

# 2100: Post-Infusion Follow-Up

A transplant center designated as a *Comprehensive Report Form* center will submit data on the Pre-TED and Pre-TED Disease Classification Forms, followed by either the Post-TED Form or the Comprehensive Report Forms. The type of follow-up forms required for a specific recipient is determined by the CIBMTR's form selection algorithm (see Section 1 in the [Center Reference Guide](#)).


The Post-Infusion Form (2100) must be completed at the following time points: 100 days, 6 months, annually for 6 years post-HCT, and biennially thereafter. This form should be completed as closely to these time points as possible. The following recipient data should be collected from an actual examination (or other recipient contact) by the transplant center physician or the local physician who is following the recipient post-HCT: vital status, hematopoietic reconstitution post-HCT, neutrophil recovery, platelet recovery, current hematologic findings, immune reconstitution, chimerism studies, engraftment syndrome, acute Graft-versus-Host Disease (GVHD), chronic GVHD, infections, organ function, new malignancy, functional status, and subsequent HCT.

## Subsequent HCT:

If a recipient receives a subsequent HCT between time points (100 day, 6 months, annually), the CRF form sequence will start over again with another Pre-TED.

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

Contact [CIBMTR Center Support](#) if the subsequent Pre-TED does not come due automatically.

 If the recipient received a subsequent transplant (excluding an autologous rescue), the answers to all questions should reflect the clinical status of the recipient the day prior to the start of the preparative regimen or, if no preparative regimen was given, the answers to all questions should reflect the clinical status of the recipient the **day prior to HCT infusion**.

## Lost to Follow Up:

Occasionally, centers may lose contact with recipients for a variety of reasons, including the recipient moving, changing physicians, or death. If contact with a recipient appears lost, please consider calling the recipient at home or work, sending a letter, communicating with the treating or referring physician, or contacting the hospital billing department. If no documentation exists and several unsuccessful attempts have been made to contact the recipient, they are considered lost to follow-up and the form may be marked as such using the [Lost to Follow-Up Tool](#) in FormsNet3 for each reporting period in which no contact exists.

[Links to Sections of Form:](#)

[Q1 – 8: Vital Status](#)

[Q9 – 15: Granulopoiesis / Neutrophil Recovery](#)

[Q16 – 19: Megakaryopoiesis / Platelet Recovery](#)

[Q20 – 28: Growth Factor and Cytokine Therapy](#)

[Q29 – 38: Current Hematologic Findings](#)

[Q39 – 54: Immune Reconstitution](#)

[Q55 – 72: Chimerism Studies](#)

[Q73 – 83: Engraftment Syndrome](#)

[Q84 – 133: Acute Graft vs. Host Disease](#)

[Q134 – 203: Chronic Graft vs. Host Disease](#)

[Q204 – 210: Current GVHD Status](#)

[Q211 – 226: Infection Prophylaxis](#)

[Q227 – 248: Infection](#)

[Q249 – 310: Organ Function](#)

[Q311: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder](#)

[Q312 – 335: Functional Status](#)

[Q336 – 339: Subsequent HCT](#)

#### Manual Updates:

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

If you need to reference the historical Manual Change History for this form, please review the table below or reference the retired manual section on the [Retired Forms Manuals](#) webpage.

Date	Manual Section	Add/Remove/Modify	Description
9/15/2023	<a href="#">2100: Acute Graft vs. Host Disease</a>	Modify	Instructions updated to clarify reporting the date of maximum grade of acute GVHD when there is organ staging variation: <i>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, regardless of any variation in the organ staging. For further clarification, review acute GVHD grading scenario D above. If <b>Not applicable</b> was reported for Maximum overall grade of acute GVHD, this question must be left blank. If the same maximum overall grade was achieved, but the specific organ staging varied, report the date of the maximum organ staging consistent with the overall grade reported in Maximum overall grade of acute GVHD. For example, a recipient developed stage 2 liver GVHD that later progressed to stage 3 liver GVHD within the reporting period. The date the recipient had stage 3 liver GVHD should be reported as the date of maximum grade, even though stage 2 and stage 3 liver GVHD are both captured as grade 3.</i>
9/15/2023	<a href="#">2100: Acute</a>	Add	Acute GVHD Grading Scenario <b>D</b> added to reflect updated instructions of reporting the date of maximum grade when there is organ staging variation: <b>D. A</b>

	<a href="#">Graft vs. Host Disease</a>		<i>recipient developed stage 1 skin involvement and stage 1 liver involvement (overall grade II) 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 3, along with GI stage 1 (overall grade II). In this case, grade II would be reported as the Maximum overall grade of acute GVHD with the maximum date reported as 1/1/2019 the first date of maximum overall grade of acute GVHD. Additionally, when reporting the organ staging at the time of maximum overall grade, skin stage 1 and liver stage 1 should be reported. Skin stage 3 and GI stage 1 will not be captured.</i>
8/25/2023	<a href="#">2100: Post-Infusion Follow-Up</a>	Modify	Diagnosis of COVID-19 after the start of the preparative regimen Any COVID-19 infections diagnosed after the start of the preparative regimen should be reported in the following questions on the Post-HCT Follow-Up (2100) form. <del>An associated Respiratory Virus Post-Infusion Data (2149) form will be generated.</del> <b>Effective August 25, 2023, the Respiratory Virus Post-Infusion Data (2149) form for transplants on the CRF track will no longer be required. Additionally, an unscheduled Respiratory Virus Post-Infusion Data (2149) form cannot be created for these recipients.</b>
7/19/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Blue PTLD info box added to Q311: <b>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.</b>
7/19/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Modify	Clarified in Q311 which option to select for PTLD: <i>Indicate whether a new or secondary malignancy, lymphoproliferative disorder, or myeloproliferative disorder has developed. Do not report recurrence, progression, or transformation of the recipient's primary disease (disease for which the transplant was performed), or relapse of a prior malignancy.</i> <i>New malignancies, lymphoproliferative disorders, or myeloproliferative disorders include but are not limited to:</i> <ul style="list-style-type: none"> <li>• Skin cancers (basal, squamous, melanoma)</li> <li>• New leukemia</li> <li>• New myelodysplasia</li> <li>• Solid tumors</li> <li>• PTLD (post-transplant lymphoproliferative disorder) (report as <del>lymphoma or lymphoproliferative disease</del> <b>NHL</b> )</li> </ul>
5/3/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Not applicable / previously reported blue box added to Q9: <b>Not applicable and Previously reported options: When Not applicable is reported for 100-day reporting period, for all future reporting periods, select Previously reported.</b>
5/3/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Not applicable / previously reported blue box added to Q16: <b>Not applicable and Previously reported options: When Not applicable is reported for 100-day reporting period, for all future reporting periods, select Previously reported.</b>

	<a href="#">Form</a>		
5/1/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Instructions for Q333 clarified: <i>Select the work status that best describes the recipient's current or most recent employment during this reporting period. If the recipient is <b>Retired</b>, specify their retirement status. If the recipient's status is anything other than <b>Full time</b>, indicate if the recipient claimed medical disability due to any illness.</i>
5/1/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Instructions for Q328 updated on what to not consider when reporting smoked tobacco cigarettes: <i>The intent of this question is to determine the recipient's history of smoking cigarettes only. Do not report the use of cigars, pipe tobacco, chewing tobacco, <b>electronic cigarettes, vaping</b> or other drugs. Report <b>Yes</b> if the recipient has smoked tobacco cigarettes since the date of the last report and capture the average number of packs (20 cigarettes per pack) smoked a day, if known. If the recipient has not smoked tobacco cigarettes since the date of the last report, or their smoking history is not known, report <b>No</b> or <b>Unknown</b>.</i>
2/16/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Examples of immunosuppression added to Q208
2/16/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Modify	Examples updated for Q1: <b>Example 8.</b> <i>The recipient had a subsequent non-genetically modified cellular therapy. The recipient has their first transplant on 1/21/15 and a non-genetically modified (e.g., DLI) (excludes DLI) cellular therapy infusion on 2/15/15. There was no lymphodepleting therapy administered.</i> <b>Example 9.</b> <i>The recipient had a subsequent Donor Lymphocyte Infusion (DLI). The recipient has their first transplant on 1/21/2215 and receives a DLI on 2/27/2022. There was no lymphodepleting therapy administered prior to the DLI. What to report: <u>100 Day Date of Contact:</u> The date of contact reported will be appropriate to the reporting period. Do not complete the follow up form early. Combined follow up will not be applied, a single F2199 is required for each DLI in the reporting period, then HCT reporting continues.</i>
2/15/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Clarification added on how to report the mucositis grade: <b>Mucositis requiring therapy:</b> <i>inflammation and ulceration of mucous membranes that line the digestive tract, usually due to chemotherapy and radiotherapy. Specify the grade as <b>0 (none), I (mild) – oral soreness, erythema, II (moderate) – oral erythema, ulcers, solid diet tolerated, III (severe) – oral ulcers, liquid diet only, or IV (life-threatening – oral ulcers, oral alimentation impossible in question 304. The highest grade in the reporting period should be reported. Do not report mucositis which did not require treatment or intervention during the reporting period.</b></i>
2/15/2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	The 'No Documentation of Contact Date' red warning box added above Q1: <b>No Documentation of Contact Date</b> <i>The contact date data field cannot be left blank and is required to be reported. In cases where the recipient passed away</i>

	<a href="#">Form</a>		<i>and there is no documentation to report the date of death, the guidelines for reporting estimated dates must be used.</i>
1/27/ 2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Red warning box regarding reporting persistent GVHD for the Day 100 reporting added for Q136: <b>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.</b>
1/27/ 2023	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Add	Red warning box regarding reporting persistent GVHD for the Day 100 reporting added for Q96: <b>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.</b>
9/23/ 2022	<a href="#">2100:Post-Infusion Follow-Up Form</a>	Modify	Version 8 of the 2100: Post-Infusion Follow-Up section of the Forms Instructions Manual released. Version 8 corresponds to revision 8 of the Form 2100

*Last modified: Sep 18, 2023*

# Q1 – 8: Vital Status

The date of actual contact with the recipient to determine medical status for this follow-up report is based on a medical evaluation conducted by a clinician with responsibility for the recipient's care. Report the date of the medical evaluation performed closest to the designated time period of the form (e.g., Day+100, 6 months, or annual follow-up visit). Time windows are provided to guide selection of dates for reporting purposes. Recipients are not always seen within the time windows used for reporting follow-up dates, and some discretion is therefore required when determining which date to report. If the recipient is not seen within the time windows, report the date closest to the date of contact within reason.

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



## Reporting the 1-Year Date of Contact

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

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

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

Time Point	Approximate Range
100 days	+/- 15 days (Day 85-115)
6 months	+/- 30 days (Day 150-210)
1 year	+ 60 days (Day 365 – 425)
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 available.

**Example 1.** *The 100-day date of contact doesn't fall within the ideal approximate range.*

The autologous recipient was transplanted on 1/1/13 and is seen regularly until 3/1/13. After that, the recipient was referred home and not seen again until 7/1/13 for a restaging exam and 7/5/13 for a meeting to discuss the results.

What to report:

100 Day Date of Contact: 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)

6 Month Date of Contact: 7/5/13 (note the latest disease assessment would likely be reported as 7/1/13)

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

The autologous recipient was transplanted on 1/1/12 and is seen regularly until 3/1/12. After that, the recipient was referred home and not seen again until 1/1/13 for a restaging exam and 1/4/13 for a meeting to discuss the results.

What to report:

100 Day Date of Contact: 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)

6 Month Form: Indicate the recipient is lost to follow-up in FormsNet3

1 Year Date of Contact: 1/4/13 (note the latest disease assessment would likely be reported as 1/1/13)

#### Additional Information

- A date of contact should never be used multiple times for the same recipient's forms.
  - For example, 6/1/13 should not be reported for both the 6 month and 1-year form. Instead, determine the best possible date of contact for each reporting period; if there is not a suitable date of contact for a reporting period, this may indicate that the recipient was lost to follow-up.
- If the recipient has a disease evaluation just after the ideal date of contact, capturing that data on the form may be beneficial.
  - For example, if the recipient's 90 day restaging exam was delayed until day 115 and the physician had contact with the recipient on day 117, the restaging exams can be reported as the latest disease assessment and day 117 would be the ideal date of contact, even though it is just slightly after the ideal approximate range for the date of contact.

#### Date of Contact & Death

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

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

**Example 3.** *The recipient has died before their six-month anniversary.*

The recipient is transplanted on 1/1/20, was seen regularly through the first 100 days. They had restaging exams on 4/4/20 and was seen on 4/8/20, and then died on 5/13/20 in the hospital emergency room.

What to report:

100 Day Date of Contact: 4/8/20 (note the latest disease assessment would likely be reported as 4/4/20)

6 Month Date of Contact: 5/13/20 (though the death does not occur within the ideal approximate range for 6 months)

**Example 4.** *The recipient has died after their six-month anniversary.*

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

What to report:

100 Day Date of Contact: 4/23/13 (note the latest disease assessment would likely be reported as 4/22/13)



6 Month Date of Contact: 7/16/13 (note the latest disease assessment would likely be reported as 6/25/13)

### **Date of Contact & Subsequent Infusion**

If the recipient has a subsequent infusion (HCT or cellular therapy), 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 (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 transplant events.

**Example 5.** *The recipient had a 2nd transplant with a preparative regimen.*

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

What to report:

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

**Example 6.** *The recipient had a subsequent transplant without a preparative regimen.*

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

What to report:

100 Day Date of Contact: 4/11/13 (+/- 15 days)

6 Month Date of Contact: 5/30/13

**Example 7.** *The recipient had a subsequent genetically modified cellular therapy with lymphodepleting therapy administered prior to infusion.*

The recipient has their first transplant on 2/1/15 and a genetically modified (e.g. CAR-T) cellular therapy infusion on 3/1/15. The recipient was admitted on and received their first dose of lymphodepleting therapy 2/28/15.

What to report:

100 Day Date of Contact: 2/27/15 (regardless of actual contact on that date). Both HCT and cellular therapy forms will be completed but all applicable HCT follow-up forms will be reset to the new event date (i.e., Forms 4100+2100). See [How Forms Come Due](#) in the Data Management Manual for more information on combined follow up.

**Example 8.** *The recipient had a subsequent non-genetically modified cellular therapy.*

The recipient has their first transplant on 1/21/15 and a non-genetically modified (e.g. DLI) 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.

**Example 9.** *The recipient had a subsequent Donor Lymphocyte Infusion (DLI).*

The recipient has their first transplant on 1/21/2022 and receives a DLI on 2/27/2022. There was no lymphodepleting therapy administered prior to the DLI.

What to report:

100 Day Date of Contact: The date of contact reported will be appropriate to the reporting period. Do not complete the follow up form early. Combined follow up will not be applied, a single F2199 is required for each DLI in the reporting period, then HCT reporting continues.

### **1-Year Date of Contact**

When reporting the date of contact for the 1-year reporting period, if the recipient is alive, report a contact date on or after Day 365. The date of contact should not be reported prior to Day 365 for the 1-year reporting period. This ensures the recipient is included in the numerator for the transplant center's Center Specific Analysis (CSA).

**Example 10.** *A recipient is evaluated before and after Day 365 but not on Day 365.*

The recipient had an allogeneic transplant on 1/5/13 and is seen regularly until 6/20/13. After that, the recipient was referred home and not seen again until 1/1/14 for a restaging exam and again on 1/15/14 to review the results. Day 365 is 1/5/14.

What to report:

1-Year Date of Contact: 1/15/14 (since this date is  $\geq$  Day 365)

**Example 11.** *A recipient is evaluated before and after Day 365 but not on Day 365.*

The recipient is transplanted on 2/28/19 and seen regularly until 8/28/19. The next visit is on 2/20/20 for blood work and the lab results are phoned to the recipient on 2/21/20. The recipient was not evaluated again until 4/1/20. Day 365 is 2/28/20.

What to report:

1-Year Date of Contact: 4/1/20

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### **Question 2: Specify the recipient's survival status at the date of last contact.**

Indicate the survival 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.

### **Question 3: Did the recipient receive a subsequent HCT?**

Indicate whether the recipient received a second (or third, etc.) hematopoietic stem cell infusion. Hematopoietic stem cells are defined as mobilized peripheral blood stem cells, bone marrow, or cord blood.

The source of the hematopoietic stem cells may be allogeneic unrelated, allogeneic related, or autologous. For more information on how to distinguish infusion types (example: HCT versus DCI), see [Appendix D](#).

If the recipient has received a subsequent HCT since the date of the last report, ensure the date of actual contact reported in question 1 is the date immediately prior to the start of the preparative regimen for the subsequent HCT. If no preparative regimen was given, report the date prior to infusion.

#### Questions 4: Has the recipient received a cellular therapy? (e.g., CAR-T, DCI)

##### Therapy Over Multiple Reporting Periods

If course of cellular therapy carries over an **HCT** reporting period, and has already been reported on a prior form, do not re-report that course of cellular therapy. For example, if a course of cellular therapy includes three infusions, and the third infusion overlaps from the one year to two year **HCT** reporting period, do not report a cellular therapy since the date of the last report on the two year **HCT** follow up form

Indicate whether the recipient received a cellular therapy for any reason within the reporting period. The most common type of post-HCT cellular therapy are donor cellular infusions (DCI) and donor lymphocyte infusions (DLI). These infusions are not intended to promote hematopoiesis. If the recipient received additional cells due to engraftment issues, or if they received an infusion of unmanipulated CD34+ cellular product (stimulated peripheral blood stem cells, bone marrow, or cord blood), report as a subsequent HCT rather than a cellular therapy. For more information on how to distinguish infusion types (example: HCT versus DCI), see [Appendix D](#).

A DCI is a form of cellular therapy that uses cells from the original donor and is commonly used to create a graft-versus-leukemia / tumor (GVL / GVT) effect. The recipient does not receive a preparative regimen prior to receiving the donor cells because the purpose of a DCI is to activate the immune system rather than repopulate the marrow. The recipient may, however, be given therapy prior to the infusion for the purpose of disease control. The types of cells used in a DCI include, but are not limited to lymphocytes, unstimulated peripheral blood mononuclear cells, dendritic cells, and / or mesenchymal cells.

Other forms of cellular therapy may include cytotoxic T-lymphocytes (CTL) to treat infections or chimeric antigen receptor T-cells (CAR T-cells) to treat persistent, progressive, or recurrent disease.

##### Reporting Multiple Cellular Therapy Infusions

**FormsNet3<sup>SM</sup>**: Complete the DLI, genetically modified, and date of cellular therapy questions for each cellular therapy infusion administered in this reporting period by adding additional instance(s) in FormsNet3SM.

**Paper form submission**: Copy the DLI, genetically modified, and date of cellular therapy questions and complete for each cellular therapy infusion administered in this reporting period.

