is diagnosed on 5/25/2015. Immunosuppression is given and symptoms quickly resolve with no active acute GVHD beginning 6/10/2015. The six month date of contact is 6/20/2015. Another flare of acute GVHD is clinically diagnosed on 8/15/2015.

100 Day Post-TED Form:

Did acute GVHD develop since the date of last report: Report **Yes** to indicate a new clinical diagnosis of acute GVHD.
Date of acute GVHD diagnosis: Report the initial date of diagnosis (2/1/2015).
Did acute GVHD persist since the date of last report: Leave blank. This question will be skipped whenever a diagnosis date has been entered.
Overall grading and organ staging at diagnosis: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

Six Month Post-TED Form:

Did acute GVHD develop since the date of last report: Report **No** to indicate acute GVHD persists from a previous report. Notes, the flare of acute GVHD was < 30 days from symptoms resolution so it doesn't count as a new reportable episode.
Date of acute GVHD diagnosis: Leave blank. This question will be skipped whenever *Did acute GVHD develop since the date of last report* is answered **No**.
Did acute GVHD persist since the date of last report: Report **Yes** to indicate GVHD persists from a previous report.
Overall grading and organ staging at diagnosis: Leave blank. Answering **Yes** for *Did acute GVHD persist since the date of last report* prevents the center from re-reporting diagnosis information already captured on the 100 day form.

One Year Post-Infusion Data Form:

Did acute GVHD develop since the date of last report: Report **Yes** to indicate a flare of acute GVHD occurred at least 30 days after resolving during a prior reporting period.
Date of acute GVHD diagnosis: Report the diagnosis date of the flare occurring during the reporting period (8/15/2015).
Did acute GVHD persist since the date of last report: Leave blank. This question will be skipped whenever a diagnosis date has been entered.
Overall grading and organ staging at diagnosis: Answer these questions based on the assessments performed at the time of diagnosis of the flare of acute GVHD (8/15/2015).

B. A recipient receives an infusion on 1/1/2015 and develops acute skin GVHD on 2/1/2015 and then

chronic eye GVHD on 3/1/2015. Both acute and chronic symptoms resolve by the 100 day date of contact (4/5/2015). While tapering their immunosuppression, the recipient has a flare of their acute skin GVHD on 5/30/2015. Treatment continues and symptoms completely resolve by the six month date of contact (6/20/2015).

100 Day Post-Infusion Data Form:

Did acute GVHD develop since the date of last report: Report **Yes** to indicate a new clinical diagnosis of acute GVHD.
Date of acute GVHD diagnosis: Report the initial date of diagnosis (2/1/2015).
Did acute GVHD persist since the date of last report: Leave blank. This question will be skipped whenever a diagnosis date has been entered.
Overall grading and organ staging at diagnosis: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).
Maximum overall grade and organ staging: Answer these questions based on any symptoms and treatment documented from the onset of acute GVHD (2/1/2015) up to the diagnosis of chronic GVHD (3/1/2015). This instruction is provided in the Acute / Chronic GVHD note box above.

Six Month Post-Infusion Data Form:

Did acute GVHD develop since the date of last report: Report **No** to indicate acute GVHD did not develop during the reporting period.
Date of acute GVHD diagnosis: Leave blank. This question will be skipped whenever *Did acute GVHD develop since the date of last report* is answered **No**.
Did acute GVHD persist since the date of last report: Report **No** to indicate acute GVHD did not persist from a previous report.

If chronic GVHD has been diagnosed in a prior reporting period, report **No** for *Did acute GVHD develop since the date of last report* and *Did acute GVHD persist since the date of last report*. Any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD must be reported in the chronic GVHD section of the form. Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section. This instruction has been provided in the Acute / Chronic GVHD note box above.

Question 28: Date of acute GVHD diagnosis

Report the date of clinical diagnosis of acute GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed a rash one week prior to the physician clinically diagnosing acute skin GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

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

For more information regarding reporting partial or unknown dates, see General Instructions, General

Guidelines for Completing Forms.

> **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 29: Did acute GVHD persist since the date of last report?

This question will only be enabled in FormsNet3^{SM} if the center has reported **No** for the question *Did acute GVHD develop since the date of last report* and, therefore, has not reported a date of diagnosis. If prompted to answer this question, report **Yes** if acute GVHD was diagnosed in a prior reporting period and **any** of the following conditions are met:

- The recipient's acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).
- The recipient's acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred **within 30 days** of symptom resolution / quiescence.
- The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see Acute / Chronic GVHD note box above).

Report **No** for *Did acute GVHD develop since the date of last report* and *Did acute GVHD persist since the date of last report* questions if the recipient had no active acute GVHD symptoms during the reporting period **OR** all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see Acute / Chronic GVHD note box above).

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

Question 30: Overall grade of acute GVHD at diagnosis

Indicate the overall grade of acute GVHD at the time of diagnosis. For reporting purposes, "at diagnosis" is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic). The acute GVHD grading scale is based on **clinical evidence** (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on *clinical* severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, **overall grading remains clinical** and is based on the criteria published by Przepiorka et al., *Bone Marrow Transplant* 1995; 15(6):825-8, see the GVHD Grading and Staging table below.

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

If acute GVHD was present, but the grade at diagnosis was not documented and it cannot be determined from the grading and staging table, report **Not applicable**.

Examples may include:

- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description below)

Upper GI GVHD
If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

GVHD Grading and Staging

Stage	Skin	Liver	Gut
1	Rash on <25% of skin[1]	Bilirubin 2-3 mg/dl[2]	Diarrhea > 500 ml/day[3] or persistent nausea[4] *Pediatric*: 280-555 ml/m^2/day or 10-19.9 mL/kg/day
2	Rash on 25-50% of skin	Bilirubin 3-6 mg/dl	Diarrhea >1000 ml/day *Pediatric*: 556-833 ml/m^2/day or 20-30 mL/kg/day
3	Rash on >50% of skin	Bilirubin 6-15 mg/dl	Diarrhea >1500 ml/day *Pediatric*: >833 ml/m^2/day or > 30 mL/kg/day
4	Generalized erythroderma with bullous formation	Bilirubin >15 mg/dl	Severe abdominal pain, with or without ileus, and / or grossly bloody stool
Grade[5]			
I	Stage 1-2	None	None
II	Stage 3	Stage 1	Stage 1

III	—	Stage 2-3	Stages 2-4
IV[6]	Stage 4	Stage 4	—

[1] Use “Rule of Nines” (Percent Body Surfaces table) or burn chart to determine extent of rash.

[2] Range given as total bilirubin. Downgrade one stage if an additional cause of elevated bilirubin has been documented.

[3] Volume of diarrhea applies to adults. For pediatric patients, the volume of diarrhea should be based on body surface area. Downgrade one stage if an additional cause of diarrhea has been documented.

[4] Persistent nausea with or without histologic evidence of GVHD in the stomach or duodenum.

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

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

Questions 31 – 36: List the stage for each organ at diagnosis of acute GVHD

Report the stage of each organ at diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic).

> **Skin:** Select the stage that reflects the body surface area involved with a maculopapular rash attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. See the Percent Body Surfaces table below to determine the percent of body surface area involved with a rash. Do not report ongoing rash not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

Percent Body Surfaces

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

Lower GI GVHD and Stool Output Not Documented

If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, leave the lower GI stage data field blank, override the FormsNet3 error as "not documented," and specify the volume of stool output was not documented. In this case, report **Not applicable** for the overall grade unless stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status *or* stage 2 or 3 acute liver GVHD was also documented at the time point being reported (*at diagnosis or maximum grade during the current reporting period*.

Lower intestinal tract (use mL/day for adult recipients and mL/m^2/day for pediatric recipients): Select the stage that reflects the volume of diarrhea attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Use mL/day for adult recipients and mL/m^2/day for pediatric recipients. Input and output records may be useful in determining the volume of diarrhea. Do not report diarrhea ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

Upper intestinal tract: Select the stage that reflects the presence of persistent nausea or vomiting attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report nausea or vomiting ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

Liver: Select the stage that reflects the bilirubin level attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report hyperbilirubinemia ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

Other site(s) involved with acute GVHD: Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement.

Question 37: Maximum Overall Grade of Acute GVHD

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

If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. Acute GVHD grading scenario D below has been provided for further clarification.

Report the recipient's maximum acute GVHD grade in the reporting period; **this may differ from the grade**

at diagnosis or may be the same. If acute GVHD was present, but the maximum grade was not documented and it cannot be determined from the grading and staging table, report **Not applicable**.

Examples may include:

- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description above)

Upper GI GVHD
If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

Acute GVHD Grading Scenarios:

A. A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging / grading can be determined using the GVHD Grading and Staging table above.

B. A recipient developed acute liver GVHD with elevated LFTs (i.e., transaminases) with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, this would not be reported as acute GVHD.

C. A recipient developed stage 2 skin involvement, which showed improvement in response to topical steroids. However, the recipient then developed hyperbilirubinemia attributed to stage 1 liver involvement; the skin involvement at that time was stage 1. In this case, grade II would be reported (assuming this was the extent of the recipient's acute GVHD in the reporting period).

D. A recipient developed stage 2 skin involvement which resolved in response to topical steroids. Later in the reporting period, the recipient was diagnosed with mild chronic eye GVHD. Shortly thereafter, they were diagnosed with a stage 3 flare of acute skin GVHD. In this case, grade I would be reported. Do not consider any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD when completing the acute GVHD section of the form.

E. A recipient developed stage 1 skin involvement on 1/1/2019 which resolved in response to topical steroids and tacrolimus. Later in the reporting period, on 2/14/2019, they have a flare of the skin GVHD, this time at stage 2. In this case, grade I would be reported in question 29 with the date of diagnosis of the more severe flare (2/14/2019). Additionally, the skin symptoms would be reported as stage 2 in question 31.

Question 38: First date of maximum overall grade of acute GVHD

Report the first date of maximum acute GVHD involvement, based on clinical grade. If the recipient had

multiple instances in which their GVHD reached the same maximum grade, report the earliest date. However, if the same maximum overall grade was achieved, but the specific organ staging varied, report the date of the maximum organ staging which is consistent with the overall grade reported in *Maximum overall grade of acute GVHD* question. Acute GVHD grading scenario E above has been provided for further clarification.

