2100: 100 Days Post-HCT (Revision 3)

A transplant center designated as a *Comprehensive Report Form* center will submit data on the Pre-TED Form, 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 General Instructions, Center Type and Data Collection Forms).

The 100 Day Post-HCT Form (2100) captures specific data occurring from the start of the preparative regimen to 100 days post-HCT. The following recipient data should be collected from an actual examination (or other recipient contact), as close to day 100 as possible, 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, subsequent HCT, and Donor Cellular Infusion (DCI) information.

Subsequent HCT:

If this form reports a subsequent stem cell infusion, report data from the start of the first preparative regimen to the day before the preparative regimen begins for the subsequent HCT. If no preparative regimen is given for the subsequent transplant, report data from the start of the first preparative regimen to the day before the subsequent HCT. When reporting the date of actual contact (question 1), report the dates specified above (either the date the day before subsequent preparative regimen begins or date the day before subsequent transplant), regardless of whether there is actual patient contact on that date. This is an exception to standard date-of-contact reporting to ensure all dates are captured within the sequence of forms when reporting subsequent HCTs.

If a recipient receives a subsequent HCT prior to the 100 day follow-up time period, the Comprehensive Research Form sequence will start over again with a Pre-TED Form (2400) and another Baseline Form (2000). **For recipients of multiple transplants, transplant centers are not granted access to the new Pre-TED Form in FormsNet3^{SM} until the Form 2100/2200/2300 from the previous transplant has been completed.** Transplant centers can use the FormsNet3^{SM} application to determine if a Pre-TED is due by either: 1) accessing the Forms Due Report, or 2) entering the recipient's unique ID (CRID) in the Patient Forms Due field. Contact your center's CIBMTR CRC if you have questions about the forms due for a recipient.

> ! If the recipient receives an **autologous HCT as a result of a poor graft or graft failure**, the Comprehensive Research 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.

Lost to Follow Up:

Occasionally, centers may lose contact with recipients for a variety of reasons, including their moving, changing physicians, or death. If contact with a recipient appears lost, please consider calling the recipient at home or work, sending a letter, communicating with the treating or referring physician, contacting the hospital billing department, or beginning a search request with the CIBMTR. If your center receives documented information that a recipient is alive or dead, the form should be filled out with the recipient vital status. If no documentation exists and several unsuccessful attempts have been made to contact the recipient, they are considered lost to follow-up, and the center should indicate this status in FormsNet for each reporting period in which no contact exists.

Manual Updates:

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

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

Date	Manual Section	Add/ Remove/ Modify	Description
8/ 29/ 16	2100: 100 Days Post-HCT	Add	Added text to the information banner beneath question 72: The CD20+ data field can capture CD19+ or CD20+ cells. *The CD56+ data field can capture CD56+ or CD16+ cells.*
8/ 26/ 16	2100: 100 Days Post-HCT	Add	Added text to Table 3 to clarify how centers should report chimerism testing performed on sorted marrow samples.
8/ 26/ 16	2100: 100 Days Post-HCT	Add	Added the following information text to question 452: If the recipient receives a subsequent HCT prior to day 100, do not include the start date of the preparative regimen for the subsequent HCT (or the date of the subsequent infusion if no preparative regimen was given).
3/ 31/ 16	2100: 100 Days Post-HCT	Add	Added the following informational text to question 74: The CD20+ data field can capture CD19+ or CD20+ cells
2/ 16/ 16	2100: 100 Days Post-HCT	Add	Added Codes for Indication of Therapy Table for questions 9-33. *[see table in text]*
2/9/ 16	2100: 100 Days Post-HCT	Modify	Modified pediatric acute GVHD Gut guidelines to question 151. See table for details.
1/ 22/ 16	2100: 100 Days Post-HCT	Modify	Updated footnote 4 below acute GVHD staging and grading table: Persistent nausea with *or without* histologic evidence of GVHD in the stomach or duodenum.
9/ 17/ 15	2100: 100 Days Post-HCT	Remove	Removed information box in Engraftment Syndrome Section: If this was an autologous or syngeneic HCT, continue with the Infection section at question 201.
6/ 26/ 15	2100: 100 Days Post-HCT	Modified	Updated language in warnings to Chimerism Studies, and added warnings to Engraftment Syndrome and GVHD [Acute and Chronic] sections that state autologous and sygeneic HCTs should skip the applicable sections.
6/ 12/ 15	Manual-wide	Modify	Language relating to the Lost-to-Follow-Up (2802) has been removed.
6/ 12/ 15	2100: 100 Days Post-HCT	Modify	Modified the informational text prior to question 110: ~~ATG given *before* Day 0 as GVHD prophylaxis should be reported in the preparative regimen section on the Baseline Form (questions 107-111) and on the Pre-TED form (questions 168-172).~~ ~~Report ATG given *after* Day 0 as GVHD prophylaxis in the acute GVHD prophylaxis section on the 100 Day Post-HCT Data Form (questions 111-113) and on the Pre-TED form (questions 317-319).~~ ~~Please note, ATG given pre and post transplant for GVHD prophylaxis would be reported in both the preparative regimen and GVHD prophylaxis sections of the~~