**Question 5: Was this infusion a donor lymphocyte infusion (DLI)?**

As previously mentioned, 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-HCT, often by the same donor as the HCT
- Indication is suboptimal donor chimerism, immune reconstitution, GVHD treatment, prevent or treat disease relapse (as reported on the Pre-TED (2400) Form)
- Composition of cells are un-manipulated lymphocytes

If the infusion meets the above definition of DLI, select **Yes**.

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

**Question 6: 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) Form(s) come due.

**Question 7: Are any of the products, associated with the 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.

If more than one product is infused, indicate **Yes** if any of the products are genetically modified. This question is used to determine the follow up schedule of the cellular therapy.

**Question 8: Date of cellular therapy**

Report the date of cellular therapy infusion. If multiple infusions were received in the reporting period, report the earliest. If infusions are continuing from a previous instance of a course of cellular therapy, only report in the period during which the first infusion was received. This question is used to make the Pre-CTED (4000) form come due and is not answered for DLIs.

**Section Updates:**

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q1	2/16/2023	Modify	<p>Examples updated: <b>Example 8.</b> <i>The recipient had a subsequent non-genetically modified cellular therapy. The recipient has their first transplant on 1/21/15 and a non-genetically modified (e.g. <del>DLI</del>) (excludes DLI) cellular therapy infusion on 2/15/15. There was no lymphodepleting therapy administered.</i> <b>Example 9.</b> <i>The recipient had a subsequent Donor Lymphocyte Infusion (DLI). The recipient has their first transplant on 1/21/2215 and receives a DLI on 2/27/2022. There was no lymphodepleting therapy administered prior to the DLI. What to report: <u>100 Day Date of Contact</u>: The date of contact reported will be appropriate to the reporting period. Do not complete the follow up form early. Combined follow up will not be applied, a single F2199 is required for each DLI in the reporting period, then HCT reporting continues.</i></p>	Updated to reflect release of DLI (2199) Form
Q1	2/15/2023	Add	<p>The 'No Documentation of Contact Date' red warning box added: <b>No Documentation of Contact Date</b> <i>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.</i></p>	Added for clarification

Last modified: Sep 14, 2023

# Q9 – 15: Granulopoiesis / Neutrophil Recovery

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

## \* Combined Follow-Up

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

Absolute neutrophil recovery (ANC) recovery is defined as an ANC of  $\geq 500/\text{mm}^3$  (or  $\geq 0.5 \times 10^9/\text{L}$ ) for three consecutive laboratory values obtained on different days.\* Date of ANC recovery is the date of the first of three consecutive laboratory values where the ANC is  $\geq 500/\text{mm}^3$ . At some institutions, the laboratory reports display the ANC value once there are sufficient white blood cells to perform a differential count. At other institutions, the laboratory reports do not display the ANC, and it must be calculated from the white blood cell count (WBC) and the percent of segmented and band neutrophils (if the differential was performed on a machine, the percent neutrophils will include both segmented and band neutrophils). If the laboratory report displays an automated ANC value of exactly  $500/\text{mm}^3$ , the actual ANC value should be calculated from the manual differential if available. The calculated value from the manual differential will determine ANC recovery. If your institution's laboratory reports do not display the ANC value, use the following calculation to determine the ANC:

### Example 1. Calculating Absolute Neutrophil Count (ANC)

	% segmented neutrophils	
+	% band neutrophils	
=	% neutrophils	
x	white blood cell count/ $\text{mm}^3$	
=	absolute neutrophil count/ $\text{mm}^3$	
<b>Example:</b>		
(Divide percentage by 100 to convert to decimal)		
	0.45 segmented neutrophils	
+	0.05 band neutrophils	
=	0.50 neutrophils	
x	1000/ $\text{mm}^3$ white blood cell count	
=	500/ $\text{mm}^3$ absolute neutrophil count	
ANC $500/\text{mm}^3 = 0.5 \times 10^9/\text{L} = 0.5 \times 10^6/\text{mL} = 0.5 \times 10^3/\text{mm}^3$		

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

Tracking the date of ANC recovery may not always be straightforward. In some cases, the ANC may fluctuate for a period of time before the recipient fully recovers. In other cases, the ANC may remain above  $\geq 500/mm^3$  for several days immediately post-HCT and then fall below  $\geq 500/mm^3$ . Do not begin counting ANC values of  $\geq 500/mm^3$  towards recovery until the ANC has dropped to the lowest level (nadir) post-HCT. If the recipient was transplanted using a non-myeloablative (NST) or reduced intensity (RIC) regimen, or was transplanted for an immunodeficiency (e.g., SCID, WAS), the recipient's ANC may never drop below  $\geq 500/mm^3$ . If this is the case, an ANC recovery date will not be reported, and the "not applicable" option should be chosen. However, if the recipient's ANC drops below  $\geq 500/mm^3$  for even one day, this should be considered the nadir and "not applicable" should not be chosen. See the following example for more information regarding tracking the date of ANC recovery.

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

### Example 2: Tracking ANC Recovery

*Transplant Date = May 6*

*Contact Date = August 15*

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	<i>Date of initial recovery: ANC <math>\geq 500/mm^3</math> (report this date in question 7)</i>
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 $\geq$ 500/mm <sup>3</sup> ) for timeframe
August 15 (contact date)	2250	0.43	968	

### Example 3: 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	<i>Date of initial recovery: ANC <math>\geq</math> 500/mm<sup>3</sup> (report this date in question 7)</i>
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	<i>Date of first decline: ANC <math>\leq</math> 500/mm<sup>3</sup> (report this date in question 9)</i>



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	<i>Date of recovery: ANC <math>\geq</math> 500/mm<sup>3</sup> (report this date in question 12)</i>
May 30-August 14	—	—	—	ANC $\geq$ 500/mm <sup>3</sup> for timeframe
August 15 (contact date)	2245	0.72	1616	

### Question 9: Was there evidence of initial hematopoietic recovery?

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

Check only **one** response:

- Select **Yes** if ANC  $\geq$  500/mm<sup>3</sup> (or  $\geq$   $0.5 \times 10^9$ /L) was achieved and sustained for 3 laboratory values.
- Select **No** if ANC  $\geq$  500/mm<sup>3</sup> (or  $\geq$   $0.5 \times 10^9$ /L) was not achieved.
- Select **Not applicable** if the recipient's ANC never dropped below 500/mm<sup>3</sup> (or  $\geq$   $0.5 \times 10^9$ /L) at any time after the start of the preparative regimen.
- Select **Previously reported** if the recipient's initial hematopoietic recovery was recorded on a previous report.



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

### Question 10: Date ANC $\geq$ 500/mm<sup>3</sup> (first of 3 lab values)

Enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC was  $\geq$  500/mm<sup>3</sup> (or  $\geq$   $0.5 \times 10^9$ /L). For an example of tracking ANC, see Example 2 and Example 3 above.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### Question 11: Following the initial hematopoietic recovery, was there subsequent decline in ANC to $<$ 500/mm<sup>3</sup> for $\geq$ 3 days?

Indicate **Yes** or **No** if there was subsequent decline in ANC  $<$  500/mm<sup>3</sup> (or  $<$   $0.5 \times 10^9$ /L) (three consecutive

laboratory values obtained on different days where the ANC declined to  $< 500/\text{mm}^3$ .

### \* 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) recovery, the first decline, and the last recovery.

#### Question 12: Date of decline in ANC $< 500/\text{mm}^3$ for $\geq 3$ 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  $< 500/\text{mm}^3$  (or  $< 0.5 \times 10^9/\text{L}$ ).

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

#### Question 13: Did recipient recover and maintain ANC $\geq 500/\text{mm}^3$ following the decline?

Indicate **Yes** or **No** if there was evidence of ANC recovery following the decline (three consecutive laboratory values obtained on different days where the ANC was  $\geq 500/\text{mm}^3$  (or  $\geq 0.5 \times 10^9/\text{L}$ ).

#### Question 14 – 15: 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  $\geq 500/\text{mm}^3$  (or  $\geq 0.5 \times 10^9/\text{L}$ ) following the decline. See Example 3 above.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

#### Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
Q6-12	5/18/2022	Add	Combined Follow-Up blue box added: <i>In scenarios where a cellular therapy was given after an HCT and this form is now being completed based on the subsequent cellular therapy date, these questions do not apply and are disabled.</i>	Added for clarification
Q9	5/3/2023	Add	Not applicable / previously reported blue box added: <i>When <b>Not applicable</b> is reported for 100-day reporting period, for all future reporting periods, select <b>Previously reported</b>.</i>	Added for clarification



# Q16 – 19: Megakaryopoiesis / Platelet Recovery

**!** The megakaryopoiesis / platelet recovery section can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.

## **\* Combined Follow-Up**

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

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

Report the date of the first of three-consecutive laboratory ( $\geq 20 \times 10^9/L$  and  $\geq 50 \times 10^9/L$ ) obtained on different days, as shown in Example 10 below. Note that platelet recovery may take place well after the recipient has returned to the referring physician for care. It is essential that information and laboratory values be obtained from the referring physician.

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

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

### Example 1: Reporting Platelet Recovery

	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			
<b>Report 1/8/08 as date platelet count <math>\geq 20 \times 10^9/L</math></b>											

### Example 2: Reporting Platelet Recovery ( $\geq 20 \times 10^9/L$ and $\geq 50 \times 10^9/L$ )

Date	Day	Platelet Count

June 13	0	10,000	<i>Date of last platelet transfusion</i>
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	<i>1st of 3 consecutive laboratory values <math>\geq 20 \times 10^9/L</math> (report this date in question 15)</i>
June 21	8	40,000	
June 22	9	50,000	<i>1st of 3 consecutive laboratory values <math>\geq 50 \times 10^9/L</math> (report this date in question 18)</i>
June 23	10	56,000	
June 24	11	65,000	
June 25	12	72,000	

This section relates to initial platelet recovery. All dates should reflect no transfusions in the previous 7 days. To report dates in this section, use the first of 3 consecutive laboratory values obtained on different days.

**Question 16: Was an initial platelet count  $\geq 20 \times 10^9/L$  achieved?**

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


Check only **one** response:

- If **Yes** if platelet count  $\geq 20 \times 10^9 / L$  was achieved and sustained for 3 consecutive laboratory values, obtained on different days without platelet transfusions administered in the previous 7 days
- If **No** if platelet count was not  $\geq 20 \times 10^9 / L$  or if platelet transfusions were administered in the previous 7 days.
- Check **Not applicable**, if the recipient's platelets never dropped below  $20 \times 10^9/L$  at any time post-HCT and a platelet transfusion was never required. If the recipient's platelet count drops below  $20 \times 10^9/L$  and/or the recipient received a platelet transfusion even once, do not use this option. This option is only applicable in the 100-day reporting period.
- Check **Previously reported**, if this is the 6 month or annual follow-up, and initial platelet recovery has already been reported on a previous form.

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

### Question 17: Date platelets $\geq 20 \times 10^9/L$

Enter the **first** date of three consecutive laboratory values obtained on different days where the platelet count was  $\geq 20 \times 10^9/L$ . Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in Example 1 above, when determining the recovery date.

 **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  $\geq 20 \times 10^9/L$  is demonstrated, follow the examples below when determining an estimated date.

#### Reporting Scenarios:

**A.** The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is  $22 \times 10^9/L$  on January 2,  $24 \times 10^9/L$  on January 3, and  $28 \times 10^9/L$  on January 4. The recipient does not come into the clinic for evaluation until one month later. The recipient has not received any more platelet transfusions and the platelet count is well above  $20 \times 10^9/L$ . Report January 8 (day seven post-platelet transfusion) for the date of platelet recovery.

**B.** The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is  $\geq 20 \times 10^9/L$  on January 2, January 3, and January 4. The recipient is then discharged back to their primary care physician. The transplant center receives a follow-up note from the

primary care physician that states “recipient recovered their platelets in January of 2011.” Report an estimated date of recovery using the guidelines available in [General Instructions, General Guidelines for Completing Forms](#).

### Question 18: Was an initial platelet count $\geq 50 \times 10^9/L$ achieved?

Indicate whether a platelet count of  $\geq 50 \times 10^9/L$  was achieved following this HCT.

Check only **one** response:

- If **Yes** if platelet count  $\geq 50 \times 10^9 / L$  was achieved and sustained for 3 consecutive laboratory values, obtained on different days without platelet transfusions administered in the previous 7 days
- If **\*No** if platelet count was not  $\geq 50 \times 10^9 / L$  or if platelet transfusions were administered in the previous 7 days.
- Check **Not applicable** if the recipient’s platelets never dropped below  $50 \times 10^9/L$  at any time post-HCT and a platelet transfusion was never required. If the recipient’s platelet count drops below  $50 \times 10^9/L$  and / or the recipient received a platelet transfusion even once, do not use this option. This option is only applicable in the 100-day reporting period.
- Check **Previously reported**, if a platelet count of  $\geq 50 \times 10^9/L$  was achieved and reported previously.

### Question 19: Date platelets $\geq 50 \times 10^9/L$

Enter the **first** date of three consecutive laboratory values obtained on different days where the platelet count was  $\geq 50 \times 10^9/L$ . Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in Example 2 above, when determining the recovery date.

If three laboratory values were not obtained on consecutive days, but a sequential rise of  $\geq 50 \times 10^9/L$  is demonstrated, follow the examples included in the instructions for question 15 above.

### Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q13 – 16	5/18/2022	Add	Combined Follow-Up blue instruction box added: <i>In scenarios where a cellular therapy was given after an HCT and this form is now being completed based on the subsequent cellular therapy date, these questions do not apply and are disabled.</i>	Added for clarification
Q16	5/3/2023	Add	Not applicable / previously reported blue box added: <b>Not applicable and Previously reported options: When Not applicable is reported for 100-day reporting period, for all future</b>	Added for clarification

			<i>reporting periods, select <b>Previously reported</b>.</i>	
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*Last modified: May 03, 2023*



# Q20 – 28: Growth Factor and Cytokine Therapy

! The Growth Factor and Cytokine Therapy section can only be completed on the 100-day follow-up form. These questions will not be answered for all subsequent reporting periods.

## \* Reporting Multiple Growth Factor and Cytokine Therapy

**FormsNet3<sup>SM</sup>:** Complete *Specify hematopoietic, lymphoid growth factor or cytokine received* questions for each hematopoietic, lymphoid growth factor, and / or cytokine administered in this reporting period by adding additional instance(s) in FormsNet3SM.

**Paper form submission:** Copy *Specify hematopoietic, lymphoid growth factor or cytokine received* questions for each hematopoietic, lymphoid growth factor, and / or cytokine administered in this reporting period

### Questions 20 – 28: Specify hematopoietic, lymphoid growth factor or cytokine received

A growth factor is a substance that stimulates cell growth, differentiation, and proliferation. Cytokines can act as growth factors or have an inhibitory effect on cell growth.

Select all agents given during the reporting period. For each agent administered during the reporting period, report the start date and the reason it was given.

**G-CSF (granulocyte-colony stimulating factor):** Alternate names: filgrastim, pegfilgrastim, Neupogen, Neulasta, Lenograstim.

**GM-CSF (granulocyte / macrophage-colony stimulating factor):** Alternate names: sargramostim, Leukine.

**Erythropoietin (EPO):** Alternate names: Epogen, Procrit, darbepoietin alfa (Aranesp). EPO stimulates red blood cell production. If EPO is given, specify the drug given in question 23.

**Thrombopoietin:** Alternate names: megakaryocyte growth and development factor. A glycoprotein hormone which regulates the production of hormones.

**KGF (keratinocyte growth factor):** Alternate names: palifermin, Kepivance. KGF acts to stimulate the growth of cells that line the surface of the mouth and intestinal tract. KGF may also be given to treat oral mucositis or as GVHD prophylaxis. Report if administered to stimulate cell growth or to treat oral mucositis. If KGF is administered as GVHD prophylaxis, report in the Acute Graft vs. Host Disease section of this form.

**Blinded growth factor or cytokine trial:** If the recipient is on a blinded randomized trial, specify the trial

agent administered. Additionally, update this form (2100) once the trial is over to specify whether the recipient received the trial drug or placebo.

**Other agent:** Specify any other hematopoietic growth factor, lymphoid growth factor, or cytokine administered.

**Section Updates:**

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

*Last modified: Sep 23, 2022*

## Q29 – 38: Current Hematologic Findings

! Current Hematologic Findings sections can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.

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

### Questions 29 – 38: Provide the most recent laboratory values recorded

These questions are intended to determine the hematological status of the recipient after the infusion. Testing may be performed multiple times within the reporting period; however, report only the most recent (closest to the contact date) laboratory values.

Report the date of the most recent complete blood count and select all hematologic results available. Report the associated laboratory value and unit (if applicable).

For hematocrit, check the box if red blood cells were transfused within 30 days prior to the testing.

For platelets, check the box if platelets were transfused within seven days prior to the testing.

### **Section Updates:**

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

*Last modified: Sep 23, 2022*

## Q39 – 54: Immune Reconstitution

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

These questions are intended to determine whether the recipient recovered their immune function post-HCT. Along with hematopoietic recovery, the infused allogeneic hematopoietic progenitor cells (HPCs) also generate a new immune system. This process may be slowed by immunosuppressants given to prevent GVHD.

### Question 39: Select all known immunoglobulin values (check all that apply)

Antibodies are produced by the immune system in response to foreign substances such as bacteria, viruses, or fungi. There are several types of immunoglobulins; the CIBMTR requests information on IgG, IgM, and IgA.

- **IgG** antibodies are present in all body fluids. They play a key role in fighting bacterial and viral infections.
- **IgA** antibodies are present in the nose, airway, digestive tract, ears, eyes, saliva, tears, and blood. They protect surfaces of the body that are exposed to outside foreign substances.
- **IgM** antibodies are present in blood and lymph fluid. They are the first type of antibody produced by the immune system in response to an infection.

If immunoglobulin testing was performed, select all immunoglobulins (antibodies) tested during the reporting period and answer the subsequent questions as follows. If immunoglobulin testing was not completed during the reporting period, select **No immunoglobulin testing performed**.

### Questions 40 – 44: Specify the immunoglobulin values

Report the sample collection date for the immunoglobulin testing and indicate **Yes** or **No** if the sample collection date was used for all immunoglobulin testing.

If immunoglobulin values were assessed on different dates, report the date of the most recent *IgG* test. If the exact collection date is not known, use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](#) and select **Date estimated**.

In addition, for each immunoglobulin tested, report the value and specify the units of measurement.

**\* IVIG Given without Immunoglobulin Testing**  
In some cases, IVIG may be given for low immune function without immunoglobulin testing. The transplant center should verify that IgG levels were not tested at another facility, as it is

unusual for IVIG to be given without knowing what the IgG level is. In these cases, **No immunoglobulin testing performed** should be selected for\_ Select all known immunoglobulin values and Were supplemental intravenous immunoglobulins (IVIG) received\_ should be answered **Yes**, even though testing was not done

#### Questions 45 – 46: Were supplemental intravenous immunoglobulins (IVIG) received?

Intravenous immunoglobulin (IVIG) is a substance made from antibodies derived from the blood of a donor. It is administered intravenously to treat autoimmune disorders, infections, or other conditions and can be given to prevent infections in recipients who have received a HCT or organ transplant.