Questions 30 – 35: List the stage for each organ at the time of maximum overall grade of acute GVHD

Skin: Select the stage that reflects the body surface area involved with a maculopapular rash attributed to acute GVHD at the time of maximum overall grade of acute GVHD in the reporting period. See the Percent Body Surfaces table below to determine the percent of body surface area involved with a rash. Do not report ongoing rash not attributed to acute GVHD at the time of maximum overall grade of acute GVHD.

Percent Body Surfaces

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

Lower intestinal tract (use mL/day for adult recipients and mL/m^2/day for pediatric recipients): Select the stage that reflects the volume of diarrhea attributed to acute GVHD at the time of maximum overall grade of acute GVHD. Use mL/day for adult recipients and mL/m^2/day for pediatric recipients. Input and output records may be useful in determining the volume of diarrhea. Do not report diarrhea ongoing but not attributed to acute GVHD at the time of maximum overall grade of acute GVHD.

Report an overall grade of IV if stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status is documented at the time point being reported (see GVHD Staging and Grading Table). Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.

Upper intestinal tract: Select the stage that reflects the presence of persistent nausea or vomiting attributed to acute GVHD at the time of maximum overall grade of acute GVHD in the reporting period. Do not report nausea or vomiting ongoing but not attributed to acute GVHD at the time of maximum overall grade of acute GVHD.

Liver: Select the stage that reflects the bilirubin level attributed to acute GVHD at the time of maximum

overall grade of acute GVHD in the reporting period. Do not report hyperbilirubinemia ongoing but not attributed to acute GVHD at the time of maximum overall grade of acute GVHD.

Other site(s) involved with acute GVHD: Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. Report only other organ involvement at the time of maximum overall grade of acute GVHD in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of maximum overall grade of acute GVHD. Specify the other organ system involvement.

Question 36: Did chronic GVHD develop since the date of last report?

Indicate whether a new clinical diagnosis of chronic GVHD was documented during the reporting period. If chronic GVHD was diagnosed during the reporting period, report **Yes**.

If the recipient had a flare of chronic GVHD occurring after at least a 30-day period of symptom quiescence, report **Yes**. Report **No** if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent chronic GVHD which is captured in the question *Did chronic GVHD persist since the date of last report*.

Report **No** if chronic GVHD was not clinically diagnosed – initially or as a flare – in the reporting period; this includes instances where chronic GVHD persists from a prior reporting period.

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

Question 37: Date of chronic GVHD diagnosis

Report the date of clinical diagnosis of chronic GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed shortness of breath one month prior to the clinical diagnosis of pulmonary chronic GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

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

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

> **Persistent GVHD and Day 100 Reporting Period**
> Previously, reporting **Yes** for *Did chronic 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 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 38: Did chronic GVHD persist since the date of last report?

Indicate whether chronic GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive chronic GVHD, or a prior history of GVHD. If **Yes**, questions concerning chronic GVHD at the time of diagnosis will be skipped. See question 37 for instructions on reporting a chronic GVHD flare.

If the recipient has no active symptoms during the reporting period, report **No**.

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

Question 39: Maximum grade of Chronic GVHD (according to best clinical judgement)

Report the maximum chronic GVHD involvement, based on clinical grade, since the date of the last report. The intent of this question is to capture the maximum grade based on the best clinical judgment. If the maximum clinical grade is not documented, request documentation from the recipient's primary care provider. Guidelines on how to report the maximum grade of chronic GVHD are outlined below:

- **Mild**: Signs and symptoms of chronic GVHD do not interfere substantially with function and do not progress once appropriately treated with local therapy or standard systemic therapy (e.g., corticosteroids and/or cyclosporine or FK 506)
- **Moderate**: Signs and symptoms of chronic GVHD interfere somewhat with function despite appropriate therapy or are progressive through first line systemic therapy (e.g., corticosteroids and/or cyclosporine or FK 506)
- **Severe**: Signs and symptoms of chronic GVHD limit function substantially despite appropriate therapy or are progressive through second line therapy

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

Organ Scoring of Chronic GVHD

Organ	Score 0	Score 1	Score 2	Score 3
Skin % BSA[1]	No BSA involved	1-18% BSA	19-50% BSA	>50% BSA
Skin Features	No sclerotic features	N/A	Superficial sclerotic features, but not "hidebound"	Deep sclerotic features; "hidebound;" impaired mobility; ulceration
Mouth	No symptoms	Mild symptoms **with** disease	Moderate symptoms with disease signs **with** partial	Severe symptoms with disease signs **with** major limitation of oral intake

		signs but not limiting oral intake significantly	limitation of oral intake	
Eyes	No symptoms	Mild dry eye symptoms not affecting ADL (requirement of lubricant drops ≤ 3x/day)	Moderate dry eye symptoms partially affecting ADL (requiring lubricant drops > 3x/day or punctal plugs) **WITHOUT** new vision impairment due to keratoconjunctivitis sicca (KCS)	Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) **OR** unable to work because of ocular symptoms **OR** loss of vision due to keratoconjunctivitis sicca (KCS)
GI Tract	No symptoms	Symptoms without significant weight loss (< 5%)	Symptoms associated with mild to moderate weight loss (5-15%) within 3 months **OR** moderate diarrhea without significant interference with daily living	Symptoms associated with significant weight loss (> 15%) within 3 months, requires nutritional supplement for most calorie needs **OR** esophageal dilation **OR** severe diarrhea with significant interference with daily living.
Liver	Normal total bilirubin and ALT or AP < 3 x ULN	Normal total bilirubin with ALT ≥ 3 to 5 x ULN or AP ≥ 3 x ULN	Elevated total bilirubin but ≤ 3 mg / dL or ALT > 5 x ULN	Elevated total bilirubin > 3 mg / dL
Lungs Symptom Score:	No symptoms	Mild symptoms (SOB after climbing one flight of steps)	Moderate symptoms (SOB after walking on flat ground)	Severe symptoms (SOB at rests; requires O2)
Lungs Lung Score:	FEV1 ≥ 80%	FEV1 60-79%	FEV1 40-59%	FEV1 ≤ 39%
Joints and Fascia	No symptoms	Mild tightness of arms or legs, normal or mild decreased range of motion **AND** not affecting ADL	Tightness of arms or legs **OR** joint contractures, erythema thought to be due to fasciitis, moderate decrease of range of motion **AND** mild to moderate limitation of ADL	Contractures **WITH** significant decrease of range of motion **AND** significant limitation of ADL (unable to tie shoes, button shirts, dress self, etc.)
Genital	No signs	Mild signs and	Moderate signs and may	Severe signs with or without

Tract[2]		females with or without discomfort on exam	have signs of discomfort on exam	symptoms
Other Features[3]	No GVHD	Mild	Moderate	Severe

NIH Consensus Criteria, 2014

[1] Features to be scored by BSA: Maculopapular rash, lichen planus-like features, sclerotic features, papulosquamous lesions or ichthyosis, keratosis pilaris-like GVHD.

[2] Scoring is based on severity of the signs instead of symptoms, based on limited available data and the opinions of experts. Female or male genital GVHD is not scored if a practitioner is unable to examine the patient.

[3] May include ascites, pericardial effusion, pleural effusion(s), nephrotic syndrome, myasthenia gravis, peripheral neuropathy, polymyositis, weight loss without GI symptoms, eosinophilia > 500/µL, platelets < 100,000/µL, others.

Question 40: Date of maximum grade of chronic GVHD

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

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

Question 41: Specify if chronic GVHD was limited or extensive

The grading system for chronic GVHD is divided into two categories: limited and extensive. Definitions are based on Sullivan KM, *Blood* 1981; 57:267.
Report **Limited** if chronic GVHD includes only localized skin involvement and / or liver dysfunction. Report **Extensive** if **any** of the following symptoms are attributed to chronic GVHD:

- Generalized skin involvement and / or liver dysfunction
- Liver histology showing chronic aggressive hepatitis, bridging necrosis, or cirrhosis
- Involvement of the eye: Schirmer's test with <5 mm wetting, or
- Involvement of the salivary glands or oral mucosa demonstrated on labial biopsy (labial biopsy not required), or
- Involvement of any other target organ

The intent of this question is to capture if chronic GVHD was limited or extensive throughout the entire

reporting period and is not dependent on the maximum grade and date of chronic GVHD. If the criteria to report extensive was met at any time in the reporting period, report **Extensive**.

Question 42: Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, ≤10 mg/day for adults, <0.1 mg/kg/day for children)

> **Steroids and Non-Steroid Immunosuppression for GVHD**
> GVHD treatment questions will only be completed if the center has reported **Yes** acute and/or chronic GVHD develop or persisted since the date of last report. If **No** has been reported, then the GVHD treatment questions will be left blank.

> **Corticosteroids**
> Corticosteroids are captured differently depending on whether they are used topically or systemically. Use the following guidelines when determining how to report corticosteroids used to treat acute GVHD:
> Topical Creams for Skin: Do not report topical ointments or creams used to treat skin GVHD including corticosteroid creams such as Triamcinolone or Hydrocortisone.
> Other Topical Treatments: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. Do not consider these medications when answering the question regarding systemic steroids.
> Systemic Treatments: Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in the question regarding systemic steroids.

Indicate whether the recipient is still taking systemic steroids to treat or prevent GVHD on the date of contact. Refer to the guidelines included in the question text if the recipient is taking low dose steroids or steroids for adrenal insufficiency.

Indicate **Not applicable** in any of the following scenarios:

- The recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD.
- This form is being completed for a subsequent infusion and the recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen is given).
- The recipient stopped taking systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD in a previous reporting period and did not restart systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) during the current reporting period.

Indicate **Unknown** if there is no information to determine if the recipient is still taking systemic steroids. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD on the date of contact.

If the recipient has died prior to the discontinuation of systemic steroids used to treat or prevent acute and / or chronic GVHD, select **Yes**.

See the examples below for more information:

Example 1: In the 100-day reporting period, a recipient is on Prednisone at 7 mg per day for the entire reporting period. Question 43 should be answered as “Not applicable” since the dose of systemic steroids were never > 10 mg / day.