Indicate **Yes** or **No** if the recipient received IVIG within the current reporting period (regardless if immunoglobulin testing was performed in the reporting period). If **Yes**, report the most recent date when IVIG was received. If the exact administration date is not known, use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](#).

If the recipient did not receive IVIG in the reporting period or it is unknown if administered, select **No**.

#### Question 47: Select all known lymphocyte values from the most recent testing (check all that apply)

Lymphocyte analyses are often performed post-HCT to evaluate the reconstitution of the immune system. Certain lymphocyte groups repopulate earlier than others post-HCT.

If lymphocyte testing was performed, select all lymphocytes tested during the reporting period and answer the subsequent questions as follows.

- **CD3 (T cells)**
- **CD4 (T helper cells)**
- **CD8 (cytotoxic T cells)**
- **CD19 (B lymphocyte cells)**
- **CD20 (B lymphocyte cells)**
- **CD56 (natural killer (NK) cells)**

If lymphocyte testing was not completed during the reporting period, select **No lymphocyte analyses performed**.

#### **CD19 and CD20 (B lymphocyte cells)**

If both CD19 and CD20 lymphocyte values are tested, it is not necessary to report both values. Only one of the two B lymphocyte cell values is required for reporting.

#### **Lymphocyte Analyses Units of Measurement**

The following units of measurement are equivalent to each other:

$$10^9/L = 10^3/mm^3$$

$$10^6/L = 1/mm^3 = 1/\mu L \text{ cells} / \mu L$$

### Questions 48 – 54: Specify the lymphocyte analyses

Report the sample collection date for the lymphocyte analysis. If multiple lymphocyte analyses were complete in the reporting period, report the date of the most recent analysis.

If the exact collection date is not known, use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](#).

For each lymphocyte tested, report the value, and specify the units of measurement.

If only the percentages of the lymphocyte subsets are available, it is necessary to calculate the absolute value of each lymphocyte subset for reporting purposes. This can be done by multiplying the percentage of each subset by the absolute lymphocyte count. See the example below:

#### Example 1: Calculating lymphocyte counts

*Absolute Lymphocyte Count:  $4.8 \times 10^9/L$*

Phenotype	Lab Report Percentage	Calculation (Percentage x ALC)	Absolute Value
CD3	74%	$(0.74) \times 4.8$	<b>CD3:</b> $3.55 \times 10^9/L$
CD3CD4	40%	$(0.40) \times 4.8$	<b>CD4:</b> $1.92 \times 10^9/L$
CD3CD8	34%	$(0.34) \times 4.8$	<b>CD8:</b> $1.63 \times 10^9/L$
CD19	NT	—	<b>CD19:</b> Unknown
CD20	NT	—	<b>CD20:</b> Unknown
CD56	NT	—	<b>CD56:</b> Unknown

#### Section Updates:

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

*Last modified: Sep 23, 2022*

## Q55 – 72: Chimerism Studies

### \* Autologous Transplants

If this was an autologous HCT, continue with the Engraftment Syndrome section starting with question 108. Chimerism testing and graft-versus-host disease sections should only be completed for allogeneic HCTs.

### \* Syngeneic Transplants

If this was a syngeneic HCT, continue with the Engraftment Syndrome section. Chimerism testing is not collected for syngeneic HCTs.



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

Chimerism studies are performed to determine the percent of blood or marrow cells post-transplant that are produced from donor hematopoietic stem cells and the percent that are produced from host (recipient) hematopoietic stem cells. Different types of blood cells and a variety of laboratory tests can be used to determine if a chimera (presence of both donor- and host-derived cells) exists. If cytogenetic testing was performed to look for disease markers, and the donor and recipient are different sexes, the test may also be used to determine if a chimera exists. If the donor and recipient are of the same sex, cytogenetic testing using the common staining technique, known as giemsa banding (G-banding), cannot be used to determine if there is a chimera. However, quinicrine banding (Q-banding) can be used to identify if the cells are of donor origin or not in a same-sex transplant, as this staining technique highlights inherited chromosome polymorphisms on certain human chromosomes including 3, 4, 13, 15, 21, 22, and Y. This is not a commonly used staining technique and is only helpful when the polymorphism is documented pre-HCT.

### \* Chimerism Studies

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

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

### Questions 55 – 56: Were chimerism studies performed post-HCT? (Allogeneic infusions only)

Indicate whether chimerism studies were performed within the reporting period. Select **Yes** if chimerism studies were performed and indicate whether documentation was submitted to CIBMTR (e.g., chimerism laboratory reports).

If chimerism studies were not performed within the reporting period, select **No**.

### Question 57: Were chimerism studies assessed for more than one donor / multiple donors?

Indicate whether this HCT included product(s) from multiple donors. When a multi-donor chimerism exists and includes a donor or donors from a previous HCT, report as a multi-donor chimerism even though there may only be one donor for the current transplant.

### Questions 58 – 72: Provide date(s), method(s) and other information for all chimerism studies performed prior to the date of contact (question 1)

#### Reporting Multiple Chimerism Studies

FormsNet3 application: Complete the chimerism study questions for each chimerism study by adding additional instance(s) in the FormsNet application.

Paper form submission: Copy the chimerism study questions and complete for each chimerism study being reported.

**When reporting chimerism studies for multiple donors, there should be one instance for each donor for each chimerism test result.**

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

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

#### Reporting GRID

If donor ID to report is a GRID, report the GRID in the non-NMDP ID data field, even if this is a NMDP donor. The GRID will be added as a separate data field during the next form revision of the Post-Infusion (2100) Follow-Up Form.

### Chimerism – Single Donor

Data Field	Description
GRID	Enter the donor's GRID – a 19-character donor identifier composed of three elements: Issue Organization Number (ION), Registration Donor Identifier, and Checksum. Review the <a href="#">Donor Information</a> section of the Pre-TED (2400) for more information.
NMDP cord blood unit ID	If the donor or one of the donors was an NMDP cord blood unit, enter the 9-digit NMDP cord blood unit ID. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation.
Registry	If the donor was a non-NMDP unrelated donor, report the non-NMPD unrelated donor ID.



donor ID	Examples include, but are not limited to Anthony Nolan, Australia Bone Marrow Donor Registry, and REDOME. This ID is often located on the product label, the paperwork accompanying the product, and registry-specific search/product documentation.
Non-NMDP cord blood unit ID	If the donor or one of the donors was a non-NMDP cord blood unit, enter the non-NMDP registry donor ID. This ID is often located on the product label, the paperwork accompanying the product, and registry-specific search/product documentation.
Date of birth or donor age	If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry, provide the date of birth, if known; if date of birth is not known, provide the donor's age at donation.
Donor sex	If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry, provide the biological sex.
Date sample collected	Enter the date the sample was collected for the chimerism test.
Method	Report the test method used for the reported chimerism study. Cytogenetic testing methods include karyotyping and fluorescent in situ hybridization (FISH). Cytogenetic methods are only valid for sex mismatched transplants with the exception of quinacrine banding. VNTR / STR is one of the most common molecular methods for assessing chimerism. See <a href="#">Chimerism Methods table</a> below for additional details on chimerism testing methods.
Cell source	Report whether the specimen taken for chimerism testing was from bone marrow or peripheral blood source.
Cell type	Indicate the cell type tested. If the specimen was not sorted for a specific cell line, indicate <b>Unsorted / whole</b> . See <a href="#">Chimerism Cell Types table</a> below for additional details on cell markers unique to certain cell lines.
Total cells examined	Cytogenetic testing methods include karyotyping and fluorescent in situ hybridization (FISH), each of which examines a specific and relatively low number of cells – generally 15 to 200, depending on specimen and test method. If a cytogenetic method was used, enter the total number of cells that were examined. If a non-cytogenetic test was used, leave these boxes blank.
Number of donor cells	Cytogenetic methods, karyotyping and FISH, examine a specific and relatively low number of cells – generally 15 to 200, depending on specimen and test method. If a cytogenetic method was used, enter the total number of cells that were examined and found to be of donor origin. If a non-cytogenetic test was used, leave these boxes blank. If this is reported, the “percent of donor cells” (next question) will not need to be answered.
Percent donor cells	Molecular testing methods include VNTR / STR, RFLP, and AFLP. Report the percentage of donor cells identified by molecular testing. If the test result did not detect any recipient cell population within the sensitivity of the assay, report 100% donor cells. If the test result did not detect any donor cell population within the sensitivity of the assay, report 0% donor cells. If the test detected recipient cells, but indicated donor cells “> x%,” report “x + 1” percent donor cells. If the test detected donor cells but indicated donor cells “< x%,” report “x – 1” percent donor cells.

## Chimerism Methods

Method	Description
Karyotyping for XX / XY	Cells are grown in culture, stained, and examined under a microscope to identify the <b>number</b> of cells matching the sex of the donor. This method is only valid when donor and recipient are sex mismatched.
Fluorescent in situ hybridization (FISH) for XX / XY	Cells are exposed to fluorescent DNA probes which attach to X and Y chromosomes. A microscope is used to identify the <b>number</b> of cells matching the sex of the donor. This method is only valid when donor and recipient are sex mismatched. <i>Do not report FISH testing for disease-specific abnormalities in the chimerism section of the Post-TED.</i>
Restricted fragment length polymorphisms (RFLP)	A restriction fragment is a portion of DNA which has been cut out by an enzyme. RFLP testing begins by isolating DNA from the sample. Enzymes are used to cut the DNA at specific loci resulting in many unique restriction fragments. The fragments are separated according to size by electrophoresis. The unique pattern of separation is used to identify the <b>percent</b> donor DNA present in the sample.
Variable number tandem repeat (VNTR), micro- or minisatellite	VNTR refers to a portion of DNA containing a repeating sequence of base pairs (micro- or minisatellite). The number of times a micro- or minisatellite repeats within specific loci can differ between individuals. These differences are used to distinguish donor DNA from recipient DNA. VNTR testing involves obtaining samples from the recipient and donor prior to transplant. Specific loci are compared to determine which loci contain VNTRs unique to the donor. After transplant, DNA is isolated from recipient samples. Donor-specific VNTRs are amplified by PCR techniques. The sample is then analyzed to determine the <b>percent</b> donor DNA present.
Small tandem repeat (STR), micro- or minisatellite	STR also refers to a portion of DNA containing a repeating sequence of base pairs (micro- or minisatellite). The number of times a micro- or minisatellite repeats within specific loci can differ between individuals. These differences are used to distinguish donor DNA from recipient DNA. STR testing involves obtaining samples from the recipient and donor prior to transplant. Specific loci are compared to determine which loci contain STRs unique to the donor. After transplant, DNA is isolated from recipient samples. Donor-specific STRs are amplified by PCR techniques. The sample is then analyzed to determine the <b>percent</b> donor DNA present.
Amplified fragment length polymorphisms (AFLP)	A restriction fragment is a portion of DNA which has been cut out by an enzyme. AFLP testing begins by isolating DNA from the sample. Enzymes are used to cut the DNA at specific loci resulting in many unique restriction fragments. Many restriction fragments are amplified using PCR techniques. The fragments are separated according to size by electrophoresis. The unique pattern of separation is used to identify the <b>percent</b> donor DNA present in the sample. <i>Report AFLP testing using the VNTR/STR method option on the 2450 form.</i>

## Chimerism Cell Types

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

**Section Updates:**

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

*Last modified: Sep 23, 2022*

## Q73 – 83: Engraftment Syndrome

! The Engraftment Syndrome section can only be completed on the 100-day follow-up form. These questions will be skipped for all subsequent reporting periods.

### \* Combined Follow-Up

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

### Questions 73 – 74: Did engraftment syndrome occur?

Engraftment syndrome typically occurs during neutrophil recovery post-HCT and is characterized by capillary leak syndrome, non-infectious fever, erythrodermatous skin rash, and non-cardiogenic pulmonary edema. Engraftment syndrome is usually seen following autologous transplants but can occur after allogeneic transplants. It is associated with increased transplant mortality, generally from pulmonary and associated multi-organ failure. Corticosteroid therapy is often an effective treatment for engraftment syndrome, mainly for the treatment of pulmonary symptoms.

Indicate whether the recipient developed engraftment syndrome.

If the recipient developed engraftment syndrome during the reporting period, report **Yes** and indicate the date of diagnosis. If the recipient did not develop engraft syndrome, report **No**.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### Questions 75 – 76: Specify the symptoms of engraftment syndrome (check all that apply)

Specify the engraftment syndrome symptoms the recipient developed in the reporting period. Check all that apply. If **Other symptom** is selected, specify the symptom present.

### Questions 77 – 80: Was a biopsy performed?

Indicate **Yes** or **No** if a biopsy was performed to evaluate engraftment syndrome. If **Yes**, specify the site(s) and indicate whether documentation (pathology report) was attached to the form in FormsNet3 or otherwise submitted to the CIBMTR. If **Other site** is selected, specify the biopsy site.

For further instructions on how to attach documents in FormsNet3<sup>SM</sup>, refer to the [training guide](#).

If no biopsies were done to evaluate for engraftment syndrome, report **No**.

**Questions 81 – 82: Specify therapy given for engraftment syndrome (check all that apply)**

Specify any therapy given for engraftment syndrome. If **Other therapy** is selected, specify the treatment(s) administered. If therapy was not given, select **None**.

**Question 83: Did engraftment syndrome resolve?**

Indicate whether engraftment syndrome resolved during the reporting period. If engraftment syndrome was still present on the date of contact, report **No**.

**Section Updates:**

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

*Last modified: Sep 23, 2022*

# Q84 – 133: Acute Graft vs. Host Disease (GVHD)

## \* Autologous Transplants

If this was an autologous infusion, continue with the Infection Prophylaxis section. The graft-versus-host disease sections should only be completed if an allogeneic donor was used.



## ! Acute GVHD Prophylaxis

Acute GVHD prophylaxis questions can only be completed on the 100-day follow-up form. These questions will be skipped for all subsequent reporting periods.

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

Factors influencing the severity of GVHD are related to three main categories: 1) donor or graft, 2) recipient, and 3) treatment. Influential risk factors include the degree of genetic disparity between the donor and the recipient (HLA match), female donor to male recipient, donor parity, older donors, and T-cell dose, graft type and GVHD prophylaxis. The occurrence of acute GVHD becomes a risk factor for the development of chronic GVHD. Recipient age and prior infections are also factors. In the past, GVHD was classified as acute or chronic based on its time to diagnosis following transplant, and other clinical and histological (biopsy or post-mortem) features. Today, there has been increased recognition that acute and chronic GVHD are not dependent upon the time since HCT, so determination of acute or chronic should rest on clinical and histological features. **However, organ staging, and overall grade should only be calculated from the clinical picture, not histology.** Acute GVHD usually begins between 10 and 40 days after HCT but can appear earlier or later. The organs most commonly affected by acute GVHD are the skin, gut, and / or liver. Other sites, such as the lung, may be involved.

## \* Ex Vivo Manipulation for GVHD Prophylaxis

Ex vivo manipulation performed for GVHD prophylaxis should not be reported in the GVHD prophylaxis section of this form.

**Questions 84 – 93: Select specific therapy used after the start of the preparative regimen to prevent acute GVHD. (Check all that apply) (Note: do not include growth factors reported in questions 20 – 28, or ex vivo T-cell depletion reported on the Product Insert. Do not include drugs given as part of the preparative regimen)**

Following an allogeneic HCT, specific immunosuppressive therapy may be administered to prevent GVHD or to immunosuppress the host marrow. Most transplant centers have specific GVHD prophylaxis protocols

and graft rejection protocols. Any agent a recipient receives as a result of these protocols should be included in this section. The type of acute GVHD prophylaxis is included in almost every analysis of allogeneic transplantation.

The prophylactic drug options listed on the form are intended to be **systemic** (IV or oral administration).

The Post-Infusion Follow-Up (2100) Form lists the generic immune suppression drug names. The following website provides the trade names under which generic drugs are manufactured: [http://www.rxlist.com/drugs/alpha\\_a.htm](http://www.rxlist.com/drugs/alpha_a.htm).

If GVHD prophylaxis is used for a syngeneic (monozygotic or identical twin) or autologous HCT, upload documentation in FormsNet3 using the attachment feature. Contact [CIBMTR Center Support](#) with questions.

Specify the therapy given after the start of the preparative regimen to prevent acute GVHD or graft rejection. Check all that apply. If acute GVHD prophylaxis was not given, report **None**.

**Abatacept (Orencia):** Immunomodulator that works to block the activity of T-cells.

**Alemtuzumab (Campath):** Monoclonal antibody that targets common antigens found on B-cells and T-cells (part of the body's immune system). If this drug was given as acute GVHD prophylaxis and report the total ordered dose administered in milligrams.

**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 horse or rabbits immunized against human lymphocytes. Also report the animal source. If **Other** is selected, specify the source.

**Blinded randomized trial:** If the recipient is on a blinded randomized trial, specify agent being studied in the trial in question 86. Additionally, update the Post-Infusion Follow-Up (2100) once the trial is over to specify whether the recipient received the trial drug or placebo.

**Corticosteroids (systemic) (e.g., prednisone, dexamethasone):** Usually combined with cyclosporine when used for prophylaxis. Only report systemic steroids in this section.

**Cyclophosphamide (Cytoxan):** Given in high doses near the date of infusion as prophylaxis. Continue with question 87 and report the total administered dose in milligrams. See the GVHD Prophylaxis note above for additional instructions on how to report this drug.

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

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

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

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

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

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

**Other in vivo monoclonal antibody:** Antibody preparations that are infused for GVHD prophylaxis. Specify if an in vivo monoclonal antibody other than Alemtuzumab (Campath) or an in vivo immunotoxin was used.

**Other agent:** If the drug is not listed on the form, select this option and specify the other agent being given as GVHD prophylaxis.

- Do not include ex vivo T-cell depletion. Report ex vivo T-cell depletion on the HCT Infusion Form (Form 2006).
- Do not include agents used to prevent infection. Report infection prophylaxis agents in the Infection section.
- Do not include topical corticosteroids or ursodeoxycholic acid (ursodiol, actigal).

### **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** when asked if acute GVHD developed or persisted in each subsequent reporting period. See Acute GVHD Diagnosis Scenarios included in the instructions below.

### **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 94: Did acute GVHD develop?

Questions *Did acute GVHD develop* and *Did acute GVHD persist* on the Post-HCT Follow-Up Data (2100) Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. Acute GVHD is one of the main outcomes reported in allogeneic transplantation. If the recipient had active acute GVHD during the reporting period, either *Did acute GVHD develop* OR *Did acute GVHD persist* must be answered **Yes** unless there has been a prior / concurrent diagnosis of chronic GVHD (refer to the Acute/Chronic GVHD blue box above). There will not be a situation where **Yes** is reported for both *Did acute GVHD develop* and *Did acute GVHD persist*. If *Did acute GVHD develop* is answered **Yes** and a diagnosis date has been reported, *Did acute GVHD persist* will be disabled in FormsNet3<sup>SM</sup>. Centers should report **Yes** for *Did acute GVHD develop* 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 blue box above).

If the recipient has 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 *Did acute GVHD develop* and **Yes** for *Did acute GVHD persist*. *Did acute GVHD persist* 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* and *Did acute GVHD persist*.

Report **No** for questions *Did acute GVHD develop* and *Did acute GVHD persist* 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 blue 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 a HCT on 1/1/2015 and develops acute GVHD which is clinically diagnosed on 2/1/2015. At least one of their symptoms, attributed to acute GVHD, persists beyond the 100-day date of contact which is 4/5/2015. Treatment continues and symptoms completely resolve on 5/1/2015. Immunosuppression is tapered until a flare of acute GVHD is diagnosed on 5/25/2015. Immunosuppression is given and symptoms quickly resolve with no active acute GVHD beginning 6/10/2015. The six-month date of contact is 6/20/2015. Another flare of acute GVHD is clinically diagnosed on

8/15/2015.

*100 Day Post-Infusion Data Form:*

*Did acute GVHD develop:* 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:* Leave blank. This question will be skipped whenever an acute diagnosis date has been entered.

*Biopsy and organ staging at diagnosis questions:* Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

*Six Month Post-Infusion Data Form:*

*Did acute GVHD develop:* Report **No** to indicate acute GVHD persists from a previous report. Note, the flare of acute GVHD was < 30 days from symptoms resolution so it doesn't count as a new reportable episode.

*Date of acute GVHD diagnosis:* Leave blank. This question will be skipped whenever *Did acute GVHD develop* is answered **No**.

*Did acute GVHD persist:* Report **Yes** to indicate GVHD persists from a previous report.

*Biopsy and organ staging at diagnosis questions:* Leave blank. Answering **Yes** for question 93 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:* 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:* Leave blank. This question will be skipped whenever an acute diagnosis date has been entered.

*Biopsy and organ staging at diagnosis questions:* Answer these questions based on the assessments performed at the time of diagnosis of the flare of acute GVHD (8/15/2015).

**B.** A recipient receives a HCT on 1/1/2015 and develops acute skin GVHD on 2/1/2015 and then chronic eye GVHD on 3/1/2015. Both acute and chronic symptoms resolve by the 100-day date of contact (4/5/2015). While tapering their immunosuppression, the recipient has a flare of their acute skin GVHD on 5/30/2015. Treatment continues and symptoms completely resolve by the six-month date of contact (6/20/2015).

100 Day Post-Infusion Data Form:

*Did acute GVHD develop:* 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:* Leave blank. This question will be skipped whenever an acute diagnosis date has been entered.

*Biopsy and organ staging at diagnosis* questions: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

*Maximum organ involvement and treatment* questions: 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 blue note box above.

#### Six Month Post-Infusion Data Form:

*Did acute GVHD develop:* 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* is answered **No**.

*Did acute GVHD persist:* 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* and *Did acute GVHD persist*. 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 blue note box above.

#### **Question 95: Date of acute GVHD diagnosis**

The date of acute GVHD diagnosis is important as CIBMTR tries to analyze GVHD as a time-to-event endpoint, for which a date is required. This type of analysis can then adjust for recipients who relapse or die before Day 100.

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

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

If the exact clinical diagnosis date is unknown, but the treatment start date is known, report the date treatment started as the date of acute GVHD diagnosis.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).



#### **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 96: Did acute GVHD persist?

This question will only be enabled in FormsNet3<sup>SM</sup> if the center has reported **No** for the question *Did acute GVHD develop?* and, therefore, has not reported a date of acute GVHD 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 note above question 91).

Report **No** for *Did acute GVHD develop* and *Did acute GVHD persist* 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 blue 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 97: Was acute GVHD evaluated by biopsy (histology)? (at diagnosis)

Histological tests may be performed to confirm the clinical diagnosis of GVHD; however, the staging and grading of GVHD should be based on clinical evidence, not histological results.

Indicate **Yes** or **No** if a biopsy was used to diagnose acute GVHD. If biopsy was not performed or unknown if performed at diagnosis, report **No**.

### Questions 98 – 104: Specify result(s)

For each organ listed, indicate the test result documented on the pathology report as either **Positive**, **Suggestive**, **Negative**, **Inconclusive / equivocal**, or **Not done**.

**Suggestive or Inconclusive / equivocal** should be reported if in the final diagnosis or comments section of the pathology report, those words are used.

Biopsy report may use the term "consistent with GVHD" which could be interpreted as either **Positive** or **Suggestive**, depending on the comments listed in the report.

If the biopsy was performed on an “other site,” specify the site biopsied.

Additionally, indicate whether documentation was submitted to the CIBMTR (e.g., pathology report). For further instructions on how to attach documents in FormsNet3, refer to the [training guide](#).

### Question 105: 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. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD, not its severity. However, **overall grading remains clinical** and is based on the criteria published by Przepiorka et al., *Bone Marrow Transplant* 1995; 15(6):825-8, see the GVHD Grading and Staging table below.

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

- 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

Extent of Organ Involvement			
Stage	Skin	Liver	Gut
1	Rash on <25% of skin <sup>1</sup>	Bilirubin 2-3 mg/dl <sup>2</sup>	Diarrhea > 500 ml/day <sup>3</sup> or persistent nausea <sup>4</sup> <i>Pediatric</i> : 280-555 ml/m <sup>2</sup> /day or 10-19.9 mL/kg/day
2	Rash on 25-50% of skin	Bilirubin 3-6 mg/dl	Diarrhea >1000 ml/day <i>Pediatric</i> : 556-833 ml/m <sup>2</sup> /day or 20-30 mL/kg/day
3	Rash on >50% of skin	Bilirubin 6-15 mg/dl	Diarrhea >1500 ml/day <i>Pediatric</i> : >833 ml/m <sup>2</sup> /day or > 30 mL/kg/day
4	Generalized erythroderma with bullous formation	Bilirubin >15 mg/dl	Severe abdominal pain, with or without ileus, and / or grossly blood stool

<b>Grade<sup>5</sup></b>			
<b>I</b>	Stage 1-2	None	None
<b>II</b>	Stage 3	Stage 1	Stage 1
<b>III</b>	—	Stage 2-3	Stages 2-4
<b>IV<sup>6</sup></b>	Stage 4	Stage 4	—

1. Use “Rule of Nines” (Table 4) or burn chart to determine extent of rash.

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

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

4. Persistent nausea with or without histological evidence of GVHD in the stomach or duodenum.

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

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

### Questions 106 – 111: Indicate the stage for each organ involvement at time of diagnosis of acute GVHD

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

Reporting each organ staging is important as this will allow CIBMTR to recalculate the overall acute GVHD grade, based on difference schemes, if necessary.

**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 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

<b>Body Area</b>	<b>Percent</b>	<b>Total Percentage</b>
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/kg/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<sup>2</sup>/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 ongoing nausea or vomiting which is not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

**Liver:** Select the stage that reflects the bilirubin level attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report ongoing hyperbilirubinemia which is 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 ongoing symptoms which are not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. If **Yes** is reported, specify the other site(s) of involvement.

#### **Question 112: Maximum overall grade of acute GVHD**

Indicate the overall maximum grade of acute GVHD since the date of the last report. This is an important data field since most studies are specifically interested in grade II – IV or grade III – IV acute GVHD. 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 but is not used for staging or grading. 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.

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.

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

Report the recipient's maximum acute GVHD grade in the reporting period; **this may differ from the grade at diagnosis or may be the same**. If acute GVHD was present, but the maximum grade was not documented and it cannot be determined from the grading and staging table, report **Not applicable**.

Examples may include:

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

### Upper GI GVHD

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

#### Acute GVHD Grading Scenarios:

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

**B.** A recipient developed 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).

**C.** 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.

**D.** A recipient developed stage 1 skin involvement and stage 1 liver involvement (overall grade II) 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 3, along with GI stage 1 (overall grade II). In this case, grade II would be reported as the *Maximum overall grade of acute GVHD* with the maximum date reported as 1/1/2019 the *first date of maximum overall grade of acute GVHD*. Additionally, when reporting the organ staging at the time of maximum overall grade, skin stage 1 and liver stage 1 should be reported. Skin stage 3 and GI stage 1 will not be captured.



### Question 113: 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, regardless of any variation in the organ staging. For further clarification, review acute GVHD grading scenario D above. If **Not applicable** was reported for *Maximum overall grade of acute GVHD*, this question must be left blank.

### Questions 114 – 119: Specify organ involvement at time of maximum grade

Report the stage of involvement for each organ on the date reported for maximum overall grade of acute GVHD. Refer to the GVHD Grading and Staging Table above for staging guidelines. Also, see additional information included for each organ in the instructions for the organ staging at diagnosis questions above.

### Question 120: Corticosteroids (topical GI) (e.g. beclomethasone, budesonide)

Indicate **Yes** or **No** if topical corticosteroids were used to **treat GI GVHD**. Do not report topical therapies used for skin or lung GVHD in this question. Also, do not report systemic corticosteroids such as prednisone or dexamethasone. Systemic therapies are captured below.

#### Corticosteroids

Corticosteroids are captured differently depending on whether they are used topically or systemically. Use the following guidelines when determining how to report corticosteroids used to treat acute GVHD:

Topical Creams for Skin: Do not report topical ointments or creams used to treat skin GVHD including corticosteroid creams such as Triamcinolone or Hydrocortisone.

Other Topical Treatments: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. If these treatments are given for acute GI GVHD during the reporting period, report **Yes** for *Corticosteroids*. If these treatments were given for other organ involvement of GVHD, contact the CIBMTR Customer Service Center to determine the best option for reporting this therapy.

Systemic Treatments: Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in *Select systemic treatment used to treat acute GVHD*.

#### Reporting Multiple Systemic Therapies

**FormsNet3<sup>SM</sup> application**: Complete the GVHD specific therapy questions for each reported systemic therapy by adding an additional instance in the FormsNet3<sup>SM</sup> application.  
**Paper form submission**: Copy the GVHD specific therapy questions and complete for each reported therapy.

### Questions 121 – 133: Was specific therapy given for acute GVHD?

Specify the systemic therapy used to treat acute GVHD during the reporting period. Report any prophylactic

drugs as therapy for acute GVHD if they were continued after the date of diagnosis.

If systemic therapy was given to treat acute GVHD during the reporting period, specify the drugs given and indicate if the treatment was continued from prophylaxis. If the drug was continued from prophylaxis, select **Yes** and continue with *Specify if the treatment was continued from prophylaxis*. If the drug was started in a prior reporting period and continued into the current reporting period, select **Previously reported**. The **Previously reported** option is not applicable for the Day 100 reporting period.

If the drug was not continued from prophylaxis and was not started in the prior reporting period and continued into the current reporting period, select **No** and report the therapy start date. When reporting the date started, report the first day the drug was given on or after the GVHD diagnosis date (reported in *Date of acute GVHD diagnosis*).

If **Alemtuzumab (Campath)** is selected, report the total administered dose in milligrams during the reporting period. Do not report the prescribed or daily doses.

If **ALG, ALS, ATG, ATS** is selected, report the total administered dose in milligrams during the reporting period. Do not report the prescribed or daily doses. In addition, specify the animal (horse or rabbit) source. If **Other** is selected, specify the source.

If **Anti CD25 (Zenapax, Daclizumab, AntiTAC), Blinded randomized trial, In vivo immunotoxin, Other in vivo monoclonal antibody**, or **Other JAK2** inhibitor is selected, specify the agent.

If the therapy is not listed on the form, select **Other agent** and specify the therapy.

If no therapy was given, indicate **None**.

### Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q113	9/15/2023	Modify	Instructions updated to clarify how to report the date of maximum grade of acute GVHD when there is organ staging variation <i>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, <b>regardless of any variation in the organ staging.</b> For further clarification, review acute GVHD grading scenario D above. If <b>Not applicable</b> was reported for Maximum overall grade of acute GVHD, this question must be left blank. <del>If the same maximum overall grade was achieved, but the specific organ staging varied, report the date of the maximum organ staging consistent with the overall grade reported in Maximum</del></i>	Updated for clarification

			<del>overall grade of acute GVHD. For example, a recipient developed stage 2 liver GVHD that later progressed to stage 3 liver GVHD within the reporting period. The date the recipient had stage 3 liver GVHD should be reported as the date of maximum grade, even though stage 2 and stage 3 liver GVHD are both captured as grade 3.</del>	
Q112	9/15/ 2023	Add	Acute GVHD Grading Scenario <b>D</b> added due to clarify how to report the maximum grade of GVHD when there is organ staging variation: <b>D. A recipient developed stage 1 skin involvement and stage 1 liver involvement (overall grade II) 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 3, along with GI stage 1 (overall grade II). In this case, grade II would be reported as the Maximum overall grade of acute GVHD with the maximum date reported as 1/1/2019 the first date of maximum overall grade of acute GVHD. Additionally, when reporting the organ staging at the time of maximum overall grade, skin stage 1 and liver stage 1 should be reported. Skin stage 3 and GI stage 1 will not be captured.</b>	Updated for clarification
Q96	1/27/ 2023	Add	Red warning box regarding reporting 'persistent' GVHD for the Day 100 reporting period added: <b>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.</b>	Due to change in FormsNet validations

Last modified: Sep 18, 2023

# Q134 – 203: Chronic Graft vs. Host Disease (GVHD)

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## \* Autologous Transplants

If this was an autologous HCT, continue with the Infection Prophylaxis section of the form starting. Chimerism testing and graft-versus-host disease sections should only be completed for allogeneic HCTs.

Report any chronic graft-versus-host disease occurring in this reporting period in response to allogeneic HCT or cellular therapy. Chronic GVHD affects 25-50% of long-term survivors of allogeneic transplants and usually develops after day 100. However, it has been documented as occurring as early as day 60. The mechanism of tissue damage differs from acute GVHD and a greater variety of organs may be affected. For further information on acute GVHD, refer to the [Acute GVHD](#) section of the manual.

### Question 134: Did chronic GVHD develop?

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.

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 135: 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 136: Did chronic GVHD persist?**

Indicate whether chronic GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive chronic GVHD, or a prior history of GVHD. If **Yes**, continue with *Maximum grade of chronic GVHD (according to best clinical judgment)*; questions concerning chronic GVHD at the time of diagnosis will be skipped. See *Did chronic GVHD develop* 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 137: Onset of chronic GVHD was**

Indicate whether the onset of chronic GVHD was:

- **Progressive** – acute GVHD present within 2 weeks prior to onset of chronic GVHD
- **Interrupted** – prior acute GVHD resolved for greater than 2 weeks, then chronic GVHD developed
- **De novo** – acute GVHD never developed

#### **Question 138 Were signs of acute GVHD present at the time of chronic GVHD diagnosis (overlap syndrome)?**

Chronic GVHD can be separated into two different categories; classical chronic GVHD and overlap syndrome. Overlap syndrome is a condition where there are features of both acute and chronic GVHD at the time of diagnosis. Indicate whether signs of acute GVHD were present at the time of diagnosis of chronic GVHD (overlap syndrome). Refer to *Did acute GVHD develop* in the [Acute GVHD](#) section for instructions on how to complete the acute and chronic GVHD sections for recipients with overlap syndrome.

#### **Question 139 – 141: Karnofsky / Lansky score at time of chronic GVHD diagnosis**

The Karnofsky Scale is designed for recipients aged 16 years and older and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. If the recipient is less than one year old, leave these questions blank.

Indicate the score (10-100) that best represents the recipient's activity status at diagnosis of chronic GVHD.

The only valid scores are 10-100, zero is not a valid response for this scale, nor are values not ending in zero, such as “85.” The Karnofsky/Lansky scale can be found in [Appendix L, Karnofsky/Lansky Performance Status](#).

For further information on reporting Karnofsky / Lansky Scores refer to the instructions for reporting performance scores in the [Functional Status](#) section below.

#### **Question 142: Platelets (at diagnosis of chronic GVHD)**

Report the lowest platelet count recorded within 14 days (+ / -) of the diagnosis of chronic GVHD, whether or not the recipient has received a platelet transfusion. Indicate the units of measurement.

#### **Question 143: Total serum bilirubin (at diagnosis of GVHD)**

Report the highest total serum bilirubin value (and units) within 14 days (+ / -) of the diagnosis of chronic GVHD. Indicate the units of measurement.

#### **Question 144: Was chronic GVHD evaluated by biopsy (histology)? (at diagnosis)**

Histological tests may be performed to confirm the clinical diagnosis of GVHD; however, the scoring of GVHD should be based on clinical evidence, not histological results.

Indicate **Yes** or **No** whether a biopsy was used to diagnose chronic GVHD. If a biopsy was not performed or it is unknown if performed at diagnosis, report **No**.

#### **Questions 145 – 151: Specify result(s)**

For each organ listed, indicate the test result documented on the pathology report as either **Positive**, **Suggestive**, **Negative**, **Inconclusive / equivocal**, or **Not done**.

**Suggestive** or **Inconclusive / equivocal** should be reported if in the final diagnosis or comments section of the pathology report, those words are used. Biopsy reports may use the term “consistent with GVHD” which could be either **Positive** or **Suggestive**, depending on the other comments in the report.

If the biopsy was performed on an “other site,” specify the site biopsied.

#### **Questions 152 – 184: Specify organs involved and NIH scoring at diagnosis of chronic GVHD (check all that apply)**

Report the organ involvement and NIH score of chronic GVHD for each organ / system listed at the time of diagnosis. For each involved organ, specify any features present at time of diagnosis. Refer to the Organ Scoring of Chronic GVHD Table below for the [NIH Consensus Criteria, 2014](#) for organ scoring of chronic GVHD.

Signs or symptoms occurring at the time of diagnosis may be partially or entirely attributed to GVHD. Alternatively, reportable features may be observed at diagnosis, but attributed entirely to non-GVHD causes. In any case, select the organ if any reportable signs / symptoms are documented during the reporting period

regardless of whether those features are attributed to GVHD.

Features **entirely** explained by non-GVHD causes will be excluded when determining the overall severity of chronic GVHD but are still collected on the form. Spaces have been provided to document non-GVHD causes.

Specify all features observed at the time of diagnosis and report the score for each organ using the criteria from the Organ Scoring of Chronic GVHD Table below. If any reported features are attributed **entirely** to non-GVHD causes, specify the non-GVHD cause(s) in the appropriate field. If a sign or symptom is caused by a combination of chronic GVHD and other causes, then the section on “non-GVHD causes” does not need to be completed. Further instruction has been provided under each organ below.