Example 2: At the beginning of the 6-month reporting period, a recipient is on 20 mg of Prednisone per day. After three months, the dose is decreased to 10 mg per day and is maintained at that level until the end of the reporting period. In this scenario, question 43 should be answered as “No” since the recipient received greater than 10 mg of systemic steroids within the reporting period but on the date of contact, the dose was ≤ 10 mg / day.

Example 3: Throughout the 100-day reporting period, a recipient is on 30 mg Methylprednisolone given every other day. In this scenario the average daily dose is approximately 15 mg / day. Hence, question 43 should be captured as “Yes,” as the dose of systemic steroids is > 10 mg / day.

Question 43: Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for GVHD?

> **Steroids and Non-Steroid Immunosuppression for GVHD**
> GVHD treatment questions will only be completed if the center has reported **Yes**, acute and/ or chronic GVHD develop or persisted since the date of last report. If **No**,has been reported, then the GVHD treatment questions will be left blank.

Indicate whether the recipient is still taking systemic non-steroidal immunosuppressive agents (including PUVA) to treat or prevent acute and / or chronic GVHD on the date of contact. Descriptions of many immunosuppressive agents are included below. Only report systemic non-steroidal immunosuppressive agents and not topical non-steroids immunosuppressive agents, such as Restasis and or Protopic.

If the recipient did not receive systemic non-steroidal immunosuppressive agents to treat or prevent acute and / or chronic GVHD during the reporting period, report **Not applicable**.

Indicate **Not applicable** in any of the following scenarios:

- The recipient has never received systemic non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD.
- This form is being completed for a subsequent infusion and the recipient has never received systemic non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen was given).
- The recipient stopped systemic taking non-steroidal immunosuppressive agents (including PUVA) to

treat or prevent GVHD in a previous reporting period and did not restart non-steroidal immunosuppressive agents (including PUVA) during the current reporting period.
- The recipient only received *topical* non-steroidal immunosuppressive agents (i.e., systemic non-steroidal immunosuppressive agents were never administered).

Indicate **Unknown** if there is no information to determine if the recipient is still taking non-steroidal immunosuppressive agents. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD in the reporting period.

Systemic Immunosuppressive Agents:

Aldesleukin (Proleukin): Increases production of several white blood cells including regulatory T-cells. This drug is also known as interleukin-2.

ALG (Anti-Lymphocyte Globulin), ALS (Anti-Lymphocyte Serum), ATG (Anti-Thymocyte Globulin) ATS (Anti-Thymocyte Serum): Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes.

Azathioprine (Imuran): Azathioprine inhibits purine synthesis. Usually it is used at low doses in combination with other treatments.

Bortezomib (Velcade): A proteasome inhibitor.

Cyclosporine (CSA, Neoral, Sandimmune): Calcineurin inhibitor which decreases cytokine production by T-cells. Usually given for ≥ 3 months.

Cyclophosphamide (Cytoxan): Given in high doses near the date of infusion as single agent prophylaxis.

Extra-corporeal photopheresis (ECP): The recipient's blood is removed from the body, exposes to psoralen and ultraviolet light, and re-infused.

FK 506 (Tacrolimus, Prograf): Inhibits the production of interleukin-2 by T-cells.

Hydroxychloroquine (Plaquenil): Hydroxychloroquine inhibits transcription of DNA to RNA and is commonly used as an anti-malarial drug.

Interleukin Inhibitor: Interleukin inhibitors suppress production of white blood cells and are grouped according to their target. Examples of IL-2 inhibitors include daclizumab (Zynbryta) and basiliximab (Simulect). Examples of IL-6 inhibitors include tocilizumab (Actemra) and siltuximab (Sylvant).

In vivo monoclonal antibody: Antibody preparations that are infused in the recipient following infusion.

In vivo immunotoxin: Antibody preparations linked to a toxin that is infused in the recipient following infusion.

Janus Kinase 2 Inhibitors: Suppress function of T-effector cells. Examples: ruxoloitinib (Jakafi, Jakavi) and tofacitinib (Xeljanz, Jakvinus).

Methotrexate (MTX) (Amethopterin): Inhibits the metabolism of folic acid. It is most often used with cyclosporine and is usually for a short duration of time.

Mycophenolate mofetil (MMF) (CellCept, Myfortic): Inhibits the de novo pathway used for lymphocyte proliferation and activation.

Pentostatin (Nipent): Inhibits adenosine deaminase, which blocks DNA (and some RNA) synthesis.

Sirolimus (Rapamycin, Rapamune): Inhibits the response to interleukin-2, blocking the activation of T-cells.

Tyrosine Kinase Inhibitor (TKI): Suppress function of tyrosine kinases thereby downregulating the function of many other cellular proteins / processes including fibrosis and inflammation. Examples: imatinib (Gleevec, Glivec), nilotinib (Tasigna), and dasatinib (Sprycel).

UV Therapy: UVA or UVB radiation administered to affected areas of the skin in order to suppress proliferation of cells responsible for GVHD.

PUVA (Psoralen and UVA): Psoralen is applied or taken orally to sensitize the skin, and then the skin is exposed to UVA radiation.

UVB: Broadband- or Narrowband-UVB radiation is applied to the affected areas of the skin.

Section Updates:

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

Last modified: Apr 21, 2025

Q47-177: Toxicities

Effective April 30th, 2025, report only toxicities (e.g. CRS, neurotoxicity, etc.) that are **directly** attributed to the CAR-T product / infusion. It is no longer required to report any toxicity regardless of causality. Treatment given post-infusion may have the effect of re-activating the product and inducing toxicities (e.g. CRS), these toxicities should **NOT** be captured in this section of the form. Contact CIBMTR Center Support with questions.

TED vs CRF reporting
All toxicities are listed on the F4100, however, some questions will be disabled for TED reporting level, and will only be enabled for the CRF reporting level (where an associated F4101 is due with the F4100). For more information on TED vs CRF level reporting for cellular therapy see [link]. Questions that are disabled for TED reporting level are noted.

Combined follow up
In scenarios where both HCT and cellular therapy forms are being completed, toxicities should still be reported when an HCT follows a cellular therapy. It is possible to have CAR-T cell reactivation post-HCT.

Question 47: Did the recipient experience Cytokine Release Syndrome (CRS)?

Cytokine Release Syndrome (CRS) is defined by development of a constellation of signs and symptoms that are seen after the infusion of monoclonal antibodies or cellular therapy products. It results from the rapid release of several inflammatory cytokines as a consequence of immune response triggered by a drug (i.e., monoclonal antibody) or cellular product. This rapid cytokine release into the circulation results in fever (must be ≥100.4F or ≥38C), nausea, chills, hypotension, tachycardia, asthenia, headache, rash, sore throat, respiratory failure or death. This section attempts to collect different clinical and laboratory information to understand the severity of this event.

Indicate **Yes** or **No** if CRS occurred or persisted into the current reporting period.

Question 48: Was the date of diagnosis previously reported?

If the CRS was diagnosed in a previous reporting period, and the symptoms continue into this reporting period, and the date has already been reported, select **Yes**. If CRS was not diagnosed in a previous reporting period, report **No**.

Question 49: Date of diagnosis:

Report the date (YYYY-MM-DD) when the first symptom of CRS was documented by a physician or other health care provider in the progress note or chart.

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

Questions 50-52: Specify therapy given for CRS: (check all that apply)

Disabled for TED reporting level

Check all that apply from the list of the drug(s) given to treat CRS in this reporting period. Specify the therapy if **Other therapy** is selected.

> ✻ Supportive care treatments **should not** be reported as treatment for CRS. Examples of what **not to report** as other therapy include, but are not limited to, acetaminophen (Tylenol®), albumin, antibiotics, IV fluids, or any brand name or specific corticosteroids administered.

If **Tocilizumab** was given to treat the CRS, report the number of doses given. This information is important in the grading of the CRS event.

If a drug was started as planned prophylaxis but the recipient develops CRS and the drug is continued, this is considered a change in intent from prophylaxis to treatment and the drug should also be reported as therapy for CRS.

Questions 53-63: Indicate symptoms of CRS (check all that apply)

Indicate which symptoms of CRS the recipient experienced in the current reporting period, check all symptoms that apply. For each symptom reported, also report the date of onset. If there were multiple occurrences of a symptom (e.g., fever), report the first occurrence.

If CRS is persisting from a prior reporting period, report the symptoms that worsened or carried over in this reporting period.

Fevers (≥100.4F or ≥38C): A disorder characterized by elevation of the body's temperature above the upper limit of normal. Do not report fever if less than 100.4F / 38C in this field. Fever less than 100.4F / 38C does not qualify as a symptom of CRS. Report the date of fever onset. If there were multiple fevers in the reporting period, report the first occurrence. If the recipient self-reported a fever from a home test, and the date is documented in the medical records, report the date of the home test.

Hypotension requiring therapy: Abnormally low blood pressure requiring treatment with volume resuscitation using intravenous isotonic fluids or vasopressors such as norepinephrine, dopamine, dobutamine, epinephrine, phenylephrine, or vasopressin. The use of vasopressors to control blood pressure is an indirect assessment of severity of CRS. Report the date of hypotension onset. Report therapy given for hypotension. Examples of what not to report as **Other therapy** include, but are not limited to, antibiotics, corticosteroids, any brand names, hypertension or antiarrhythmic drugs, or any drug used for CRS treatment (e.g. Anakinra, Tocilizumab).

Options for number of vasopressors include 1 or >2 and can be used to determine the grade. One important consideration here is the use of vasopressin, which can be used with fluids or other

vasopressors to stabilize the blood pressure. In order to assess severity, only patients who received two or more vasopressor agents at the same time excluding vasopressin, should be marked as >2 vasopressors. Addition of vasopressin to other vasopressor agents does not reflect the same level of acuity compared to a patient requiring 2 or more vasopressors without vasopressin. Only use the option of number of vasopressors as >2 for patients who are receiving multiple vasopressors at the same time excluding vasopressin. Select the number of vasopressors used for therapy.

Specify any vasopressor(s) used at the same time as a single therapy to treat hypotension. And report if hypotension was controlled with therapy. Controlled means not worsening clinically or resolving the hypotension / managing it without the need for additional agents such as pressors.