If a recipient has signs / symptoms of both acute and chronic GVHD during the reporting period, refer to *Did acute GVHD develop* in the Acute GVHD section above for additional instructions. Scenarios C and D below have also been provided for further clarification.

### **GVHD Reporting Scenarios:**

- A.** A recipient developed a maculopapular rash covering 25% BSA as well as deep sclerotic features. Both features are attributed to chronic GVHD. In this case, report **Yes** and **Score 3** for skin involvement (based on findings of deep sclerotic features).
- B.** A recipient developed a maculopapular rash covering 25% BSA as well as dry eyes. Both findings were identified and diagnosed at the same time. The skin rash was attributed to acute GVHD while dry eyes were entirely attributed to chronic GVHD. In this case, report **Yes** and **Score 2** for skin involvement. Report **Yes** and **Score 1** for eye involvement. Any acute findings identified on or after the date of chronic GVHD diagnosis must be reported in the chronic GVHD section. The skin rash would not be reported in the acute GVHD section of the form unless identified and diagnosed prior to any findings of chronic GVHD.
- C.** A recipient developed a maculopapular rash covering 25% BSA. This was diagnosed as acute GVHD, treated, and completely resolved during the 100-day reporting period. During the six-month reporting period, the recipient developed mild dry eyes which was diagnosed as chronic GVHD. Shortly thereafter, the recipient was also diagnosed with an acute flare of skin GVHD.

**100 Day Reporting Period:** Report the acute GVHD findings (maculopapular rash) in the acute GVHD section of the form. Report **No** for *Did chronic GVHD develop* and *Did chronic GVHD persist* to indicate chronic GVHD was not diagnosed during the 100-day reporting period.

**6 Month Reporting Period:** Report acute and chronic GVHD findings in the chronic GVHD section of the form. Report **No** for *Did acute GVHD develop* and *Did acute GVHD persist* to indicate no acute GVHD symptoms were identified during the reporting period. Even though acute skin GVHD was diagnosed, it is not necessary to report these symptoms in both acute and chronic sections of the form. Once a chronic GVHD diagnosis is made, report all signs / symptoms of GVHD (acute and chronic) in the chronic GVHD section of the form.

**D.** A recipient is diagnosed with acute skin GVHD early in the reporting period. This is treated and quickly resolves. During the same reporting period, the recipient later develops chronic GVHD of the mouth. Shortly after the diagnosis of chronic GVHD, the recipient has a flare of their skin GVHD.

**Acute GVHD data fields:** Report any signs or symptoms of acute GVHD documented prior to the diagnosis of chronic GVHD in the acute GVHD section of the form. In this case, the initial diagnosis of skin GVHD as well as any treatments initiated prior to the diagnosis of chronic GVHD will be reported in acute GVHD data fields.

**Chronic GVHD data fields:** Report any signs or symptoms of GVHD (acute or chronic) documented on or after the diagnosis of chronic GVHD in the chronic GVHD section of the form. In this case, the initial diagnosis of mouth GVHD as well as the subsequent flare of skin GVHD will be reported in chronic GVHD data fields. Any treatments continued or initiated on or after the date of diagnosis of chronic GVHD will be reported in chronic GVHD data fields.

**E.** A recipient developed a maculopapular rash covering 25% BSA as well as dry eyes. The skin rash was entirely attributed to a drug reaction while the dry eyes were attributed to chronic GVHD and a prior conjunctivitis. In this case, report **Yes** and **Score 2** for skin involvement. The center should also specify the observed rash was entirely attributed to a drug reaction in the data field *abnormality present but explained entirely by non-GVHD documented cause (for skin)*. Report **Yes** and **Score 1** for eye involvement. Do not specify conjunctivitis as a non-GVHD cause in the data fields *abnormality present but explained entirely by non-GVHD documented cause (for eye)* because the observed symptoms were not entirely explained by this diagnosis.

**F.** A recipient developed maculopapular rash covering 55% BSA as well as superficial sclerotic features of the skin. The rash is attributed to a drug reaction and the sclerotic findings are entirely attributed to chronic GVHD. In this case, report **Yes** and **Score 3** as well as **sclerotic features** for skin involvement. The center should also specify the observed rash was entirely attributed to a drug reaction in the data fields *abnormality present but explained entirely by non-GVHD documented cause (for skin)*.

**G.** A recipient develops acute skin GVHD and chronic lung GVHD on the same day in the six-month reporting period on 12/1/2019. Chronic GVHD (lung) resolved on the contact date for the six-month reporting period on 2/15/2020; however, acute GVHD (skin) persists at the one-year reporting period.

Six Month Post-Infusion Data Form:

**Acute GVHD data fields:** Report **No**, acute GVHD did not develop or persist. In this case, since acute and chronic GVHD were diagnosed on the same day, only chronic GVHD will be reported.

**Chronic GVHD data fields:** Report both the skin and lung symptoms as chronic GVHD with the date of diagnosis of 12/1/2019 in the chronic GVHD section of the form. In this case, the initial diagnosis of both skin and lung GVHD along with any treatment will be captured in the chronic GVHD section of the form.

One Year Post-Infusion Data Form:



**Acute GVHD data fields:** Do not report any signs or symptoms of acute GVHD documented during this reporting period in the acute GVHD section of the form. All symptoms of GVHD will be capture in the chronic GVHD section.

**Chronic GVHD data fields:** Report all signs or symptoms of GVHD (acute or chronic) documented during the reporting period in the chronic GVHD section of the form. In this case, the symptoms of skin GVHD will be reported in chronic GVHD data fields. Any treatments continued to treat the skin GVHD will be reported in chronic GVHD data fields.

### Organ Scoring of Chronic GVHD

Organ	Score 0	Score 1	Score 2	Score 3
Skin %BSA <sup>1</sup>	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 signs but not limiting oral intake significantly	Moderate symptoms with disease signs with partial limitation of oral intake	Severe symptoms with disease signs with major limitation of oral intake
Eyes	No symptoms	Mild dry eye symptoms not affecting ADL (requirement of lubricant drops ≤ 3x/day)	Moderate dry eye symptoms partially affecting ADL (requiring lubricant drops > 3x/day or punctal plugs) WITHOUT new vision impairment due to keratoconjunctivitis sicca (KCS)	Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) OR unable to work because of ocular symptoms OR loss of vision due to keratoconjunctivitis sicca (KCS)
GI Tract	No symptoms	Symptoms without significant weight loss (< 5%)	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	Normal total bilirubin with ALT ≥ 3 to 5 x	Elevated total bilirubin but ≤ 3 mg / dL or ALT >5 x ULN	Elevated total bilirubin > 3 mg / dL

	and ALT or AP < 3 x ULN	ULN or AP ≥ 3 ULN		
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 Tract <sup>2</sup>	No signs	Mild signs and females with or without discomfort on exam	Moderate signs and may have signs of discomfort on exam	Severe signs with or without symptoms
Other Features <sup>3</sup>	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.

**Skin:** Ranges from skin discoloration to severe scarring and tightness. Includes, but is not limited to:

- Sclerosis: thickening of the skin, which may cause loss of suppleness
- Maculopapular rash / erythema: reddish skin with small confluent bumps / redness
- Lichen planus-like features: erythematous / violaceous flat-topped papules or plaques with or without surface reticulations or a silvery or shiny appearance.
- Papulosquamous lesions or ichthyosis: dry, scaly, or thickened skin

- Keratosis pilaris: small acne-like bumps and rough patches
- Poikiloderma: atrophy, pigmentary changes, and telangiectasia

In addition to reporting the NIH score BSA involved, report the skin features score and the skin GVHD features present at diagnosis.

If any skin abnormalities were present, but explained entirely by non-GVHD causes, specify any documented causes.

**Mouth:** Refers to white plaques, scarring, and ulcers occurring in the mouth and throat.

- Lichen planus-like features: whitish lacy patches that usually appear first on inner cheeks, but can involve roof of mouth, gums, and / or tongue

If any mouth abnormalities were present, but explained entirely by non-GVHD causes, specify any documented causes.

**Eyes:** Recipients may have dry eyes and corneal ulcers due to keratoconjunctivitis sicca.

- Keratoconjunctivitis sicca (KCS): dry eye syndrome

Indicate **Yes**, **No**, or **Not done** if KCS was confirmed by an ophthalmologist at diagnosis.

If any eye abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes.

**Gastrointestinal tract (GI):**

- Esophageal web / proximal stricture or ring: extension of esophageal tissue
- Dysphagia: difficulty swallowing
- Anorexia
- Nausea
- Vomiting
- Diarrhea
- Weight loss: weight loss  $\geq$  5%
- Failure to thrive

If any GI abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes.

**Liver:** Record all types of liver abnormalities either clinical or histological.

- Liver involvement may be manifested by elevation of liver function tests. Three are considered in the scoring system: total bilirubin, alkaline phosphatase; SGPT [ALT].

If any liver abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes.

**Lung:** This ranges from mild impairment on pulmonary function tests to severe disorders.

If pulmonary function tests were performed, specify FEV1 percent.

If any lung abnormalities were present, but explained entirely by non-GVHD documented causes, specify causes.

#### **Joints and fascia:**

- Contractures: loss of joint mobility due to skin or fascia changes

If any joint or fascia abnormalities were present, but explained entirely by non-GVHD causes, specify causes.

#### **Genital tract:**

- Female: Vaginitis / stricture: pain, ulceration, inflammation, eventually scarring / narrowing of the vaginal opening.
- Male: Pain, burning sensation, lichen planus or lichen sclerosis features, scarring, stenosis.

Indicate if the recipient was sexually active at the time of diagnosis of chronic GVHD.

If any genital tract abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes.

#### **Question 185: Maximum grade of chronic GVHD (according to best clinical judgment)**

Report the maximum chronic GVHD involvement since the date of last report, based on clinical grade, as documented by the recipient's provider. The intent of this question is to capture the maximum grade based on the best clinical judgment. **If the maximum clinical grade is not documented, request documentation from a clinician trained in GVHD grading.** 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 tacrolimus)
- **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 tacrolimus)
- **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.

#### Question 186: Date of maximum grade of chronic GVHD

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

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

#### Question 187: Specify if chronic GVHD was limited or extensive

Another grading system for chronic GVHD is divided into two categories: limited and extensive. Definitions are based on Sullivan KM, *Blood* 1981; 57:267.

Report the extent of chronic GVHD since the date of last report. Report **Limited** if chronic GVHD includes only localized skin involvement and/or liver dysfunction. Report **Extensive** if **any** of the following symptoms are attributed to chronic GVHD:

- Generalized skin involvement and / or liver dysfunction
- Liver histology showing chronic aggressive hepatitis, bridging necrosis, or cirrhosis
- Involvement of the eye: Schirmer's test with < 5 mm wetting, or
- Involvement of minor salivary glands or oral mucosa 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**.

#### Questions 188 – 189: Select other indicators, clinical features, or complications related to chronic GVHD (check all that apply)

Select other indicators, clinical features, or complication related to chronic GVHD (check all that apply)

- **Ascites (serositis):** Accumulation of fluid in the peritoneal cavity
- **Pericardial effusion:** Accumulation of fluid in the pericardial cavity
- **Pleural effusion(s):** Buildup of fluid between the chest and the tissues which line the lungs
- **Nephrotic Syndrome:** Kidney disorder that causes the body to excrete too much protein in the urine
- **Myasthenia gravis:** Weakness of muscles caused by antibodies to acetylcholine receptors
- **Peripheral neuropathy:** Nerve damage, usually in the hands and feet
- **Polymyositis:** Inflammation causing muscle weakness on both sides of the body
- **Weight loss >5% without GI symptoms**

- **Eosinophilia:** Elevation in eosinophils in the peripheral blood (> 500 cells /  $\mu\text{L}$ )
- **Platelets:** Decrease in platelets in the blood (< 100,000 /  $\mu\text{L}$ )
- **Other indicator:** If selected, specify the other indicator
- **None**

### Question 190: Corticosteroids (topical GI) (e.g. beclomethasone, budesonide)

Indicate **Yes** or **No** if corticosteroids (topical GI) were given for chronic GVHD. Examples include beclomethasone and budesonide. Do not include dexamethasone, mouth rinses or eye drops administered as treatment for chronic GVHD and corticosteroids (topical GI) given as a GVHD prophylaxis.

#### Reporting Multiple Systemic Therapies

**FormsNet3<sup>SM</sup> application:** Complete the chronic GVHD treatment questions for each reported systemic therapy by adding an additional instance in the FormsNet3<sup>SM</sup> application.  
**Paper form submission:** Copy the chronic GVHD treatment questions and complete for each reported therapy.

### Questions 191 – 203: Select systemic treatment used to treat chronic GVHD

Select all systemic agents used to treat chronic GVHD during the reporting period, including any prophylactic medications continued after the diagnosis of chronic GVHD. If systemic therapy was not given for treatment of chronic GVHD, select **None**. Review the Chronic GVHD treatment reporting scenarios below for examples.

If systemic therapy was given to treat chronic GVHD during the reporting period, specify the drugs given and indicate if the treatment was continued from prophylaxis in question 189. If the drug was continued from prophylaxis or acute GVHD treatment, select **Yes**. If the drug was started in a prior reporting period and continued into the current reporting period, select **Previously reported**. The **Previously reported** option is not applicable for the Day 100 reporting period.

If the drug was not continued from prophylaxis / acute GVHD treatment and was not started in the prior reporting period and continued into the current reporting period, select **No** and report the therapy start date. When reporting the date started, report the first day the drug was given on or after the GVHD diagnosis date (reported *Date of chronic GVHD diagnosis*). If treatment is started and subsequently escalated during the same reporting period, report the earliest date treatment was actually given during the reporting period. Additionally, report the earliest start date if a drug is started multiple times during the same reporting period.

Report the total dose administered during the reporting period if a dose is required.

Refer to the acute GVHD treatment questions above for a description of most agents listed. Agents not described under acute GVHD are described below under Additional Agents. “Systemic” refers to drugs given by mouth, intramuscularly (IM), or intravenously (IV). “Topical” refers to drugs applied to the surface of skin or mouth, eye drops, or inhalation therapy. An exception to this would be the drug budesonide; it is a drug given by mouth for treatment of lower gut GVHD, but it is considered a “topical” drug since it is not

absorbed.

### Chronic GVHD Treatment Reporting Scenarios:

**A.** During the one-year reporting period, a recipient on cyclosporine for GVHD prophylaxis was diagnosed with chronic skin GVHD (5/1/2016). This was initially treated with topical steroids in addition to continuing their cyclosporine at the current dose. The chronic skin GVHD worsened shortly thereafter. On 5/15/2016, prednisone was started, and the dose of cyclosporine was increased. Symptoms persisted into the two-year reporting period but improved shortly thereafter. Upon resolution of symptoms, prednisone and cyclosporine doses were tapered.

#### *One Year Post-HCT Data Form*

*Corticosteroids:* Report **No** to indicate no topical GI corticosteroids were given. Topical steroids applied to the skin should not be reported here.

*Select systemic treatment used to treat chronic GVHD:* Select **Cyclosporine** to indicate systemic therapy was escalated to treat chronic GVHD.

*Specify if the treatment was continued from prophylaxis / acute GVHD treatment:* Report **Yes** to indicate cyclosporine was continued from prophylaxis / aGVHD treatment

Complete a second instance of the chronic GVHD treatment questions to capture the **Corticosteroids**, report **No** for *Specify if the treatment was continued from prophylaxis / acute GVHD treatment* and the start date as 5/15/2016.

#### *Two Year Post-HCT Data Form*

*Corticosteroids:* Report **No** to indicate no topical GI corticosteroids were given. Topical steroids applied to the skin should not be reported here.

*Select systemic treatment used to treat chronic GVHD:* This question will be left blank as no therapy was escalated or started to treat chronic GVHD within this reporting period.

**B.** During the one-year reporting period, a recipient on sirolimus for GVHD prophylaxis was diagnosed with chronic mouth and gut GVHD (7/1/2016). This was initially treated with topical steroids (oral dexamethasone and budesonide) in addition to continuing sirolimus at the current dose. Prednisone was started 7/30/2016 due to minimal improvement. The chronic mouth and gut GVHD resolved and dexamethasone, budesonide, as well as prednisone were discontinued. Sirolimus was continued. Later in the one-year reporting period, a severe flare of chronic gut GVHD occurred (10/15/2016). This was first treated by restarting prednisone on the date of diagnosis; however, no response was observed. Ruxolitinib was started on 10/20/2016 and symptoms resolved.

#### *One Year Post-HCT Data Form*

*Corticosteroids:* Report **Yes** to indicate topical GI corticosteroids were given. Budesonide should be reported here.

*Select systemic treatment used to treat chronic GVHD:* Report **Sirolimus** to indicate systemic therapy

was given to treat chronic GVHD.

*Specify if the treatment was continued from prophylaxis / acute GVHD treatment:* Report **Yes** to indicate sirolimus was continued from prophylaxis / aGVHD treatment. Note, topical steroids, including dexamethasone and budesonide, should not be considered when completing the systemic chronic GVHD therapy questions.

Complete a second instance of chronic GVHD treatment questions to capture **Ruxolitinib**, report **No** for *Specify if the treatment was continued from prophylaxis / acute GVHD treatment*, and the start date as 10/20/2016.

Complete a third instance of chronic GVHD treatment questions to capture **Corticosteroids**, report **No** for *Specify if the treatment was continued from prophylaxis / acute GVHD treatment*, with a start date of 7/30/2016. Report the earliest start date if a medication is started multiple times during the reporting period.

**C.** During the six-month reporting period, a recipient off all immunosuppression was diagnosed with chronic mouth GVHD (9/15/2016). This was initially treated with topical steroids (oral dexamethasone). Cyclosporine was started on 9/20/2016 due to minimal response. Symptoms resolved by the one-year date of contact (10/1/2016) at which time dexamethasone was discontinued. The recipient remained on cyclosporine. During the one-year reporting period, a flare of chronic mouth GVHD occurred on 11/15/2016 while attempting to taper cyclosporine. This was treated by increasing the dose of cyclosporine on the date of diagnosis of the flare.

#### *Six Month Post-HCT Data Form*

**Corticosteroids:** Report **No** to indicate the recipient was initially treated with topical steroids.

**Select systemic treatment used to treat chronic GVHD:** Report **Cyclosporine** to indicate systemic therapy was given to treat chronic GVHD.

*Specify if the treatment was continued from prophylaxis / acute GVHD treatment:* Report **No** and specify 9/20/2016 as the treatment start date. This is the date cyclosporine was started as treatment for chronic GVHD. Note, topical steroids, including dexamethasone, budesonide, etc. should not be considered when completing systemic chronic GVHD treatment questions.