Hypoxia requiring minimal supplemental oxygen (FiO2<40%): A lower than normal concentration of oxygen in arterial blood requiring supplemental oxygen of <40% FiO2. One example here is the delivery of supplemental oxygen with a low-flow nasal cannula or blow-by device. Report the date of onset.

Hypoxia requiring more than minimal supplemental oxygen (FiO2>40%): A lower than normal concentration of oxygen in arterial blood requiring supplemental oxygen of >40% FiO2. Also specify if positive pressure ventilatory support is required, such as CPAP, BiPAP, intubation or mechanical ventilation. Do not report use of CPAP for sleep apnea. Examples here include the requirement of supplemental oxygen delivered through a high-flow nasal cannula, facemask, opti-flow, non-rebreather mask or Venturi mask. Report the date of onset.

Source: Common Terminology Criteria for Adverse Events (CTCAE) v5.0

Questions 64-65: Was positive pressure ventilatory support required (CPAP, BiPAP, intubation, and mechanical ventilation):

This option outlines the need of devices considered as positive pressure ventilation which could be non-invasive like continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP or BPAP), or invasive, which requires endotracheal intubation with mechanical ventilation.

Patients who use BiPAP or CPAP for obstructive sleep apnea are not considered the same here and should not be reported in this question. The intent of this question is the treatment of respiratory insufficiency or failure.

If positive pressure ventilatory support was required, select **Yes** and report the start date. If the recipient required multiple types of positive ventilatory support, report the start date of the first method. If positive pressure ventilatory support was not required, or it unknown if it was required, report **No** or **Unknown**.

Questions 66-67: Did cytokine release syndrome resolve?

If the cytokine release syndrome resolved, select **Yes** and report the resolution date (YYYY-MM-DD).

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

If the cytokine release syndrome did not resolve in this reporting period, select **No**.

It is possible a patient could experience CRS like symptoms after the CRS event has previously resolved. In these situations, please report the date of onset, the worst grade of both events, and the resolution of the second event if applicable. Please contact CIBMTR Center Support for a review of these types of scenarios.

Question 68: Were features resembling macrophage activation syndrome (MAS) / hemophagocytic lymphohistiocytosis (HLH)-like toxicities present?

Macrophage activation syndrome (MAS) and hemophagocytic lymphohistiocytosis (HLH) are a severe systematic inflammatory syndromes caused by excessive activation and expansion of T lymphocytes and macrophagic histiocytes. HLH is recognized as both a familial disorder and a sporadic disorder associated with an infection, malignancy, and rheumatologic disorders[1]. Diagnostic clinical criteria for MAS/HLH include fever, cytopenias, high triglyceride levels, high ferritin levels, high soluble IL-2 receptor levels, low fibrinogen levels or organomegaly. MAS/HLH has also been reported following chimeric antigen receptor (CAR) T-cell therapy. Some patients may present with CRS and progress into this more aggressive syndrome, where the MAS/HLH falls into the spectrum of CRS. But MAS/HLH may also develop independently which can be due to the recipient's underlying disease (especially lymphoma[1]). The intent of this question is to capture whether MAS/HLH occurred in the recipient regardless of CRS occurring.

1. Jordan, MB, Allen, CE, Greenberg, J, et al. Challenges in the diagnosis of hemophagocytic lymphohistiocytosis: recommendations from the North American Consortium for Histiocytosis (NACHO). Pediatr Blood Cancer. 2019; 66:e27929.

Report the date (YYYY-MM-DD) when the first symptom of MAS / HLH-like toxicities was documented by a physician or other health care provider in the progress note or chart.

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

Question 69: Date of MAS / HLH-like toxicities onset:

Report the date (YYYY-MM-DD) when the first symptom of MAS / HLH-like toxicities was documented by a physician or other health care provider in the progress note or chart.

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

Questions 70-71: Specify therapy given for MAS / HLH-like toxicities: (check all that apply)

Disabled for TED reporting level

Check all that apply from the list of the drug(s) given to treat MAS / HLH-like toxicities in this reporting period. Specify the therapy if **Other therapy** is selected.

Supportive care treatments **should not** be reported as treatment for CRS. Examples of what **not to report** as other therapy include, but are not limited to, acetaminophen (Tylenol®) albumin, antibiotics, IV fluids, or any brand name or specific corticosteroids administered.

Questions 72: Did the recipient have splenomegaly?

Disabled for TED reporting level

Indicate if the recipient had splenomegaly (i.e., abnormal enlargement of the spleen) that could be attributed to MAS/HLH. Splenomegaly is often documented during the physician's physical assessment of the recipient and represents an abnormal finding. Splenomegaly can also be detected by imaging techniques such as ultrasonography, CT or MRI.

Questions 73: Was MAS/HLH confirmed by a bone marrow biopsy?

Disabled for TED reporting level

The pathognomonic feature of MAS is a bone marrow examination that reveals numerous well differentiated macrophages actively phagocytosing hematopoietic cells. MAS is a subset of HLH, and a bone marrow aspirate and biopsy may be performed to look for microscopic evidence of hemophagocytosis as part of the diagnostic work-up for HLH.

Report **Yes** if a bone marrow biopsy was obtained to confirm MAS/HLH. Report **No** if a bone marrow biopsy was not obtained to confirm MAS/HLH.

Questions 74-78: Specify the laboratory values collected (check all that apply)

Disabled for TED reporting level

Hypofibrinogenemia and hypertriglyceridemia support the diagnosis of HLH. The laboratory values should be at the time of diagnosis of MAS/HLH.

If **Fibrinogen** is selected, report the lowest fibrinogen level and the date the sample was collected.

If **Triglyceride** is selected, report the highest triglyceride level and the date the sample was collected.

Questions 79-80: Did macrophage activation syndrome (MAS) / hemophagocytic lymphohistiocytosis (HLH) resolve?

If the macrophage activation syndrome (MAS) / hemophagocytic lymphohistiocytosis (HLH) resolved, select **Yes** and report the resolution date (YYYY-MM-DD).

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

If the macrophage activation syndrome (MAS) / hemophagocytic lymphohistiocytosis (HLH) did not resolve, select **No**.

Questions 81: Did the recipient experience neurotoxicity?

ICANS (Immune effector Cell-associated Neurotoxicity Syndrome) is the development of different neurologic signs and symptoms reported after the infusion of genetically modified lymphocytes. This was initially thought to be part of CRS, but it was also observed in the absence of any other signs of CRS. Neurotoxicity also appears to be a spectrum of signs and symptoms that vary from fine tremors and word finding difficulties to seizure and loss of conscience. This section collects different neurologic signs, ICANS and others, that have been described after cellular therapy infusions.

Indicate **Yes** or **No** if neurotoxicity occurred or persisted in the current reporting period.

Questions 82-83: Specify therapy given for neurotoxicity: (check all that apply)

Disabled for TED reporting level

Check all that apply from the list of drug(s) given to treat neurotoxicity in this reporting period. Pulse dose of corticosteroids are intravenous (IV) high doses given intermittently over a short time period. Specify if **Other therapy** is selected. Supportive care treatments should not be reported as treatment for neurotoxicity. Examples of what not to report as other therapy include, but are not limited to, antibiotics (e.g., amoxicillin, cefepime, ciprofloxacin, piperacillin), antipsychotics (e.g., Risperdal) narcotics/opioids, or other pain killers.

If a drug was started as planned prophylaxis but the recipient develops neurotoxicity and the drug is continued, this is considered a change in intent from prophylaxis to treatment and the drug should also be reported as therapy for neurotoxicity.

Question 84: Which cognitive assessment was performed?

The CAR Toxicity (CARTOX) 10-point neurologic assessment assigns one point for each task performed correctly. A score of 10 is normal. These scales assess cognition and the level of encephalopathy more precisely. They include assessments of orientation, naming, writing, and attention with a score associated with each positive answer. Lower scores are associated with a higher level of encephalopathy.

Unresponsive patients score 0 for all scales. Some centers performed these evaluations multiple times a day. These questions attempt to capture the worst score.

The Immune Effector Cell-Associated Encephalopathy (ICE) assessment is a slightly modified version of the CARTOX-10 assessment. It includes an element for command following.

If another assessment was performed, convert to CARTOX or ICE to report here. See question 85 for a conversion of the Cornell Assessment of Pediatric Delirium (CAPD) to CARTOX or ICE.

Question 85: What was the lowest score? (e.g., CARTOX-10, ICE)

Lower scores are associated with a higher level of encephalopathy. Report the lowest score of any evaluation from the reporting period.

Unable to complete assessment should be selected when an assessment was started and couldn't be finish for any reason or the recipient couldn't perform the evaluation. This should be used rarely since evaluations may be given multiple times a day.

Assessment	CARTOX-10 (12)	ICE SCORE (IMMUNE EFFECTOR ENCEPHALOPATHY) ASSESSMENT
Orientation	Orientation to year, month city, hospital, or President/Prime Minister of country of residence: **5 points**	Orientation to year, month, city, or hospital: **4 points**
Naming	Name 3 objects (e.g., point to clock, pen, button): **3 points**	Name 3 objects (e.g., point to clock, pen, button): **3 points**
Writing	Ability to write a standard sentence (e.g., Our national bird is the bald eagle): **1 point**	Ability to write a standard sentence (e.g., Our national bird is the bald eagle): **1 point**
Attention	Count backwards from 100 by 10: **1 point**	Count backwards from 100 by 10: **1 point**
Following Commands	—	"Show me two fingers," or, "Close your eyes and stick out your tongue.": **1 point**

Source: ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biology of Blood and Marrow Transplantation, Volume 25, Issue 4, April 2019, Pages 625-638

Encephalopathy assessment for children age <12 years using the Cornell Assessment of Pediatric Delirium (CAPD)

A lower CARTOX / ICE score indicates a higher grade of neurotoxicity (symptom/signs)	Grade 1	Grade 2	Grade 3	Grade 4
Neurological assessment score	Mild (7-9)	Moderate (3-6)	Severe (0-2)	Critical/ obtunded

When converting CAPD to CARTOX or ICE, report any number in the corresponding range (e.g. CAPD of ≥9, report 0, 1, or 2)

Assessment	CARTOX	ICE	CAPD
Grade 1	7-9	7-9	1-8
Grade 2	3-6	3-6	1-8
Grade 3	0-2	0-2	≥9

For symptoms of neurotoxicity, report the HIGHEST grade observed in this reporting period.