#### *One Year Post-HCT Data Form*

**Corticosteroids:** Report **No** to indicate the recipient was initially treated with topical steroids.

**Select systemic treatment used to treat chronic GVHD:** Report **Cyclosporine** to indicate systemic therapy was given to treat chronic GVHD.

*Specify if the treatment was continued from prophylaxis / acute GVHD treatment:* Report **No** and specify 11/15/2016 as the treatment start date.

#### **Additional Agents:**

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



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

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

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

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

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

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

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

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

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

Alternative treatments may be used in combination with drug therapy (example: low dose cyclophosphamide). If alternative treatments were used, report in **Other agent**.

### Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q136	1/27/2023	Add	Red warning box regarding reporting 'persistent' GVHD for the Day 100 reporting period added: <b>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</b>	Due to change in FormsNet validations

			<i>last report.</i>	
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*Last modified: Jan 30, 2023*

## Q204 – 210: Current GVHD Status

### Question 204: Are symptoms of GVHD still present on the date of actual contact (or present at the time of death)?

This question refers to any symptoms of GVHD (acute and / or chronic) observed during the reporting period. This section of the form must be completed if the center reported **Yes**, acute, or chronic GVHD developed or persisted.

Indicate whether the recipient has active clinical signs / symptoms of acute and/or chronic GVHD on the date of contact (question 1). If the recipient has died, indicate whether GVHD symptoms were present at the time of death.

### Question 205: Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, $\leq 10$ mg/day for adults, $< 0.1$ mg/kg/day for children)

#### \* Corticosteroids

Corticosteroids are captured differently depending on whether they are used topically or systemically. Use the following guidelines when determining how to report corticosteroids used to treat acute GVHD:

Topical Creams for Skin: Do not report topical ointments or creams used to treat skin GVHD including corticosteroid creams such as Triamcinolone or Hydrocortisone.

Other Topical Treatments: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. Do not consider these medications when answering *Is the recipient still taking systemic steroids*.

Systemic Treatments: Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in *Is the recipient still taking systemic steroids*.

Indicate whether the recipient is still taking systemic steroids to treat or prevent GVHD on the date of contact. If the recipient is no longer taking systemic steroids for GVHD, report **No**. If the recipient is still receiving systemic steroids during the reporting period to treat or prevent GVHD, report **Yes**. Refer to the guidelines included in the question text if the recipient is taking low dose steroids or steroids for adrenal insufficiency.

If the recipient did not receive systemic steroids for 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 steroids ( $> 10$  mg / day for adults or  $\geq 0.1$  mg / kg / day for children) to treat or prevent GVHD.
- This form is being completed for a subsequent HCT and the recipient has never received systemic steroids ( $> 10$  mg / day for adults or  $\geq 0.1$  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  $\geq 0.1$  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  $\geq 0.1$  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**.

Review 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. *Is the recipient still taking systemic steroids* should be answered as **Not applicable** since the dose of systemic steroids was 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 202 should be answered as **No** since the dose of systemic steroids was  $\leq 10$  mg / day on the day of contact.

**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, *Is the recipient still taking systemic steroids* should be captured as **Yes**, as the dose of systemic steroids is  $> 10$  mg / day.

### Questions 206 – 207: Date final treatment of systemic steroids administered

Indicate whether the date systemic steroids was discontinued is **Known** or **Unknown**. If the final treatment date is **Known**, report the date when the final dose of systemic steroids was administered. For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### Question 208: Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for GVHD?

Indicate whether the recipient is still taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent acute and / or chronic GVHD on the date of contact. If the recipient is still taking non-steroid immunosuppressive agents, report **Yes**. If the recipient is no longer receiving non-steroid agents for GVHD, report **No**.

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

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

- The recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD.
- This form is being completed for a subsequent HCT and the recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD since the start of the preparative regimen for the most recent infusion (or since the date of the most recent infusion if no preparative regimen was given).
- The recipient stopped taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD in a previous reporting period and did not restart non-steroidal immunosuppressive agents (including PUVA) during the current reporting period.

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

If the recipient has died prior to discontinuation of non-steroidal immunosuppressive agents used to treat or prevent acute and/or chronic GVHD, select **Yes**.

#### **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  $\geq 3$  months.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

### Question 209 – 210: Date final treatment administered

Indicate whether the final administration date of non-steroidal immunosuppressive agents (including PUVA) is **Known** or **Unknown**. If the final treatment date is **Known**, report the date when the final treatment or prophylaxis dose of non-steroidal immunosuppressive agents was administered.

For more information regarding reporting partial or unknown dates, see [General Instructions, General](#)

[Guidelines for Completing Forms.](#)**Section Updates:**

<b>Question Number</b>	<b>Date of Change</b>	<b>Add/Remove/Modify</b>	<b>Description</b>	<b>Reasoning (If applicable)</b>
Q208	2/16/2023	Add	Examples of immunosuppression added	Updated to be consistent with the Post-TED (2450)

*Last modified: Feb 16, 2023*

# Q211 – 226: Infection Prophylaxis

## ✿ Infection Prophylaxis

It is important to look at the Medication Administration Record (MAR) throughout the entire reporting period to ensure medications are not missed. Also, the use of some infection prophylactic drugs may not start immediately post-HCT (example: Pentamidine). Do not report agents used as treatment for documented or suspected infections. Report prophylactic immunoglobulins in the Immune Reconstitution section.



This section can only be completed on the 100-day follow-up form. These questions will be skipped for all subsequent reporting periods.

Antimicrobial therapy is generally given to HCT recipients to help prevent infections. The following questions are intended to obtain information on the infection prophylaxis regimen received by the recipient. In general, most centers have a standard cocktail of drugs used which include an antibacterial agent (or agents), antiviral agent, antifungal agent, and an anti-pneumocystis agent. This information is often available in a transplant center SOP for infection prevention. Sometimes, recipients are on one of these medications prior to starting the preparative regimen and therefore it could be treating an infection or is being used as “secondary prophylaxis.” Information regarding primary and secondary prophylaxis can provide insight into the development of resistant infections.

## ✿ Reporting Infection Prophylaxis

When reporting infection prophylaxis, select the drug in each group the recipient received first and closest to the start of the preparative regimen, even if the drug was started prior the preparative regimen. Include any prophylactic medications started prior to day +45 post-infusion; however, only report the first drug received during the reporting period.

## ✿ Reporting Infection Prophylaxis Start Dates

When reporting the start date for all prophylaxis medications (antibacterial, antiviral, antifungal, and anti-PJP), refer to the medical administration record to confirm the date. In the case where the start date is prior to the start of the preparative regimen and the date is unknown, report the date as seven days prior to the start of the preparative regimen.

### Questions 211 – 213: Specify the first antibacterial drug given (select one)

Report the first antibacterial drug administered and closest to the start of the preparative regimen / infusion and started no later than day +45. This may include antibacterial drugs started prior to the start of the preparative regimen as long as they were continued at the start of the preparative regimen.

Only one antibacterial drug may be reported. If multiple antibacterial drugs were started on the same day,



report whichever drug is considered the standard prophylaxis agent at the transplant center. Centers should have an SOP defining infection prophylaxis. Seek physician clarification, as needed.

If **Other antibacterial drug** is selected, specify the drug. Do not include vancomycin IV or Trimethoprim/Sulfamethoxazole (Bactrim, Septra) in this data field. IV vancomycin is captured separately. Trimethoprim/Sulfamethoxazole (Bactrim, Septra) is given as PJP prophylaxis and captured below.

Report the antibacterial drug start date and ensure the date reflects the first date when the drug was administered. If the start date is prior to the start of the preparative regimen *and* the date is unknown, report the start date as seven days prior the start of the preparative regimen. Refer to the medical administration record to confirm the start date.

If no antibacterial drugs were given as prophylaxis, including prior to the start of the preparative regimen and no later than day +45, select **None**. Do not report antibacterial agents given empirically for neutropenic fever.

**Example 1:** If both amoxicillin and levofloxacin were started as prophylaxis on the same day the preparative regimen was started, the center should report whichever agent is considered standard for prophylaxis at their institution. However, if amoxicillin was administered at the start of the preparative regimen and levofloxacin was started two days later, the center should only report amoxicillin as the first antibacterial infection prophylaxis drug.

#### Questions 214 – 215: Was vancomycin IV also given as prophylaxis?

Indicate **Yes** or **No** if vancomycin IV was also given for prophylaxis at the *same time as the first antibacterial drug reported above*. If **Yes**, report the start date of vancomycin IV. It is uncommon that vancomycin is used as prophylaxis, therefore, please confirm with the physician that the intent of vancomycin IV was prophylaxis.

**Example 2:** Amoxicillin was started as prophylaxis on the same day the preparative regimen was started, and then vancomycin IV was started on day +1 post-infusion. If the amoxicillin was continued while the recipient remained on vancomycin, select **Amoxicillin** in the antibacterial section and report the start date and also report **Yes**, vancomycin IV was also given as prophylaxis with the start date (these will have separate start dates). Vancomycin IV was given *at the same time (in addition to)* as the first antibacterial drug, amoxicillin. However, if amoxicillin was stopped prior to or on the same day when vancomycin was started, **No** would be reported.

#### Questions 216 – 218: Specify the first antiviral drug given (select one)

Report the *first* antiviral drug administered and closest to the start of the preparative regimen / infusion and started no later than day +45. This may include antiviral drugs started prior to the start of the preparative regimen as long as they were continued at the start of the preparative regimen. If the start date is prior to the start of the preparative regimen *and* the start date is unknown, report the date as seven days prior the start of the preparative regimen. Only one antiviral drug may be reported.

If **Other antiviral drug** is selected, specify the drug. Do not include letermovir in this data field.

If no antiviral drugs were given, including prior to the start of the preparative regimen and no later than day +45, select **None**.

#### Questions 219 – 220: Was letermovir (prevymis) given as prophylaxis?

Letermovir is given to prevent CMV reactivation and is generally started between Day 0 and Day +28 post-HCT.

Indicate **Yes** or **No** if letermovir was also given for prophylaxis at the *same time (in addition to) as the first antiviral drug reported above*. If **Yes**, report the start date of letermovir.

#### Questions 221 – 223: Specify the first antifungal drug given (select one)

Report the *first* antifungal drug administered and closest to the start of the preparative regimen / infusion and started no later than day +45. This may include antifungal drugs started as prophylaxis prior to the start of the preparative regimen as long as they were continued at the start of the preparative regimen. Only one antifungal drug may be reported. If the start date is prior to the start of the preparative regimen *and* the start date is unknown, report the date as seven days prior to the start of the preparative regimen.

If **Other antifungal drug** is selected, specify the drug. Do not report Nystatin in this data field.

If no antifungal drugs were given, including prior to the start of the preparative regimen and no later than day +45, select **None**.

#### Questions 224 – 226: Specify the first anti-pneumocystis (PJP) drug given (select one)

Report the *first* anti-pneumocystis (PJP) drug administered and closest to the start of the preparative regimen / infusion and started no later than day +45. This may include anti-pneumocystis (PJP) drugs started prior to the start of the preparative regimen as long as they were continued at the start of the preparative regimen. Only one anti-pneumocystis (PJP) drug may be reported.

If **Other anti-pneumocystis** is selected, specify the drug.

If no anti-pneumocystis (PJP) drugs were given, including prior to the start of the preparative regimen and no later than day +45, select **None**.

#### Section Updates:

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

*Last modified: Sep 23, 2022*

## Q227 – 248: Infection

Infections occur frequently in 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.

### \* **Combined Follow-Up**

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

### \* **Reporting Multiple Infections**

**FormsNet3<sup>SM</sup> 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 preparative regimen**

Any COVID-19 infections diagnosed *after* the start of the preparative regimen should be reported in the following questions on the Post-HCT Follow-Up (2100) form. Effective August 25, 2023, the Respiratory Virus Post-Infusion Data (2149) form for transplants on the CRF 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 has a positive antibody result.
- The recipient was symptomatic and treated but COVID-19 testing was not performed and / or COVID-19 diagnostic testing was performed and negative

DO report an infection in the follow 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)

### Questions 227 – 235: Did the recipient develop a clinically significant infection?

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

### 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*.

Reporting the following infections, will cause a Fungal Infection Post-HCT Data (2146) form to come due:

1. 211 Aspergillus flavus
2. 212 Aspergillus fumigatus
3. 213 Aspergillus niger
4. 210 Aspergillus, NOS
5. 215 Aspergillus terreus
6. 214 Aspergillus ustus
7. 270 Blastomyces (dermatitidis)
8. 201 Candida albicans
9. 208 Candida non-albicans
10. 222 Cryptococcus gattii
11. 221 Cryptococcus neoformans

12. 230 Fusarium (all species)
13. 261 Histoplasma (capsulatum)
14. 241 Mucorales (all species)
15. 242 Rhizopus (all species)
16. 272 Scedosporium (all species)
17. 240 Zygomycetes, NOS
18. 503 Suspected fungal infection

Reporting the following infections will cause a Hepatitis Serology Post-HCT Data (2147) form to come due:

1. 307 Hepatitis B Virus
2. 308 Hepatitis C Virus

Reporting the following infections will cause a Human Immunodeficiency Virus Post-HCT Data (2148) form to come due:

- 309 Human Immunodeficiency Virus 1 or 2

**Site:**

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

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

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

For clarification, the following site definitions are provided:

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

**Bone:** an infection in the bone itself (Osteomyelitis)

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

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

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

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

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

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

**Liver / Spleen:** includes the gallbladder and biliary tract

**Lung:** also known as the lower respiratory tract

**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”).

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

**Skin, necrotizing fasciitis:** a severe bacterial infection of the fascia, the tissues that line and separate muscles, that causes extensive tissue death including damage to skin and overlying tissues

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

**Urinary tract, upper:** includes the kidneys and ureters

### **Date of Diagnosis:**

Report the specimen collection date of the positive microbiology culture or laboratory report as the diagnosis date. For suspected fungal infections, enter the date of a radiological test or the date treatment was started. 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](#).

### **Infection Reporting Scenarios:**

**A.** A recipient’s post-HCT CMV testing was consistently negative until 1/10/2015 when CMV PCR testing found 15,000 copies of the virus in the recipient’s peripheral blood. On 1/20/2015, the CMV PCR detects 2000 copies. The CMV PCR is still positive on 1/30/2015 but is documented as “detected but not quantifiable”. From 2/7/15, all subsequent CMV PCRs are negative until 6/3/2015 when the CMV PCR demonstrates 1300 copies.

The center should report one instance of infection to capture the CMV infection first documented on 1/10/2015. A second instance should also be reported to capture a recurrent CMV infection documented on 6/

3/2015. This is >60 days after PCR testing reverts to negative and is therefore considered a recurrence and not the same infection per the guidelines in the Definitions for the Same Infection table above. The recurrent infection would be reported on a subsequent Post-Infusion Data Form if it is diagnosed after the date of contact for the form being completed.

**B.** A recipient with concerning respiratory symptoms undergoes a bronchiolar lavage on 10/1/2014. A culture performed on the sample collected from the procedure revealed a Streptococcus, Group B infection. The recipient received systemic antibacterial antibiotics, but the infection progressed to their blood as demonstrated by a culture performed on sample collected 10/3/2014. The recipient did not have any repeat cultures performed between their initial diagnosis and testing performed on 11/1/2014.

The center should report one instance to capture the Streptococcus, Group B infection. The diagnosis date is the date of the first positive culture performed on the sample collected 10/1/2014.

- If the positive culture from 10/3/2014 was collected during the same reporting period, “lung” and “blood” should both be reported as sites of infection.
- If the positive culture from 10/3/2014 was collected after the date of contact for the current reporting period, do not report “blood” as a second site of infection.

**C.** A recipient is empirically diagnosed with septic shock on 8/15/2013, though cultures and viral tests are consistently negative. The recipient is treated with multiple antimicrobial agents which eventually leads to a resolution of all symptoms / complications. The organism responsible for the suspected infection is never identified.

As no organism was identified, the only scenario in which the center should report this as an infection is if there is documentation confirming a suspected fungal infection. In any case, the clinical diagnosis of septic shock will be reported in a following question.

### **Questions 236 – 237: Did the recipient develop Systemic Inflammatory Response Syndrome (SIRS)?**

Systemic inflammatory response syndrome refers to unregulated inflammation which may or may not be related to an infection. Using the criteria below, indicate **Yes** or **No** if the recipient developed SIRS in the reporting period. If **Yes**, report the diagnosis date.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

When determining the development of SIRS, the following criteria should be used and do not use a transplant center’s own criteria:

SIRS Criteria (adults and pediatrics):

Requires at least one or more of the following:

- Core temperature > 38.5 C or < 36 C, *and / or*



- Leukocytosis or leukopenia for age (not secondary to chemotherapy) or >10% bands

Additional symptoms may include:

- Tachycardia, otherwise unexplained persistent in absence of external stimulus, chronic drugs or painful stimuli **or** bradycardia, in < 1 year old, otherwise unexplained persistent
- Tachypnea or mechanical ventilation for an acute process not related to underlying neuromuscular disease or general anesthesia

As long as **two symptoms** are present and one of the symptoms is from the first group above, SIRS should be reported.

### Questions 238 – 239: Did the recipient develop septic shock?

Septic shock refers to the failure to maintain sufficient mean arterial pressure without intervention with vasopressors. It results from vasodilation associated with infection. If septic shock was clinically diagnosed during the reporting period, report **Yes** and indicate the diagnosis date.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### Questions 240 – 243: Did a fecal microbiota transplant (FMT) occur?

Fecal microbiota transplant (FMT) refers to the procedure involving collecting fecal matter from a pre-screened donor and transferring it to a recipient by the oral or rectal route (for example by nasogastric tube or enema) in order to restore intestinal microbial flora. FMT is commonly used as treatment for C difficile colitis or as treatment / prevention for GVHD.

If a FMT occurred during the reporting period, report **Yes**, indicate the date of FMT and specify the indication. If the indication is not listed on the form, select **Other** and specify the indication.

If multiple FMT's were received during the reporting period, report the first date of FMT performed in the reporting period. Use the process described for reporting partial or unknown dates in [General Instructions, Guidelines for Completing Forms](#) if the exact collection date is not known.



#### **COVID-19 Vaccine**

If the recipient received a COVID-19 vaccine at *any time* (including **pre- or post-infusion**) prior to July 2021 (before the COVID-19 vaccine questions were available on the Post-Infusion Follow-Up (2100) form), select **Yes** for *Was a vaccine for COVID-19 (SARS-CoV-2) received* at the first opportunity this form becomes available. When reporting the vaccine date, report the actual date the recipient received the vaccine, even if the date is outside of the reporting window or prior to infusion, override the error as **Verified Correct** and specify in the comments "Per CIBMTR instructions, report actual vaccine date and verify data field as correct."

### ✿ Combined Follow-Up

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

#### Question 244: Was a vaccine for COVID-19 (SARS-CoV-2) received?

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**.