Questions 86-135: Indicate the manifestations of neurotoxicity (check all that apply)

Disabled for TED level reporting, child questions for these manifestations: other manifestation onset, cerebral vascular accident (stroke), cognitive impairment, personality change(s).

Cerebral edema: A swelling in the brain caused by the presence of excessive fluid. Specify the type of cerebral edema, report if the cerebral edema resolved, and the date of resolution (if applicable).

Cerebral vascular accident (stroke): A disorder characterized by a decrease or absence of blood supply to the brain caused by obstruction (thrombosis or embolism) of an artery resulting in neurological damage. Report the date of onset and the type of stroke. Hemorrhagic stroke occurs when a weakened blood vessel ruptures. Two types of weakened blood vessels usually cause hemorrhagic stroke: aneurysms and arteriovenous malformations (AVMs). Ischemic strokes occur when the arteries to your brain become narrowed or blocked, causing severely reduced blood flow (ischemia).

Cognitive impairment: A disorder characterized by a conspicuous change in cognitive function[a]. Specify the type of cognitive impairment, report if the cognitive impairment resolved, and the date of resolution (if applicable). The date of resolution should be the for the category as a whole, e.g., when the last symptom resolved.

- Amnesia: A disorder characterized by systematic and extensive loss of memory[a]
- Cognitive disorder: A disorder characterized by a conspicuous change in cognitive function[a]
- Confusional state: A disorder characterized by a lack of clear and orderly thought and behavior[a]
- Concentration impairment: A disorder characterized by a deterioration in the ability to concentrate[a]
- Encephalopathy: A disorder characterized by a pathologic process involving the brain[a]
- Hallucination: A disorder characterized by a false sensory perception in the absence of an external stimulus[a]
- Leukoencephalopathy: A disorder characterized by diffuse reactive astrocytosis with multiple areas of necrotic foci without inflammation* as determined by neuroimaging (i.e., brain MRI).
- Loss of consciousness: A disorder characterized by a decrease in ability to perceive and respond[a]
- Mental status changes: a change in a person’s mood, behavior, psychomotor skills, and/or cognition
- Non-infective encephalitis: inflammation of the brain not caused by infection
- Psychomotor retardation: slowing of mental and physical activity
- Other cognitive impairment: other decline in mental abilities not included in above options

Depressed level of consciousness: A disruption in how the brain works that causes a change in behavior. This change can happen suddenly or over days and ranges from increased sleepiness to coma. Specify the most severe level, report if the depressed level on consciousness resolved, and the date of resolution (if applicable).

Leukoencephalopathy: A disorder characterized by diffuse reactive astrocytosis with multiple areas of necrotic foci without inflammation* as determined by neuroimaging (i.e., brain MRI).

Motor neuron disorder: neurological disorder effecting motor neurons that control muscle activity. Specify the type of motor neuron disorder, report if the motor neuron disorder resolved, and the date of resolution (if applicable). The date of resolution should be the for the category as a whole, e.g., when the last symptom resolved.

- Facial weakness/paralysis: weakness or inability to move facial musculature
- Hemiparesis: Weakness on one side of the body (hemiplegic), partial paralysis of the lower limbs (legs), or other sudden loss of connectivity between the CNS and muscles.
- Paraparesis: Weakness on one side of the body (hemiplegic, partial paralysis of the lower limbs (legs), or other sudden loss of connectivity between the CNS and muscles.
- Guillain-Barre syndrome: A disorder characterized by the body's immune system attacking the peripheral nervous system causing ascending paralysis[a]
- Myelitis: Inflammation of the spinal cord
- Other motor neuron disorder: other motor neuron disorder not included in above options

Movement disorder: neurologic disorder causing excess movement or lack of voluntary movement. Specify the type of movement disorder, report if the movement disorder resolved, and the date of resolution (if applicable). The date of resolution should be the for the category as a whole, e.g., when the last symptom resolved.

- Action tremor: A disorder caused by the rapid alternating contraction and relaxation of muscles with the voluntary movement of a muscle and is a common symptom of diseases of the nervous system.
- Ataxia: A disorder characterized by lack of coordination of muscle movements resulting in the impairment or inability to perform voluntary activities
- Cogwheel rigidity: muscular rigidity causing cogwheel jerks to passive movement of limbs
- Dysgraphia: neurologic disorder causing writing disabilities
- Dyskinesia: abnormal, involuntary movements
- Dysmetria: improper accuracy in voluntary movements
- Gait disturbance: A disorder characterized by walking difficulties
- Myoclonus: involuntary and sudden movement of muscle
- Resting tremor: A disorder caused by the rapid alternating contraction and relaxation of muscles (involuntary) while the body is at rest against gravity and is a common symptom of diseases of the nervous system.
- Other movement disorder: other movement disorder not included in above options

Non-infective encephalitis: inflammation of the brain not caused by infection.

Personality change: deviation from the patient's normal behavior patterns. Specify the type of personality change, report if the personality change resolved, and the date of resolution (if applicable). The date of resolution should be the for the category as a whole, e.g., when the last symptom resolved.

- Flat affect: lack of emotional expression
- Personality change: A disorder characterized by a conspicuous change in a person's behavior and thinking[a]

- Other personality change: other personality changes not included in above options

Seizure: Uncontrolled electrical activity in the brain, which may produce a physical convulsion, minor physical signs, thought disturbances or a combination of symptoms. Specify the type of seizure and severity (grade). Report the worst type of seizure if multiple types were experienced in a single reporting period.

Speech impairment: neurologic disorder causing disruption of normal speech. Specify the type of speech impairment and specify the grade of dysphasia (if applicable)

- Dysphasia: The loss of ability to understand or express speech, caused by brain damage.
- Aphasia: Grade 3 dysphasia is defined as aphasia

Other symptom: If the recipient experienced a symptom of neurotoxicity not listed above, report here and specify the symptom, and report the date of onset.

[a]Common Terminology Criteria for Adverse Events (CTCAE) v5.0 and ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biology of Blood and Marrow Transplantation, Volume 25, Issue 4, April 2019, Pages 625-638

Questions 136-137: Did neurotoxicity resolve?

Resolution means complete normalization of neurologic function. It is possible that patients might remain with residual neurologic dysfunction which would not qualify as complete resolution of this complication. If the cellular therapy associated neurotoxicity resolved, select **Yes** and report the resolution date (YYYY-MM-DD).

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

Other toxicities

Questions 138-139: Did the recipient receive immunoglobulin replacement therapy?

Disabled for TED reporting level

Replacement therapy is given to prevent infections. If the recipient received immunoglobulin replacement therapy (includes, but not limited to, IVIG or SCIG) regardless of hypogammaglobulinemia that developed post-infusion, select **Yes** and indicate if the recipient is still receiving the therapy on the contact date for this reporting period. If the last immunoglobulin replacement therapy was given less than 6 months from the date of contact, report **Yes** unless it's clearly stated in the medical record that no more immunoglobulin replacement therapy is required.

Questions 140-141: Has the recipient's immunoglobulin level recovered?

Disabled for TED reporting level

Hypogammaglobulinemia refers to low levels of circulating gammaglobulins, or immunoglobulins, in the blood and often determined by quantitative levels of immunoglobulins G (IgG), A (IgA) and M (IgM), or most commonly IgG only. Hypogammaglobulinemia is common after CAR-T infusions that target CD19+ cells, which produce immunoglobulins. The degree of hypogammaglobulinemia is associated with a higher risk of infection. Immunoglobulin replacement therapy is given to prevent infections.

Hypogammaglobulinemia can be reported as resolved if there are sustained normal levels of IgG in the blood without the need for IG infusions for 6 consecutive months.

Normal limits of IgG concentration in the blood vary with age. For adults, levels lower than 600 mg/dL of circulating IgG are considered to be hypogammaglobulinemia. Children ages 4 to 18, levels lower than 500 mg/dL are considered hypogammaglobulinemia. Children younger than four years, as levels of IgG can be much lower and still be within normal ranges for the age, the diagnosis of hypogammaglobulinemia needs to be confirmed with the treating physician.

Example 1. IgG levels were measures at 450 mg/dL on June 1; immunoglobulin replacement therapy was given on June 15. IgG levels were monitored for the next 7 months, and no further immunoglobulin replacement therapy was given. IgG levels went above 600 mg/dL on December 15 and continued to rise. Report the resolution date as the first test result that was greater than 600 mg/dL (December 15).

Example 2. IgG levels were measures at 450 mg/dL on May 15, no immunoglobulin replacement therapy is given. IgG levels were monitored and went above 600 mg/dL on June 3 and normal levels were sustained. Report resolution date as the first test result that was greater than 600 mg/dL (June 3).

Example 3. IgG levels were measures at 450 mg/dL on June 1; immunoglobulin replacement therapy was given on June 15. IgG levels were not monitored, and the recipient has returned to their primary oncologist. In the absence of any testing, the resolution date can be reported as the date 6 months after the last IG infusion.

Example 4. For an adult recipient, IgG levels were measured at 450 mg/dL on June 1; immunoglobulin replacement therapy was given on June 15. IgG levels were monitored over the next six and a half months and no further immunoglobulin replacement therapy was given. IgG levels were tested, and measured greater than 600 mg/dL, on November 29 (5.2 months after last IG infusion) and December 25 (6.2 months after the last IG infusion). The resolution date should be greater than or equal to 6 months after the last IG infusion; therefor December 25 should be reported as the resolution date.

Example 5. For an adult recipient, IgG levels were measured at 450 mg/dL on June 1; immunoglobulin replacement therapy was given on June 15. IgG levels were monitored over the next six and a half months and no further immunoglobulin replacement therapy was given. IgG levels were tested, and measured greater than 600 mg/dL, on November 29 (5.5 months after last IVIG infusion). IgG levels were measured at 450 mg/dL on December 25 (6.2 months after the last IG infusion). Hypogammaglobulinemia

cannot be reported as resolved in this case.

If the hypogammaglobulinemia resolved, select **Yes** and report the resolution date (YYYY-MM-DD) as documented by a physician or other health care provider in the progress note or chart.

Select **Not applicable** when:

- The recipient never got immunoglobulin replacement therapy because their IgG levels were never decreased
  Or
- There was no decline in IgG levels in *this* reporting period
  Or
- IgG levels were never tested in *this* reporting period

Questions 142-147: Tumor lysis syndrome

Disabled for TED reporting level

Tumor lysis syndrome (TLS) is a disorder characterized by metabolic abnormalities that result from a spontaneous or therapy-related cytolysis of tumor cells. Indicate if TLS occurred or persisted into the current reporting period.

Indicate **Yes**, **No**, or **Unknown** or No if tumor lysis syndrome occurred or persisted into the current reporting period.

If the tumor lysis syndrome was diagnosed in a previous reporting period, symptoms continue into this reporting period, and the date has already been reported, select **Yes** to the question *Was the date of onset previously reported* and report the date (YYYY-MM-DD) when the tumor lysis syndrome was documented by a physician or other health care provider in the progress note or chart.. If tumor lysis syndrome was not diagnosed in a prior reporting period, report **No** and enter the date of tumor lysis syndrome diagnosis.

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

Report the most severe grade of the tumor lysis syndrome as documented by a physician or other health care provider in the progress note or chart.

- **Grade 3:** Present
- **Grade 4:** Life-threatening consequences: urgent intervention indicated
- **Grade 5:** Death

If the tumor lysis syndrome resolved, select **Yes** and report the resolution date (YYYY-MM- DD) as documented by a physician or other health care provider in the progress note or chart.

Reporting multiple other toxicities
FormsNet3 application: Complete the *other toxicity* questions to report multiple other toxicities by adding additional instance(s) in the FormsNet3^{SM} application.
Paper form submission: Copy the other toxicity questions to report multiple other toxicities. A separate instance should be completed for each toxicity.

Questions 148-153: Other toxicity:

Disabled for TED reporting level

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

To reduce the reporting burden, other toxicities reported should be related to the cellular therapy infusion that are documented in the medical record as clinically important and relevant and do not fit into another category listed on this form.

If the recipient experienced a toxicity that does not fit in a category above, select **Yes** and specify the other toxicity.

If the recipient did not experience other toxicities, select **No**.

If the other toxicity was diagnosed in a previous reporting period, symptoms continue into this reporting period, and the date has already been reported, select **Yes** to the question *Was the date of onset previously reported* and report the date (YYYY-MM-DD) when the other toxicity was documented by either a physician / health care provider or determined by lab results.
If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Indicate **Yes** or **No** if the other toxicity resolved. If **Yes**, report the resolution date (YYYY-MM-DD) as documented by a physician or other health care provider in the progress note or chart.

Questions 154-160: Has the recipient experienced a grade 3 organ toxicity?

This question will enable only if the commercially available product Kymriah®, Breyanzi^{TM}, Abecma®, or Carvykti^{TM} is selected in question 1 and can only be completed on the 100 day and 6 month follow-up forms.

As defined by the CTCAE criteria, grade 3 toxicity represents severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care Activities of Daily Living (ADL), which refer to bathing, dressing and undressing, feeding self, using

the toilet, taking medications, and not bedridden. If **Other** is selected, then the grade 3 toxicities / symptoms that are reported should be related to the cellular therapy infusion that are documented in the medical record as clinically important and relevant and do not fit into another category listed on this form.

Reporting multiple Grade 3 toxicities
FormsNet3^{SM} application: Complete the Grade 3 organ toxicity questions to report multiple Grade 3 toxicities by adding an additional instance(s) FormsNet3 application. A separate instance should be completed for each toxicity.
Paper form submission: Copy the Grade 3 organ toxicity questions to report multiple Grade 3 toxicities. A separate instance should be completed for each toxicity.

Specify the organ affected, and specify the toxicity of that organ. The list of symptoms will dynamically filter based on the organ selected. The table below shows all option values.

Organ / System	Symptom or Event
Cardiovascular	Capillary leak syndrome, cardiac arrhythmia, hypertension, hypotension, left ventricular systolic dysfunction, myocardial infarction, new or worsening heart failure, pericardial effusion, pericarditis, restrictive cardiomyopathy, thromboembolic event
Gastrointestinal	Abdominal pain, constipation, diarrhea, dyspepsia (heartburn), gastroenteritis, intestinal obstruction (includes small intestine and colonic), mucositis oral, nausea, vomiting
Kidneys	Acute kidney injury, chronic kidney disease, cystitis noninfective
Liver	Alanine aminotransferase increased (ALT), alkaline phosphatase increased, aspartate aminotransferase increased (AST), blood bilirubin increased, hepatic failure, hepatitis
Lungs	Acute respiratory distress syndrome, dyspnea, productive cough, pulmonary edema, respiratory edema, respiratory failure
Musculoskeletal	Arthralgia (joint pain), muscle weakness, generalized or specific area (not due to neuropathy), myalgia (muscle pain)
Nervous system	Dizziness, encephalopathy, headache, tremor
Other	Anorexia, chills, dysgeusia (taste alternation), edema limbs, fatigue

If the grade 3 organ toxicity was diagnosed in a previous reporting period, symptoms continue into this reporting period, and the date has already been reported, select **Yes** to the question *Was the date of onset previously reported* and report the date (YYYY-MM-DD) when the grade 3 organ toxicity was documented by either a physician/ health care provider or determined by lab results. Else select **No** and report the date of grade 3 organ toxicity diagnosis.

If the grade 3 organ toxicity resolved, select **Yes** to the question *Did the grade 3 organ toxicity resolve?* and

report the date (YYYY-MM-DD) as documented by a physician or other health care provider in the progress note or chart.

Questions 160-166: Has the recipient experienced a grade 4 organ toxicity?

> ! This question can only be completed on the 100 day and 6 month follow-up forms.

Disabled for TED reporting level

As defined by the CTCAE criteria, grade 4 toxicity represents life-threatening consequences and urgent intervention is indicated. If **Other** is selected, then the grade 4 toxicities / symptoms that are reported should be related to the cellular therapy infusion that are documented in the medical record as clinically important and relevant and do not fit into another category listed on this form.

> ✻ **Reporting multiple Grade 4 toxicities**
> **FormsNet3 application**[SM]: Complete the Grade 4 organ toxicity questions to report multiple Grade 4 toxicities by adding an additional instance(s) FormsNet3 application. A separate instance should be completed for each toxicity.
> **Paper form submission**: Copy the Grade 4 organ toxicity questions to report multiple Grade 4 toxicities. A separate instance should be completed for each toxicity.

Specify the organ affected and specify the toxicity of that organ. The list of symptoms will dynamically filter based on the organ selected. The table below shows all option values.

Organ / System	Symptom or Event
Cardiovascular	Capillary leak syndrome, cardiac arrhythmia, hypertension, hypotension, left ventricular systolic dysfunction, myocardial infarction, new or worsening heart failure, pericardial effusion, pericarditis, restrictive cardiomyopathy, thromboembolic event
Gastrointestinal	Abdominal pain, constipation, diarrhea, dyspepsia (heartburn), gastroenteritis, intestinal obstruction (includes small intestine and colonic), mucositis oral, nausea, vomiting
Kidneys	Acute kidney injury, chronic kidney disease, cystitis noninfective
Liver	Alanine aminotransferase increased (ALT), alkaline phosphatase increased, aspartate aminotransferase increased (AST), blood bilirubin increased, hepatic failure, hepatitis
Lungs	Acute respiratory distress syndrome, dyspnea, productive cough, pulmonary edema, respiratory edema, respiratory failure
Musculoskeletal	Arthralgia (joint pain), muscle weakness, generalized or specific area (not due to neuropathy), myalgia (muscle pain)

Nervous system	Dizziness, encephalopathy, headache, tremor
Other	Anorexia, chills, dysgeusia (taste alternation), edema limbs, fatigue

If the grade 4 organ toxicity was diagnosed in a previous reporting period and symptoms continue into this reporting period and the date has already been reported, select **Yes** to the question *Was the date of onset previously reported* and report the date (YYYY-MM-DD) when the grade 4 organ toxicity was documented by either a physician/ health care provider or determined by lab results. Else select **No** and report the date of grade 4 organ toxicity diagnosis..

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

If the grade 4 organ toxicity resolved, select **Yes** and report the date (YYYY-MM-DD) as documented by a physician or other health care provider in the progress note or chart.

Questions 167-176: Specify the laboratory values collected (check all that apply)

! Specify the maximum lab results since the date of last report. If there are multiple results available for the same test, only report the maximum in the reporting period.

Collection Dates
If the same maximum value occurs multiple times during the reporting period, report the first date post-infusion when the maximum value occurs.

Disabled for TED reporting level

C-reactive protein: C-reactive protein (CRP) is a protein produced by the liver and found in the blood. CRP levels increase with tissue injury or trauma, infection or inflammation. CRP is also highly associated with IL-6 levels. Specify the maximum value since the date of the last report, the date the sample was collected, and the upper limit of normal for your institution.

Interleukin-6: Interleukin-6 is a pro-inflammatory cytokine derived from macrophages and endothelial cells that increases synthesis and secretion of immunoglobulins by B lymphocytes. Specify the maximum value since the date of the last report and the date the sample was collected.

Soluble interleukin-2 receptor α (sIL2RA or soluble CD25): Interleukin-2 receptor alpha or CD25 can shed from the surface of cells during inflammatory conditions. This test detects soluble or circulating sIL2RA. Report the maximum value since the date of the last report and the date the sample was collected.

Total serum ferritin: Ferritin is an acute phase reactant and is often found in high concentration in highly inflammatory conditions. Report the maximum value since the date of the last report and the date the sample was collected.