### ✿ Reporting Multiple COVID-19 Vaccine Doses

FormsNet3<sup>SM</sup> 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 FormsNet3SM application.

Paper form submission: Copy *Specify vaccine type, dose(s) and date received* questions and complete to report all vaccine doses received.

#### Question 245 – 246: Specify vaccine type

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

### ✿ Third versus Booster Doses

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
- One dose of Johnson & Johnson's Janssen

#### Questions 247 – 248: Select dose(s) received (check all that apply)

Report the dose of the vaccine the recipient received in the reporting period. Select all that apply.

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.

If the recipient received two doses in a reporting period, select both **First dose (with planned second dose)** and **Second dose**.

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)
227	8/25/2023	Modify	<p>Diagnosis of COVID-19 after the start of the preparative regimen</p> <p>Any COVID-19 infections diagnosed after the start of the preparative regimen should be reported in the following questions on the Post-HCT Follow-Up (2100) form. <del>An associated Respiratory Virus Post-Infusion Data (2149) form will be generated.</del> <b>Effective August 25, 2023, the Respiratory Virus Post-Infusion Data (2149) form for transplants on the CRF track will no longer be required. Additionally, an unscheduled Respiratory Virus Post-Infusion Data (2149) form cannot be created for these recipients.</b></p>	2149 is no longer required to be completed for recipients on the TED track when there is a diagnosis of COVID-19 post-infusion.

*Last modified: Aug 25, 2023*

# Q249 – 310: Organ Function

## Pulmonary Function



### Bacterial, Viral, and Fungal Pneumonia

Report pneumonia due to infection in the Infection section.

### Questions 249 – 252: Did the recipient develop non-infectious interstitial pneumonitis (IPn or ARDS) / idiopathic pneumonia syndrome (IPS)? (Report infectious pneumonia in infection section)

IPn refers to inflammation of the alveolar walls. Acute respiratory distress syndrome (ARDS) typically refers to fluid build-up within the alveoli. In either case, gas exchange is impaired resulting in oxygen deprivation. Both conditions can result from infectious or non-infectious causes.

Idiopathic pneumonia syndrome (IPS) refers to all non-infectious lung injuries that occur early after HCT (within 100-120 days) including: peri-engraftment respiratory distress syndrome (PERDS), interstitial pneumonitis without a pathogen, radiation / drug-induced lung injury, or transfusion-associated lung injury (TRALI).

Report any non-infectious pulmonary abnormalities diagnosed since the date of the last report. See below for a description of reportable abnormalities as well as common methods of assessment.

Indicate **Yes** or **No** if the recipient developed non-infectious interstitial pneumonitis (IPn or ARDS) / idiopathic pneumonia syndrome (IPS) in the reporting period. If **Yes**, report the diagnosis date and the diagnostic method(s), *other than radiographic studies*. Select all that apply.

If the diagnosis was determined at an outside center and no documentation of a clinical, pathological, or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

Documentation of diagnostic tests may be attached to the form. For further instructions on how to attach documents in FormsNet3, refer to the training guide.

### Diagnostic Methods:

- Bronchoalveolar lavage (BAL): a procedure in which a bronchoscope is guided into the lower respiratory system. Fluid is emitted from the bronchoscope and then collected for further examination.
- Transbronchial biopsy: a procedure in which forceps on the end of the bronchoscope are used to collect lung tissue samples for further examination.
- Open / thorascopic lung biopsy: An open lung biopsy is a procedure in which an incision is made between the ribs to collect a sample of lung tissue for further examination. A thorascopic lung biopsy

is a procedure in which an incision is made to the chest and an endoscope is used to collect samples of lung tissue.

- Autopsy: a post-mortem procedure used to determine the cause of death and to evaluate other disease present at the time of death.

### ✿ Reporting Multiple Other Non-Infectious Pulmonary Abnormalities

**FormsNet3<sup>SM</sup>:** Complete a separate instance of the other non-infectious pulmonary abnormality questions for each other non-infectious pulmonary abnormality the recipient developed in the reporting period by adding an additional instance in the FormsNet3SM application.

**Paper form submission:** Copy the other non-infectious pulmonary abnormality questions and complete for each other non-infectious pulmonary abnormality the recipient developed in the reporting period.

### Questions 253 – 258: Specify other non-infectious pulmonary abnormality developed (e.g. bronchiolitis obliterans, COP / BOOP, diffuse alveolar hemorrhage)

Indicate if the recipient developed any other non-infectious pulmonary abnormality.

- **Bronchiolitis obliterans (BO):** an airway obstruction as a result of inflammation of the bronchioles. This complication typically occurs late after HCT. It is often a manifestation of chronic GVHD. If bronchiolitis obliterans is a result of chronic GVHD, confirm that bronchiolitis obliterans was also reported in the chronic GVHD section of this form.
- **Cryptogenic organizing pneumonia (COP) / Bronchiolitis obliterans with organizing pneumonia (BOOP):** an idiopathic form of pneumonia which affects different parts of the lungs including the bronchioles and alveoli. This complication typically occurs late after HCT.
- **Diffuse alveolar hemorrhage (DAH):** bleeding into the alveolar space typically resulting from an injury to the pulmonary blood vessels.
- **Other non-infectious pulmonary abnormality:** any other non-infectious pulmonary abnormalities not already captured in the above categories. Do not report pleural effusions here.

If the recipient did not develop any other non-infectious pulmonary abnormality, select **None**.

If the recipient developed a non-infectious pulmonary abnormality, report the diagnosis date and specify the diagnostic method, *other than radiographic studies*. Select all that apply.

If the diagnosis was determined at an outside center and no documentation of a clinical, pathological, or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

Documentation of diagnostic tests may be attached to the form. For further instructions on how to attach documents in FormsNet3, refer to the training guide.

**Question 259 – 260: Did the recipient receive endotracheal intubation or mechanical ventilation?**

Endotracheal intubation or mechanical ventilation may be used for respiratory failure or for airway protection from severe mucositis.

Invasive positive pressure ventilation is delivered via an endotracheal tube. Do not include non-invasive positive pressure ventilation that is delivered through an alternate interface (e.g., facemask).

Indicate whether the recipient received endotracheal intubation or mechanical ventilation (invasive positive pressure ventilation) post-HCT. If **Yes**, report the date when endotracheal intubation or mechanical ventilation was started. If the recipient was intubated multiple times within the reporting period, report the first date of intubation. Report **No** if the patient received endotracheal intubation or mechanical ventilation during surgery.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

**Question 261 – 262: Was the recipient successfully extubated?**

Indicate if the recipient was successfully extubated during the reporting period. If **Yes**, report the date of extubation. If the recipient was extubated multiple times within the reporting period, please report the last date of extubation.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

**Liver Toxicity Prophylaxis and Function****Questions 263 – 264: Specify therapy used to prevent liver toxicity (check all that apply)**

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

Select all therapy the recipient received intended to prevent liver toxicity during the reporting period, including therapy given during the preparative regimen. Report only agents given to prevent liver toxicities, not those given to treat a diagnosed liver injury or toxicity.

**Liver Toxicity**

Liver toxicity questions designed to collect information on the level of liver dysfunction that is not related to acute or chronic GVHD (e.g., chemotoxicity, cyclosporine toxicity, veno-occlusive disease [VOD]). Liver dysfunction may be determined by biopsy, viral culture, or suspected by clinical evidence.

### Question 265: Did the recipient develop non-infectious liver toxicity (excluding GVHD)?

Indicate **Yes** or **No** if the recipient developed a non-infectious liver toxicity during the reporting period. Include toxicities which developed between the start of the preparative regimen and the date of last contact (question 1) when completing the 100-day follow-up form. Do not report liver complications due to GVHD in this section.

#### Reporting Multiple Other Non-Infectious Liver Toxicities

**FormsNet3<sup>SM</sup> application:** Complete a separate instance of the *Specify the etiology of the non-infectious liver toxicity etiology* questions for each other non-infectious liver toxicity the recipient developed in the reporting period by adding an additional instance in the FormsNet3<sup>SM</sup> application.

**Paper form submission:** Copy the *Specify the etiology of the non-infectious liver toxicity etiology* questions and complete for each other non-infectious liver toxicity the recipient developed in the reporting period.

### Question 266 – 268: Specify the etiology of the non-infectious liver toxicity etiology

Report the etiology of the non-infectious liver toxicity that the recipient developed in the reporting period and specify the diagnosis date.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

- **Veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS):** occurs following injury to the hepatic venous endothelium, resulting in hepatic venous outflow obstruction due to occlusion of the hepatic venules and sinusoids. This typically results in a distinctive triad of clinical signs including hepatomegaly with right upper quadrant tenderness, third space fluid retention (e.g., ascites), and jaundice with a cholestatic picture. For more information on VOD / SOS including diagnostic criteria, refer to the [VOD / SOS section](#) of the Forms Instructions Manual.
- **Cirrhosis:** Cirrhosis is a degenerative disease in which fibrous tissue forms and the lobes become filled with fat. Cirrhosis may be diagnosed using a liver biopsy, but clinical symptoms (enlarged liver), blood tests, laparoscopy, or radiology imaging are often used to determine the diagnosis of cirrhosis when a liver biopsy is not necessary.
- **Other etiology:** Liver toxicity other than VOD / SOS or cirrhosis. Do not include hepatic infections or GVHD.
- **Unknown etiology:** If there is a liver toxicity; however, there is no information about the etiology of the non-infectious liver toxicity. This option should be used sparingly and only when no judgment can be made about the etiology in the reporting period.

### Thrombotic Microangiopathy (TMA)

Thrombotic microangiopathy (TMA) is a multifactorial condition where intravascular platelet activation, formation of thrombi, and microangiopathic hemolytic anemia occur due to generalized endothelial

dysfunction. Organ injury, specifically the kidney, may occur as a result of these processes.<sup>1</sup> Characteristics of thrombotic microangiopathy includes microangiopathic hemolysis, thrombocytopenia ( $< 50 \times 10^9/L$ ), neurological changes, and pulmonary dysfunction: Other laboratory features include:

- LDH greater than the center-specific upper limit of normal
- Serum creatinine  $> 2$  mg/dL or  $>50\%$  rise over baseline
- Bilirubin greater than twice the center-specific upper limit of normal

1 Jodele, S., M. Davies, and B.L. Laskin. "Diagnostic and Risk Criteria for HSCT-associated Thrombotic Microangiopathy: A Study in Children and Young Adults." *Blood* 124.4 (2014): 645-53. Web.

**Questions 269 – 270: Did the recipient develop post-infusion thrombotic microangiopathy (TMA) or similar syndrome? (includes microangiopathy, thrombotic thrombocytopenia purpura (TTP), hemolytic uremic syndrome (HUS))**

Indicate **Yes** or **No** if the recipient developed post-infusion TMA or a similar syndrome since the date of last report. If **Yes**, report the diagnosis date.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

- Microangiopathy: Disease of the capillaries where the capillaries bleed and slow the flow of blood due to thickening and weakening of capillary walls.
- Thrombotic thrombocytopenia (TTP): Blood disorder where blood clots form in the small blood vessels of the body.
- Hemolytic uremic syndrome (HUS): Abnormal destruction of red blood cells which block the kidneys resulting in kidney failure. May be caused by *Escherichia coli*, other infections, and medications.

If the recipient did not develop post-infusion TMA or a similar syndrome, report **No**.

**Question 271: Specify signs and symptoms (check all that apply)**

Report all signs or symptoms the recipient experienced due to post-infusion TMA or a similar syndrome during the reporting period. Select all that apply.

**Questions 272 – 276: Was TMA evaluated by biopsy?**

Indicate whether TMA was evaluated by a biopsy.

If **Yes**, report if the results as **Positive, Suggestive, Negative, Inconclusive / equivocal**, or **Not done**. If **Other site** is reported, specify the biopsy site.

Indicate whether documentation was submitted to the CIBMTR (e.g., pathology report). For further instructions on how to attach documents in FormsNet3, refer to the training guide.



### Questions 277 – 278: Was therapy given for TMA?

Specify any therapy given in the reporting period for TMA. Report only agents given to treat a diagnosis of TMA. If no therapy was given, select **None**.

### Questions 279 – 280: Did the TMA resolve? (Normalization of renal function, LDH, and resolution or improvement in renal and / or neurologic dysfunction)

Indicate whether TMA resolved. If **Yes**, report the first date the recipient met the following criteria:

- Normalization of renal function (per institutional guidelines);
- Normalization of LDH (per institutional guidelines);
- Resolution / improvement of renal and neurologic dysfunction.

### Other Organ Impairment / Disorder

The intent of this section is to identify serious conditions or impairments occurring after transplant. For the purposes of this manual, the term “clinically significant” refers to conditions requiring treatment or intervention. Additional guidelines for commonly reported organ impairments and disorders are included below. Do not report complications that are expected for most transplant recipients and do not require treatment (i.e., minor complications resolving without intervention).

Report any other clinically significant organ impairment or disorder the recipient developed during the reporting period. If this form is being completed for the 100-day reporting period, include any clinically significant impairments or disorders diagnosed between the start of the preparative regimen and the date of contact (question 1).

Do not report any impairments / disorders which have persisted since the last report. If this form is being completed for the 100-day reporting period, do not report conditions which have persisted since before the start of the preparative regimen.



#### Reporting Multiple Clinically Significant Organ Impairments or Disorders

**FormsNet3<sup>SM</sup>**: Complete a separate instance of the clinically significant organ impairment or disorder questions for each other clinically significant organ impairment or disorder the recipient developed in the reporting period by adding an additional instance.

**Paper form submission**: Copy of the clinically significant organ impairment or disorder questions for each clinically other significant organ impairment or disorder the recipient developed during the reporting period.

### Questions 281 – 305: Specify impairment / disorder

Indicate if any of the organ impairments or disorders listed were diagnosed during the reporting period. If the recipient developed an impairment during the reporting period, select the impairment / disorder, enter the date of diagnosis, and answer any additional questions pertaining to the impairment / disorder. If the diagnosis was determined at an outside center and no documentation of a clinical, pathological, or

laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported.

**Do not report organ impairments or disorders diagnosed prior to the start of the preparative regimen / infusion or in a prior reporting period.**

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

## Renal

- **Acute renal failure requiring dialysis:** report whether dialysis was ordered or recommended for renal failure. Also report whether the recipient received the treatment. Symptoms of renal failure include dehydration, nausea, blood in the urine, and / or swelling of extremities.
- **Chronic kidney disease / renal impairment:** report whether there was chronic kidney disease or renal impairment (persistent decrease in glomerular filtration to  $< 60 \text{ mL/min.1.73m}^2$ ). Also report whether the recipient received treatment. If this is selected, also indicated if the recipient was placed on dialysis.

## Cardiac

- **Arrhythmia:** report whether the recipient developed an arrhythmia, including atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmia. If selected, specify the type of arrhythmia.
- **Cardiomyopathy:** a disease of the heart muscle that makes it more difficult for the heart to pump blood to the rest of the body.
- **Congestive heart failure (CHF):** inability of the heart to supply oxygenated blood to meet the body's needs. Ejection fraction  $< 40\%$ . If selected, report the ejection fraction and specify if the recipient was **Symptomatic** or **Asymptomatic**.
- **Coronary artery disease:** damage or disease in the major blood vessels of the heart. Also called CAD, atherosclerotic heart disease.
- **Unstable angina:** sometimes called acute coronary syndrome and results in unexpected chest pain due to reduced blood flow and oxygen to the heart.
- **Myocardial infarction (MI):** an obstruction in the coronary artery resulting in damage / necrosis to the cardiac muscle.
- **Hypertension (HTN) requiring therapy:** report whether the recipient was still receiving therapy for hypertension on the contact date for the reporting period.
- **Pericarditis:** swelling and irritation of the pericardium.
- **Heart valve disease:** the presence of one or more of the following:
  - Moderate or severe degree of valve stenosis or insufficiency as determined by echo, whether the valve is mitral, aortic, tricuspid or pulmonary
  - Prosthetic mitral or aortic valve
  - Symptomatic mitral valve prolapse

## Vascular

- **Deep vein thrombosis (DVT):** development of a blood clot in a deep vein. Specify if the DVT was

catheter (central line) related in question 291. This information is typically documented within the results of the ultrasound.

- **Pulmonary embolism (PE):** development of a blood clot in the arteries of the lung. Specify if the PE was catheter (central line) related in question 292. This information is typically documented within the results of the ultrasound.
- **Hyperlipidemia (high total cholesterol, low HDL cholesterol, high LDL cholesterol, and/or high triglyceride levels):** high levels of lipids (fat particles) in the blood. Hyperlipidemia is typically diagnosed by a lipid panel. If this is reported, report the diagnosis date as the date when the lipid panel was drawn. Additionally, specify which lipids were assessed and provide the results (fasting results are preferred). Check all apply.

## Neurological

- **CNS hemorrhage:** bleeding within the central nervous system.
- **Encephalopathy:** damage or disease of the brain. Symptoms of encephalopathy include memory loss, personality changes, and declining ability to concentrate and reason.
- **Neuropathy:** nerve damage, usually in hands and feet, which causes pain, weakness, and numbness.
- **Seizures:** sudden, involuntary muscle contractions due to the hyperexcitation of neurons.
- **Stroke / transient ischemic attack:** loss of brain function due to a disturbance in the blood supply to the brain. If the recipient experienced different kinds of strokes in the reporting period, report a separate instance for each type of stroke.

## Endocrine

- **Diabetes / hyperglycemia requiring chronic treatment:** high blood glucose levels. Diabetes / hyperglycemia should only be reported if insulin and / or oral medication is required for treatment. Diabetes / hyperglycemia controlled through diet and exercise should not be reported. Indicate if the recipient was still receiving treatment for diabetes / hyperglycemia on the contact date for the reporting period. Only select this option if the recipient developed diabetes / hyperglycemia requiring treatment post-infusion. Do not report this disorder if the recipient had a diagnosis and was on treatment prior to infusion.
- **Growth hormone deficiency / short stature:** a condition in which the body does not produce enough growth hormone / a reduced overall rate of growth. Indicate if the recipient received therapy for the growth hormone deficiency / short stature.
- **Hypothyroidism requiring replacement therapy:** decreased activity of the thyroid gland. Diagnosis of hypothyroidism includes high levels of thyroid-stimulating hormone (TSH). Symptoms of hypothyroidism include fatigue, depression, weakness, weight gain, musculoskeletal pain, decreased taste, hoarseness, and / or puffy face.
- **Pancreatitis:** inflammation of the pancreas.

## Genitourinary

- **Gonadal dysfunction requiring hormone replacement (testosterone or estrogen):** Females may experience early symptoms of menopause including amenorrhea. Males may experience decreased

spermatogenesis. Low levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and / or testosterone may require hormone replacement therapy.