None: None of the specified laboratory tests above were performed

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
47	4/30/ 2025	Add	Added new warning box above question 47: Effective April 30th, 2025, report only toxicities (e.g. CRS, neurotoxicity, etc.) that are **directly** attributed to the CAR-T product / infusion. It is no longer required to report any toxicity regardless of causality. Treatment given post-infusion may have the effect of re-activating the product and inducing toxicities (e.g. CRS), these toxicities should **NOT** be captured in this section of the form. Contact CIBMTR Center Support with questions.	Effective immediately, only toxicities directly attributed to the CAR-T infusion are deemed appropriate to report
47	4/30/ 2025	Remove	Removed the blue note box above question 47: ~~Report any observed toxicity or infection that occurs post-infusion in this reporting period, regardless of causality and whether or not treatment was administered. The intent is to capture all toxicities diagnosed after the cellular therapy infusion. Although treatment given post-infusion may have the effect of re-activating the product and inducing toxicities (e.g. CRS), these toxicities should still be captured in this section of the form.~~	Effective immediately, only toxicities directly attributed to the CAR-T infusion are deemed appropriate to report
50 – 52	10/24/ 2025	Add	*If **Tocilizumab** was given to treat the CRS, report the number of doses given. This information is important in the grading of the CRS event. If a drug was started as planned prophylaxis but the recipient develops CRS and the drug is continued, this is considered a change in intent from prophylaxis to treatment and the drug should also be reported as therapy for CRS.*	Added for clarification
70-71	10/25/ 2024	Modify	Correct “CRS” to “MAS / HLH-like toxicities”: Check all that apply from the list of the drug(s) given to treat ~~CRS~~ MAS / HLH-like toxicities in this reporting period.	Correction of a typo

82 – 83	10/24/ 2025	Add	*Check all that apply from the list of drug(s) given to treat neurotoxicity in this reporting period. Pulse dose of corticosteroids are intravenous (IV) high doses given intermittently over a short time period. Specify if* ***Other therapy*** *is selected. Supportive care treatments should not be reported as treatment for neurotoxicity. Examples of what not to report as other therapy include, but are not limited to, antibiotics (e.g., amoxicillin, cefepime, ciprofloxacin, piperacillin), antipsychotics (e.g., Risperdal) narcotics/opioids, or other pain killers. If a drug was started as planned prophylaxis but the recipient develops neurotoxicity and the drug is continued, this is considered a change in intent from prophylaxis to treatment and the drug should also be reported as therapy for neurotoxicity.*	Added for clarification
138-140	10/25/ 2024	Modify	Removed “IVIG” from 138, 140 Examples 1, 2, 3, 4, 5 and added “immunoglobulin replacement therapy (includes, but not limited to, IVIG or SCIG)” in 138	Updated for clarification. Ig therapy can be given via IV or sub-cutaneous (SC)
68-69	10/25/ 2024	Modify	Removed Disabled for TED reporting level	Questions are enabled for TED reporting level
68-69	10/25/ 2024	Modify	Updated the definition for MAS/HLH-like toxicity onset date: ~~Report the date (YYYY-MM-DD) when the first symptom of MAS/HLH was documented by either the date of the pathological confirmation of MAS/HLH (bone marrow or other organ biopsy) or the first date of a ferritin level > 100,000 ng/mL among patients without pathologic confirmation but with high clinical suspicion (persistent high fevers, ongoing cytopenias, high triglyceride levels, low fibrinogen levels or organomegaly).~~ Report the date (YYYY-MM-DD) when the first symptom of MAS / HLH-like toxicities was documented by a physician or other health care provider in the progress note or chart.	Updated for clarification
142-147	10/25/ 2024	Modify	Added bold text below question header: Questions 142-147: Tumor lysis syndrome **Disabled for TED reporting level**	Added for clarification
140	6/11/ 2024	Modify	Normal limits of IgG concentration in the blood vary with age. For adults, levels lower than 600 mg/dL of circulating IgG are	Clarification when to use

			considered to be hypogammaglobulinemia. Children ages 4 to ~~10~~ 18, levels lower than 500 mg/dL are considered hypogammaglobulinemia.	the not applicable option.
148	5/22/ 2024	Add	Added new note regarding combined follow up: In scenarios where an HCT was given after a cellular therapy and this form is now being completed based on the subsequent HCT date, these questions do not apply and are disabled.	Due to change in FormsNet validations
138	4/26/ 2024	Modify	Correction of required to received: **Questions 138-139: Did the recipient ~~require~~ receive immunoglobulin replacement therapy?** Replacement therapy is given to prevent infections. If the recipient ~~required~~ received immunoglobulin replacement therapy (IVIG) regardless of hypogammaglobulinemia that developed post-infusion, select Yes and indicate if the recipient is still ~~requiring~~ receiving the therapy on the contact date for this reporting period. If the last immunoglobulin replacement therapy (IVIG) was given less than 6 months from the date of contact, report Yes unless it's clearly stated in the medical record that no more immunoglobulin replacement therapy is required.	Correction of mistake in the manual
85	1/16/ 2024	Add	Added the following text to question 85: Lower scores are associated with a higher level of encephalopathy. Report the lowest score of any evaluation from the reporting period. **Unable to complete assessment** should be selected when an assessment was started and couldn't be finish for any reason or the recipient couldn't perform the evaluation. This should be used rarely since evaluations may be given multiple times a day.	Clarifying when to used 'unable to complete assessment'
140	12/12/ 2023	Modify	Select **Not applicable** when: The recipient never got immunoglobulin replacement therapy due to never having a decreased IgG level Or There was no decline in IgG levels in this reporting period Or IgG levels were never tested in this reporting period	Clarification when to use the not applicable option.
140	9/7/ 2023	Modify	Select **Not applicable** when: The recipient never got immunoglobulin replacement therapy due to never having a decreased IgG level Or There was no decline in IgG levels in this reporting period	Clarification when to use the not applicable option.
140	8/24/ 2023	Add	If the recipient never got immunoglobulin replacement therapy and their immunoglobulin levels were never decreased, select **Not applicable**.	Clarification when to use the not applicable

				option.

Last modified: Oct 31, 2025

Q178-189: Infection

> **!** COIVD-19 Infection
> The COVID-19 infection questions are disabled as of April 2024.

Infections occur frequently in cell therapy or transplant patients. The following questions are intended to capture detailed information on *clinically significant* infections diagnosed during the reporting period. A single infection may be found on multiple cultures or at multiple sites. Infections may recur following resolution of symptoms and negative testing. Use the instructions provided in this section to determine when an infection should be considered clinically significant, and therefore reported, as well as when to report new and / or recurrent infections.

> ✻ **Reporting Multiple Infections**
> **FormsNet3^{SM} application**: Complete the infection organism, site of infection, and diagnosis date questions for each reported infection by adding an additional instance in the FormsNet application to report the organism, site, and date of diagnosis.
> **Paper form submission**: Copy the infection organism, site of infection, and diagnosis date questions and complete for each reported infection to report the organism, site, and date of diagnosis.

> ✻ **Diagnosis of COVID-19 after the start of the lymphodepleting therapy:** Any COVID-19 infections diagnosed after the start of the lymphodepleting therapy should be reported in the following questions on the Cellular Therapy Essential Data Follow-Up (4100) form. Effective August 25, 2023, the Respiratory Virus Post-Infusion Data (2149) form for infusions on the cellular therapy track will no longer be required. Additionally, an unscheduled Respiratory Virus Post-Infusion Data (2149) form cannot be created for these recipients.

> ✻ **Reporting COVID-19 Reinfection**
> There have been cases of recipients recovering from COVID-19 infection, only to later test positive again. For CIBMTR purposes, a new COVID-19 infection should be reported when a recipient tests positive again >21 days from resolution (resolution defined as no signs or symptoms of infection, or a negative diagnostic test).

Possible COVID-19 Reporting Scenarios:
Do NOT report an infection in the following scenarios:

- A recipient only has a positive antibody result.
- The recipient was symptomatic and treated but COVID-19 diagnostic testing was not performed and / or COVID-19 diagnostic testing was performed and negative.

DO report an infection in the following scenarios:

- A recipient has a positive COVID-19 diagnostic result (PCR or antigen), regardless of if treatment was given or if the recipient was asymptomatic
- A recipient has a positive antibody result and a positive COVID-19 diagnostic test (PCR or antigen)

Question 178-182: Did the recipient develop a clinically significant infection since the date of the last report?

Indicate whether the recipient developed a clinically significant bacterial, viral, or fungal infection during the reporting period. For the purpose of this manual, the term “clinically significant” refers to any infection requiring treatment. Surveillance cultures in which normal flora is present and the recipient is asymptomatic do not need to be reported. If no clinically significant infections occurred during the reporting period, report **No**.

Do **not** report the following scenarios:

- Culture-negative neutropenic fever without clear source;
- Upper respiratory infections which are presumed viral, but no virus has been identified;
- Candida detected in oral or stool samples (includes oral thrush);
- Toenail fungus;
- Yeast infection in the groin, vagina, or under the breasts;
- Surveillance cultures in which normal flora is present and the recipient is asymptomatic;
- Infections persisting from a prior reporting period (including infections which have progressed to new sites since the last report); or
- Infections recurring within the time frames specified in the Definitions for Same Infection table below.

Systemic inflammatory response syndrome and septic shock may be diagnosed with or without an organism identified by relevant testing. In either case, a clinical diagnosis of these complications will be reported in the following section. If an organism is identified by molecular report, laboratory report, or other physician documentation, the infection should be captured in this section. If no organism is identified, the center should use the following guidelines to determine whether to report an infection:

- If a fungal infection is suspected (per radiology assessments) and treated, but no organism is isolated during the reporting period, select **Suspected fungal infection**.
- If a bacterial or viral infection is suspected and treated, but not confirmed, select **Suspected bacterial infection** or **Suspected viral infection**, respectively.
- If no particular organism group is identified or suspected, **do not** report an infection in this section.

For each infection, report the organism, site, and date of diagnosis.

If there are multiple positive tests within the specified timeframes listed below, the infection is considered the ‘same’ and should not be reported multiple times.

Definitions for *Same* Infection

Bacteria	Virus	Fungal
≤ 7 Days • Any bacteria ≤ 30 Days • Clostridium difficile ≤ 365 Days • Helicobacter pylori	≤ 14 Days • Adenovirus • Enterovirus • Herpes zoster • Influenza • Parainfluenza • Rhinovirus • Respiratory syncytial virus • Varicella zoster ≤ 30 Days • Human Herpes Virus – 6 ≤ 60 Days • Cytomegalovirus • Epstein-Barr virus • Herpes simplex • Polyomavirus	≤ 14 Days • Any yeasts ≤ 90 Days • Any molds

Organism:
Select the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation.

If the specific organism is not listed, use the code **777 – Other organism** and report the name of the organism in the space provided.

In some cases, an infection may be suspected but significant enough to be treated. If a fungal, bacterial, or viral infection is suspected, but not identified, report using code **502 – Suspected bacterial infection**, **503 – Suspected fungal infection** or **504 – Suspected viral infection**. As noted above, only report infections which are clinically significant.

Site:
Infections can occur virtually anywhere. In order to capture sufficient detail without excess burden, there is a list for the potential sites. An infection may occur in more than one site at the same time or at different times.

- If the infection is identified at multiple sites with the same organism and within the recurrence interval to be considered the same infection (Definitions for Same Infection table), please report all sites the organism was identified.
- If the infection is identified at multiple sites with an organism already reported but is outside of the recurrence interval to be considered the same infection, please report as a new infection.

Select the site(s) of the infection from the options provided on the form. Report all sites of infection which were confirmed by microbiology, laboratory report, or other physician documentation *during the reporting period*. This includes any new sites identified after the date of diagnosis as well as after treatment has been

initiated.

For clarification, the following site definitions are provided:

Blood: includes blood obtained from a central IV line, catheter tip, or from a direct needle stick (Peripheral draw). Blood should be the reported site for infections identified in the bone marrow.

Bone: an infection in the bone itself (Osteomyelitis)

CNS: includes CSF (cerebrospinal fluid) specimens as well as abscesses and/or inflammation noted on brain imaging (encephalitis, meningitis)

Eyes: includes infection in any part of the eye (i.e., retinitis)

Genital: includes vagina, penis, perineum, ovaries, scrotum, testes, uterus

GI tract, lower: includes jejunum, ileum, colon, rectum, and stool

GI tract, upper: includes mouth, dentition, esophagus, stomach, and duodenum

Joints: includes fibrous connective tissue and cartilage at any site of bone articulation, typically isolated to a single area (i.e., not a diffuse infection) such as the knee, elbow, or shoulder

Liver/Spleen: includes the gallbladder and biliary tract

Lung: also known as the lower respiratory tract

Skin, cellulitis: a spreading bacterial or viral infection of the skin and tissues beneath the skin

Skin, necrotizing fasciitis: a severe bacterial infection of the fascia, the tissues that line and separate muscles, which causes extensive tissue death including damage to skin and overlying tissues
Sinus and/or upper respiratory tract: all areas from the nose to the throat and sinuses, does not include lungs (report as “Lung”), mouth, or dental infections (report mouth and dental as “GI tract, upper”).

Urinary tract, lower: includes urinary tract infections and cystitis (bladder inflammation)

Urinary tract, upper: includes the kidneys and ureters

Date of Diagnosis:
Report the date of diagnosis of the infection as the collection date for the positive microbiology culture or laboratory report. For suspected fungal infections, enter the date of a radiological test or the date treatment was started as the date of diagnosis. If multiple sites of infection are identified during the reporting period, report the collection date of the first positive microbiology culture or laboratory report.

For more information regarding reporting partial or unknown dates, see General Instructions, General

Guidelines for Completing Forms.

> **COVID-19 Vaccine**
> The COVID-19 vaccine questions are disabled as of April 2024.

Questions 183-184: Pre-exposure drugs given for COVID-19 (SARS-CoV-2)?

Indicate if the recipient received pre-exposure drugs for COVID-19 in this reporting period. Specify if **Other** is selected.

Question 185: Was a vaccine for COVID-19 (SARS-CoV-2) received since the date of last report?

Indicate **Yes** if the recipient received a vaccine for COVID-19 (SARS-CoV-2) during the reporting period. If the recipient did not receive a vaccine in the reporting period, select **No**. If documentation is unclear if the recipient received a vaccine for COVID-19 in the reporting period, select **Unknown**.

Revaccination Post – Infusion
When vaccines are given post-infusion, the physician should make the determination on whether the doses are part of the primary series of vaccines, third primary dose, boosters, or revaccination. If a recipient receives a new course of COVID-19 vaccines following infusion as revaccination, report the vaccines as a new series. The most up to date CDC COVID-19 vaccine information for immunocompromised people can be found here.

> **Reporting Multiple COVID-19 Vaccine Doses**
> **FormsNet3^{SM} application**: Complete the *Specify vaccine type*, *dose(s)* and *date received* questions to report all vaccine doses received by adding an additional instance in the FormsNet3^{SM} application.
> **Paper form submission**: Copy *Specify vaccine type*, *dose(s)* and *date received* questions and complete to report all vaccine doses received.

Questions 186-187: Specify vaccine brand:

Specify the brand of COVID-19 vaccine the recipient received in the reporting period. If the recipient received a brand that is not listed, select **Other type** and specify the vaccine. If the vaccine brand is unknown, leave the field blank and override the error as **Unknown**.

> **Third dose versus Booster dose**
> To determine between a third dose and a booster dose, seek clinician clarification, as needed, using the guidelines listed below:
> **Booster dose**: Administered to recipients who have enough protection after completing their primary vaccine series but then protection decreases over time
> **Third dose**: An additional primary dose required for recipients who did not build enough

protection from their primary vaccine series, typically for immunocompromised individuals
Primary vaccine series:
- Two doses of Pfizer-BioNTech or Moderna

Questions 188-189: Select dose(s) received (check all that apply)

For the reported dose, specify the vaccine dose the recipient in the current reporting period and specify the date when the dose was received.

Select **One dose (without planned second dose)** if the recipient received a single dose, without the plans of receiving the second dose and report the date of administration.

Select **First dose (with planned second dose)** if the recipient received their first dose, with plans for receiving the second dose and report the date of administration.

Select **Second dose** if this is the recipient's planned second dose of the vaccine and report the date of administration.

Refer to the blue instructional box above for additional information regarding third and booster doses.

If the exact date is not known, use the process described in the General Instructions, Guidelines for Completing Forms and select **Date estimated**.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q178	4/19/ 2024	Add	The COVID-19 Infection red box updated to clarify these questions are now disabled.	Due to disabling of questions with the Spring 2024 release
Q183	4/19/ 2024	Modify	The COVID-19 Vaccine red box updated to clarify these questions are now disabled.	Due to disabling of questions with the Spring 2024 release
178	11/21/ 2023	Modify	DO report an infection in the following scenarios: A recipient has a positive COVID-19 diagnostic result (PCR or antigen) ~~or~~	Clarified when to

			~~if treatment was given or if the recipient was asymptomatic.~~ regardless of if treatment was given or if the recipient was asymptomatic.	report a COIVD-19 infection
178	8/25/ 2023	Modify	Diagnosis of COVID-19 after the start of the lymphodepleting therapy: Any COVID-19 infections diagnosed after the start of the lymphodepleting therapy should be reported in the following questions on the Cellular Therapy Essential Data Follow-Up (4100) form. ~~An associated Respiratory Virus Post-Infusion Data (2149) form will be generated.~~ Effective August 25, 2023, the Respiratory Virus Post-Infusion Data (2149) form for infusions on the cellular therapy track will no longer be required. Additionally, an unscheduled Respiratory Virus Post-Infusion Data (2149) form cannot be created for these recipients.	2149 is no longer required to be completed for recipients on the cellular therapy track when there is a diagnosis of COVID-19 post-infusion.
183-184	8/22/ 2023	Modify	Clarified the intention of the question: Indicate if the recipient received pre-exposure drugs for COVID-19 in this reporting period.	This question applies to each reporting period.

Last modified: Apr 23, 2024

Q190-191: Pregnancy Status

Pregnancy status
This section focuses on fertility. This is an important section due to the possibility of some genetically modified cells persisting and possible transmission to the fetus.

Pregnancy Questions
Pregnancy questions will only be answered for recipients between the ages of 10 and 60.

If a pregnancy is reported, complete the Pregnancy (3501) Form to answer questions specific to the pregnancy. The option of **Previously reported** should only be used if the same pregnancy instance has already been reported on a Pregnancy (3501) Form that was created as an unscheduled form ("on demand"). If there is a question regarding use of this option, contact CIBMTR Center Support if there are questions.

Example 1. Recipient or recipient's female partner becomes pregnant at day +68. It is reported at the time the 100-day Form Cellular Therapy Essential Data Follow-Up (4100) form is completed. These questions should be answered as **Yes**, and the Form 3501 should be completed to report all pregnancy information.

Example 2. Recipient or recipient's female partner becomes pregnant at day +68 and had received a commercially available CAR-T product (e.g., Yescarta®). Per protocol, the pregnancy should be reported at the time of knowledge of the pregnancy. The Form 3501 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. When the 100-day Cellular Therapy Essential Data Follow-Up (4100) form is completed, these questions should be answered as **Previously reported**.

Example 3. Recipient or recipient's female partner becomes pregnant at 1 year and 1 month and had received a commercially available CAR-T product (e.g., Yescarta®). Per protocol, the pregnancy should be reported at the time of knowledge of the pregnancy. The Form 3501 should be created as an unscheduled form in FormsNet3 and completed in a timely manner. The outcome of the first pregnancy does not go to term or does not result in a live birth and another pregnancy event occurs at 1 year and 11 months. It is decided to report the 2nd pregnancy event on the 2 year Cellular Therapy Essential Data Follow-Up (4100) form since it is due. These questions should be answered as **Yes** to create another Form 3501.

Question 190: Was the recipient pregnant at any time in this reporting period? (Female Only)

Indicate whether the recipient was pregnant at any time during the reporting period. Skip this question for male recipients.

If **Yes**, complete the Pregnancy (3501) form also. The **Previously reported** option should only be used if the same pregnancy instance has already been reported on a Pregnancy (3501) form that was created as an unscheduled form (on-demand). See examples above.

Contact CIBMTR Center Support with questions.

Question 191: Was the recipient's female partner pregnant at any time in this reporting period? (Male only)

Indicate whether the recipient's female partner was pregnant at any time during the reporting period. Skip this question for female recipients.

If **Yes**, complete the Pregnancy (3501) form also. The **Previously reported** option should only be used if the same pregnancy instance has already been reported on a Pregnancy (3501) form that was created as an unscheduled form (on-demand). See examples above.

Contact CIBMTR Center Support with questions.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
190 – 191	10/25/ 2024	Add	Added red warning box: **Pregnancy Questions** Pregnancy questions will only be answered for recipients between the ages of 10 and 60.	Added applicable age range

Last modified: Oct 27, 2024