- **Hemorrhagic cystitis / hematuria requiring medical intervention (catheterization of bladder, extra transfusions, urology consult):** characterized by bleeding and inflammation of the bladder wall. Hemorrhagic cystitis may result from systemic chemotherapy or radiation therapy and / or some viral infections (e.g., BK virus). Report cases with macroscopic (visible to the naked eye) or gross hematuria (WHO Grade III and IV hemorrhagic cystitis). If the etiology is infectious, also report in the Infection section. Examples of medical intervention include catheterization of bladder, extra transfusions, or a urology consult.

## Musculoskeletal

- **Avascular necrosis:** localized tissue death due to inadequate oxygen to the cells. Also known as coagulation necrosis or ischemic necrosis.
- **Osteonecrosis of the jaw:** bones of the jaw weaken and die due to potent antiresorptive medications such as bisphosphonates or RANKL inhibitors, infection, steroid use, and treatment of cancer, including radiation.
- **Osteoporosis:** bones become weak and brittle due to losing bone mass faster than it is created from aging.
- **Osteoporotic fracture:** fractures due to low bone mineral density.

## Psychiatric

- **Depression requiring therapy:** mood disorder resulting in persistent feeling of sadness and loss of interest. Common treatments include antidepressant, anxiolytic, and antipsychotic medications. Common names include Amitriptyline, Bupropion (Wellbutrin), Buspirone, and Abilify.
- **Anxiety requiring therapy:** disorder characterized by feelings of worry, anxiety, or fear which are strong enough to interfere with daily activities. Common medications include Duloxetine (Cymbalta), Diazepam (Valium), Buspirone, Pregabalin (Lyrica).
- **Post-traumatic stress disorder (PTSD) requiring therapy:** condition triggered by seeing or experiencing a traumatic event.

## Other

- **Cataracts:** loss of transparency in the lens of the eye.
- **Iron overload requiring therapy:** condition characterized by having too much iron in the body. Therapy includes phlebotomy and iron chelation. Indicate which therapy is required. Check all apply.

*Iron overload cannot be answered on the day 100 form. Iron overload questions will be answered for all subsequent reporting periods.*

- **Mucositis requiring therapy:** inflammation and ulceration of mucous membranes that line the digestive tract, usually due to chemotherapy and radiotherapy. Specify the grade as **0 (none)**, **I (mild) – oral soreness, erythema**, **II (moderate) – oral erythema, ulcers, solid diet tolerated**, **III (severe) – oral ulcers, liquid diet only**, or **IV (life-threatening) – oral ulcers, oral alimentation impossible**

in question 304. The highest grade in the reporting period should be reported. Do not report mucositis which did not require treatment or intervention during the reporting period.

*Mucositis can only be answered on the day 100 form. Mucositis questions will be skipped for all subsequent reporting periods.*

- **Other impairment or disorder:** use this category to report any clinically significant impairment(s) / disorder(s) not listed on the form. Specify the other impairment / disorder.

Do not report complications that have been reported elsewhere on the form.

- **None:** If there are no other organ impairments / disorders, select this option.

### Questions 306 – 310: Has the recipient received a solid organ transplant since the date of last report?

Indicate whether the recipient received a solid organ transplant since the date of the last report. If **Yes**, specify the organ transplanted. If **Other organ** is reported, specify organ. Additionally, report the date of the solid organ transplant and specify the solid organ donor type.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

If the recipient did not receive a solid organ transplant during the reporting period, report **No**.

Solid organ transplant questions cannot be answered on the day 100 forms. These questions will be answered for all subsequent reporting periods.

### Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q281 – 305	2/15/ 2023	Add	Clarification added on how to report the mucositis grade: <b><i>Mucositis requiring therapy: inflammation and ulceration of mucous membranes that line the digestive tract, usually due to chemotherapy and radiotherapy. Specify the grade as 0 (none), I (mild) – oral soreness, erythema, II (moderate) – oral erythema, ulcers, solid diet tolerated, III (severe) – oral ulcers, liquid diet only, or IV (life-threatening – oral ulcers, oral alimentation impossible in question 304. The highest grade in the reporting period should be reported. Do not report mucositis which did not require treatment or intervention during the reporting period.</i></b>	Added for clarification



# Q311: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder



## Combined Follow-Up

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

### **Question 311: Did a new malignancy, myelodysplastic, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the infusion was performed? (Include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders)**

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

Report relapse of the recipient's primary disease on the appropriate post-HCT disease-specific data form. Relapse of a prior malignancy will not be captured by the CIBMTR.

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

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

The following should not be reported as new malignancy:

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



## Post-Transplant Lymphoproliferative Disorder (PTLTD)

PTLTD should be reported as a new malignancy if it was confirmed via a biopsy (treatment not required) or suspected to be PTLTD 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. However, in the case of a basal cell or squamous cell skin cancer, report each discreet episode as a new malignancy. See Example 3 below for additional information.

If a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was diagnosed during the reporting period, report **Yes** and the Subsequent Neoplasm (3500) form 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 due 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.** A recipient developed a new malignancy at Day +68 and is reported at the time the Day 100 Post-Infusion Follow-up (2100) form is completed. In this scenario, report **Yes**, the recipient developed a new malignancy and a Subsequent Neoplasms (3500) form will be completed to report the new malignancy information. For all future reporting periods, select **No**.

**Example 2.** A recipient developed a new malignancy during the seven-year reporting period and the transplant center decided to create the Subsequent Neoplasms (3500) form as an unscheduled form in FormsNet3<sup>SM</sup> to report the new malignancy information immediately since a Post-Infusion Follow-Up for seven-year reporting period will not come due. When the eight-year Post-Infusion Follow-Up (2100) form is completed, **Previously reported**, will be reported since a prior Subsequent Neoplasms (3500) form has already been submitted for the new malignancy.

**Example 3.** A recipient was diagnosed with basal cell skin cancer on the neck in the one-year reporting period and two months later, within the same reporting period, there was a diagnosis of basal cell located on the nose. The lesion on the nose is not considered a metastasis from the neck, but a new discreet lesion. Report **Yes**, there was a new malignancy on the Post-HCT Follow-Up (2100) and a single Subsequent Neoplasms (3500) form will come due to report one of the basal cell malignancies. Create a second Subsequent Neoplasms (3500) form to report the other basal cell malignancy as these are discreet episodes.

#### **Section Updates:**

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q311	7/19/2023	Modify	Clarified which option to select for PTLD: <i>Indicate whether a new or secondary malignancy, lymphoproliferative disorder, or myeloproliferative disorder has developed. Do not report recurrence, progression, or transformation of the recipient's</i>	Added for clarification



			<p><i>primary disease (disease for which the transplant was performed), or relapse of a prior malignancy.</i></p> <p><i>New malignancies, lymphoproliferative disorders, or myeloproliferative disorders include but are not limited to:</i></p> <ul style="list-style-type: none"> <li>• <i>Skin cancers (basal, squamous, melanoma)</i></li> <li>• <i>New leukemia</i></li> <li>• <i>New myelodysplasia</i></li> <li>• <i>Solid tumors</i></li> <li>• <i>PTLD (post-transplant lymphoproliferative disorder) (report as <del>lymphoma or lymphoproliferative disease</del> <b>NHL</b> )</i></li> </ul>	
Q311	7/19/2023	Add	<p>Blue PTLD info box added: <b>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.</b></p>	Added for clarification

Last modified: Jul 19, 2023

# Q312 – 335: Functional Status



## Combined Follow-Up

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



*The Was the intent to complete the HCT procedure as an outpatient, Did the recipient require an unplanned admission, Was the recipient discharged prior to the date of contact, and Total number of inpatient days in first 100 days post-HCT questions will only be answered on the day 100 form. Centers will not be able to complete these questions for any subsequent reporting periods.*

### Question 312: Was the intent to complete the HCT procedure (conditioning, infusion, and period of recovery from neutropenia) as an outpatient?

Report **Yes** if the plan was to complete all conditioning, infusions, and recovery in the outpatient setting. If the plan was to admit the patient for any part of the transplant, report **No**.

Report **Yes** even if the recipient required an unplanned admission.

### Question 313: Did the recipient require an unplanned admission?

Report whether the recipient required an unplanned admission during the reporting period. This includes unplanned admissions for the purpose of completing an infusion as well as admissions to address any post-infusion complications. Report **Yes** if an unplanned admission was required. If the recipient did not require an unplanned admission, report **No**.

### Questions 314 – 315: Was the recipient discharged prior to the date of contact?

If the recipient was discharged from the hospital during the reporting period, report **Yes** and report the date the recipient was discharged. If the recipient was admitted to the hospital multiple times during the reporting period, report first discharge date. If the recipient was not discharged from the hospital during the reporting period, report **No**.

If the recipient died without ever being discharged from the hospital, report **No**.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### Question 316: Total number of inpatient days (day 0 to day 100) in first 100 days post-HST

Enter the total number of inpatient days (including day 0). If the recipient was discharged and readmitted during the first 100 days, the total should include days hospitalized after being readmitted. When counting

the total number of inpatient days, count either the day of admission or the day of discharge; do not count both.

If the recipient receives a subsequent infusion prior to day 100, do not include the start date of the preparative regimen for the subsequent infusion (or the date of the subsequent infusion if no preparative regimen was given).

### Questions 317 – 319: Recipient height (most recent)

*These questions will only be enabled / answered for pediatric patients ( $\leq 16$  years old) when the form visit ID is 6 months or greater. These questions will be disabled / not answered for all recipients on the day 100 follow-up form.*

Indicate whether the recipient's height is known. If **Known**, report the recipient's most recent height, specify the units, and report the date the height was measured. If the recipient's height was not measured during the reporting period, report **Unknown**.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### Questions 320 – 322: Recipient weight: (most recent)

Indicate whether the recipient's weight is known. If **Known**, report the recipient's most recent weight, specify the units, and report the date the weight was measured. If the recipient's weight was not measured during the reporting period, report **Unknown**.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### Questions 323 – 325: Functional status

The CIBMTR uses the Karnofsky / Lansky scale to determine the functional status of the recipient on the date of contact. The Karnofsky Scale is designed for recipients aged 16 years and older and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. If the recipient is less than one year old, leave questions 323 – 325 blank. If the recipient passed away during the reporting period, this question will be disabled.

Select the appropriate performance scale, Karnofsky or Lansky, based on the recipient's age. Using this scale, select the score (10-100) that best represents the recipient's activity status immediately prior to the date of last actual contact. Acceptable performance scores include those recorded within 14 days prior to 100 Day and Six-Month contact dates. For the annual reporting periods, performance scores may be reported if dictated within one month of the contact date. The only valid scores are 10-100; zero is not a valid response for this scale, nor are values not ending in zero, such as "85." The Karnofsky / Lansky scale can be found in [Appendix L](#).

Recipient performance status is a critical data field that has been determined to be essential for all outcome-

based studies. Determination of performance status is ideally performed by a healthcare provider. Centers are encouraged to put tools in place to facilitate this collection. If a Karnofsky / Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician's clinic note), data professionals are encouraged to discuss a determination with the physician or mid-level health care provider (NPs and PAs) rather than make an assignment themselves, based on inadequate information. Documentation from an RN who has been trained and authorized to determine performance scores may also be used.

The CIBMTR recognizes that some transplant centers prefer to assign and use the ECOG performance score as opposed to the Karnofsky / Lansky score. Although the ECOG and Karnofsky / Lansky performance score systems are based on similar principles, the scales are not the same. For example, the Karnofsky / Lansky scale is described in 10 categories, whereas the ECOG performance status is reported in six categories. Due to the overlap between the two systems, an ECOG score of "one" can represent either "80" or "90" on the Karnofsky / Lansky scale; whereas, a Karnofsky / Lansky score of "80" or "90" is converted directly to an ECOG score of "one." Therefore, the Karnofsky / Lansky scale can be more accurately converted into ECOG.

However, for centers that collect only an ECOG performance score, CIBMTR will make the following accommodations when auditing the source data:

- Centers assigning ECOG scores should do so using standard practices to ensure accuracy.
- For the purposes of CIBMTR reporting, conversion of ECOG to Karnofsky / Lansky should follow a standard and consistent practice to account for the lack of direct mapping. This practice should be clear and reproducible.



### **Pregnancy Questions**

Questions 325 and 326 will only be answered for recipients between the ages of 10 and 60.



### **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 the pregnancy questions, on the Post-HCT Data (2100) form are disabled when there is a cellular therapy and an HCT.

### **Question 326: 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 below.

Contact CIBMTR Center Support with questions.

**Question 327: 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 below.

Contact CIBMTR Center Support with questions.

**Example 1.** A recipient or recipient's female partner becomes pregnant at Day +68 and is reported at the time when the Day 100 Post-Infusion Follow-Up (2100) form is completed. The recipient or recipient's female partner is still pregnant at the six-month reporting period and then delivers the baby during the one-year reporting period. The recipient / recipient's female partner does not become pregnant again.

For the Day 100 reporting period, question 325 or 326 should be reported as **Yes** and the Pregnancy (3501) form will be completed to report the pregnancy information. For the six-month and one-year reporting periods, **Previously reported** should be selected since the recipient / recipient's female partner was still pregnant during the reporting period and a prior Pregnancy (3501) form has already been submitted for the pregnancy. For all future reporting periods, select **No**.

**Example 2.** A recipient or recipient's female partner becomes pregnant during the seven-year reporting period and the transplant center decided to create the Pregnancy (3501) form as an unscheduled form in FormsNet3<sup>SM</sup> to report the pregnancy information immediately since a Post-Infusion Follow-Up for seven-year reporting period will not come due. When the eight-year Post-Infusion Follow-Up (2100) form is completed, **Previously reported**, will be reported since a prior Pregnancy (3501) form has already been submitted for the pregnancy.

**Questions 328 – 330: Has the recipient smoked tobacco cigarettes since the date of last report?**

The intent of this question is to determine the recipient's history of smoking cigarettes only. Do not report the use of cigars, pipe tobacco, chewing tobacco, electronic cigarettes, vaping or other drugs. Report **Yes** if the recipient has smoked tobacco cigarettes since the date of the last report and capture the average number of packs (20 cigarettes per pack) smoked a day, if known. If the recipient has not smoked tobacco cigarettes since the date of the last report, or their smoking history is not known, report **No** or **Unknown**.

**Questions 331 – 332: Specify the category which best describes the recipient's current occupation**

Select the category that best describes the recipient's current occupation. If the recipient is younger than school-aged, select **Under school age**. If the recipient is a student, select **Not employed**. If **Other** is selected, specify the recipient's occupation.

Only one work status may be reported. If a recipient has multiple work opportunities during the current reporting period, report the highest level of work being performed. For example, full time work would be reported over part time work.

### Questions 333 – 335: What is the recipient’s current or most recent work status?

Select the work status that best describes the recipient’s current or most recent employment during this reporting period. If the recipient is **Retired**, specify their retirement status. If the recipient’s status is anything other than **Full time**, indicate if the recipient claimed medical disability due to any illness.

#### Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q328 – 330	5/1/ 2023	Add	Instructions updated on what to not consider when reporting smoked tobacco cigarettes: <i>The intent of this question is to determine the recipient’s history of smoking cigarettes only. Do not report the use of cigars, pipe tobacco, chewing tobacco, <b>electronic cigarettes, vaping</b> or other drugs. Report <b>Yes</b> if the recipient has smoked tobacco cigarettes since the date of the last report and capture the average number of packs (20 cigarettes per pack) smoked a day, if known. If the recipient has not smoked tobacco cigarettes since the date of the last report, or their smoking history is not known, report <b>No</b> or <b>Unknown</b>.</i>	Added for clarification
Q333 – 335	5/1/ 2023	Add	Instructions clarified: <i>Select the work status that best describes the recipient’s current or most recent employment during this reporting period. If the recipient is <b>Retired</b>, specify their retirement status. If the recipient’s status is anything other than <b>Full time</b>, indicate if the recipient claimed medical disability <b>due to any illness</b>.</i>	Added for clarification

*Last modified: Jul 19, 2023*

## Q336 – 339: Subsequent HCT



### Subsequent HCT

Complete this section only if the recipient received a subsequent HCT. The data reported in this section should reflect the clinical status immediately prior to the start of the preparative regimen for the subsequent HCT.

A new Pre-TED (2400), Disease Classification (2402), and Recipient Baseline (2000) form must be completed for the subsequent HCT. The exception to this is an autologous HCT performed for graft failure / insufficient hematopoietic recovery. The cells used for this subsequent autologous HCT would have been collected prior to the previous HCT.

For more information on how to distinguish infusion types (i.e., HCT vs DCI), see [Appendix D](#).

### Question 336: Date of subsequent HCT

Report the date when the recipient received the subsequent HCT.

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms](#).

### Questions 337: What was the indication for subsequent HCT?

Indicate the reason for the subsequent HCT (check only one).

- **Graft failure / insufficient hematopoietic recovery:** Additional hematopoietic stem cells are required because there wasn't any ANC recovery following HCT (primary graft failure), the hematopoietic recovery indefinitely declined after the initial hematopoietic recovery (secondary graft failure), or hematopoietic recovery was deemed insufficient or slow for survival following previous high-dose therapy and HCT. If autologous cells are infused for this reason, this is considered autologous rescue; in this case, reporting will continue under the prior HCT date and a new Pre-TED form is not required.
- **Persistent primary disease:** Additional hematopoietic stem cells are required because of the persistent presence of disease pre- and post-transplant (i.e., complete remission was never achieved following the previous transplant).
- **Recurrent primary disease:** Additional hematopoietic stem cells are required because of relapsed primary disease (i.e., complete remission was achieved pre- or post-transplant, but the disease relapsed following the previous transplant).
- **Planned subsequent HCT, per protocol:** Additional hematopoietic stem cells are given as defined by the protocol for a subsequent transplant / infusion. This transplant is not based upon recovery, disease status, or any other assessment.
- **New malignancy (including PTLD and EBV lymphoma):** Additional hematopoietic stem cells are required because the recipient has developed a new malignancy. This does not include a transformation or progression of the original malignancy for which the recipient was transplanted (refer to *New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder* section for

more information).

- **Insufficient chimerism:** In the case of a stable, mixed donor chimerism, the infusion of additional cells (usually lymphocytes and not mobilized hematopoietic stem cells) is typically classified as a DCI. Verify with the transplant physician that the cells given should be reported as a subsequent transplant and that stable, mixed chimerism is the reason for the transplant. In the case of declining chimerism—when the percentage of donor cells is sequentially decreasing on several studies, indicating possible impending graft failure—additional stem cells are required. Usually the donor chimerism has fallen below 30-50%.
- **Other:** If additional hematopoietic stem cells are given for a reason other than the options listed, select **Other** and specify the other indication for the subsequent transplant.

### Question 339: Source of HSCs (check all that apply)

Specify the hematopoietic stem cell source(s) of the recipient's subsequent HCT. Check all that apply.

#### Section Updates:

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

*Last modified: Sep 23, 2022*