			~~Pre-TED form.~~ For ATG, Campath, and Cyclophosphamide: If these agents are given for GVHD prophylaxis both prior to and after Day 0, they must be reported in separate sections of the Pre-TED form, and Recipient Baseline Forms. Report doses given prior to Day 0 in the preparative regimen section of the Pre-TED (questions 168-315) and Recipient Baseline (107-242). If given after Day 0 as planned GVHD prophylaxis, report in the GVHD prophylaxis section of the Pre-TED (questions 316-341) and below.
6/12/15	2100: 100 Days Post-HCT	Add	Added explanatory text to question 151: Indicate the maximum grade of acute GVHD present during this reporting period [including acute GVHD that persists from a previous HCT or donor cellular infusion (DCI)]. If acute GVHD was present, but the maximum grade was not documented nor is it able to be determined from the grading and staging table, leave the maximum overall grade blank and override the error as "Unknown." **Example 1:** A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging/grading can be determined using Table 4. **Example 2:** A recipient developed acute liver GVHD with elevated LFTs with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in Table 4; "present, grade unknown" would be the best option to report.
6/5/15	2100: 100 Days Post-HCT	Add	Added pediatric acute GVHD Gut guidelines to question 151. See table for details.
6/5/15	2100: 100 Days Post-HCT	Modify	Modified text of questions 291-295: **Organism:** From the ~~table "Codes for Commonly Reported Organisms,"~~ **drop down menu**, select the code corresponding to the identified or suspected organism … … **Site:** From the ~~table "Codes for Common Sites of Infection,"~~ **drop down menu**, select the code corresponding to the site of the infection…
5/29/15	2100: 100 Days Post-HCT	Modify	Modified text in questions 500-506 to clarify FormsNet reporting: Report the total number of cells infused and specify the exponent for each cell type. If the cells were cryopreserved, report the totals after processing, but before cryopreservation. ~~If completing the paper version, copy this page to report more thanone infusion. -The FormsNet3SM application will allow as many infusion entries as needed for the 10-week period. (In Example 5, there would be 4 entries for the first 10-week period).~~ **If multiple cellular infusions were given within the 10-week period, report the cumulative total of all cells infused; submit a log of appended documents showing the product analyses for each individual DCI product.**
5/22/15	2100: 100 Days Post-HCT	Modify	Added "Oral Beclomethasone" to the following text in question 161-187: Refer to questions 111-139 for a description of each agent listed. "Systemic" refers to drugs given by mouth, intramuscularly (IM), or intravenously (IV). "Topical" refers to drugs applied to the skin, eye drops, or inhalation therapy. An exception to this guidance would be the drugs budesonide **and oral**

			beclomethasone. They are drugs given by mouth for treatment of gut GVHD, but considered a “topical” since they’re not absorbed.

Q1-7: Vital Status

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 evaluate medical status for this follow-up report.

In general, the date of contact should be reported as close to the 100 day, six month, or annual anniversary to transplant as possible. Report the date of actual contact with the recipient to evaluate medical status for the reporting period. Preferred evaluations include those from the transplant center physician, referring physician, or other physician currently assuming responsibility for the recipient's care. In the absence of contact with a physician, other types of contact may include a documented phone call with the recipient, a laboratory evaluation, or any other documented recipient interaction on the date reported. If there was no contact on the exact time point, choose the date of contact closest to the actual time point. Below, the guidelines show an ideal approximate range for reporting each post-transplant time point:

Form	Time Point	Approximate Range
100 Days Post -HCT Data (Form 2100)	100 days	+/- 15 days (Day 85-115)

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

Example 1. The 100 day date of contact doesn't fall within the ideal approximate range.
The autologous recipient was transplanted on 1/1/13 and is seen regularly until 3/1/13. After that, the recipient was referred home and not seen again until 7/1/13 for a restaging exam and 7/5/13 for a meeting to discuss the results.

What to report:
100 Day Date of Contact: 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)
6 Month Date of Contact: 7/5/13 (note the latest disease assessment would likely be reported as 7/1/13)

Example 2. The 100 day date of contact doesn't fall within the ideal approximate range and the recipient wasn't seen again until 1 year post-HCT.
The autologous recipient was transplanted on 1/1/12 and is seen regularly until 3/1/12. After that, the

recipient was referred home and not seen again until 1/1/13 for a restaging exam and 1/4/13 for a meeting to discuss the results.

What to report:
100 Day Date of Contact: 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)
6 Month Form: Indicate the recipient is lost to follow-up in FormsNet
1 Year Date of Contact: 1/4/13 (note the latest disease assessment would likely be reported as 1/1/13)

Additional Information

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

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

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

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

Example 4. The recipient has died after their six month anniversary.
The recipient is transplanted on 1/1/13, was seen regularly through the first 100 days. They had restaging exams on 4/22/13 and was seen on 4/23/13. Based on findings in the restaging exam, the recipient was

admitted for additional treatment. The disease was found to be refractory on a 6/25/13 restaging exam, and the recipient was discharged to hospice on 7/8/13. The hospital was notified via telephone that the recipient died on 7/16/13.

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

Date of Contact & Subsequent Transplant

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

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

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

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

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

Reporting Date of Actual Contact for Subsequent HCTs
When reporting the date of actual contact prior to a subsequent HCT, report the dates specified above regardless of whether there is actual patient contact on the date. This is an exception to standard date of contact reporting to ensure all dates are captured within the sequence of forms.

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

Question 2: Did this patient receive the scheduled HCT?

If the recipient received the scheduled HCT, check "yes" and continue with question 5. If the recipient did not receive the scheduled HCT, check "no" and continue with question 3.

Questions 3-4: Reason

Select the reason the recipient did not receive the scheduled HCT. If the HCT was cancelled, continue with question 4 and specify the reason the HCT was cancelled.

Question 5: Did the recipient receive a subsequent HCT (bone marrow, mobilized peripheral blood stem cells, cord blood) prior to day 100 after the HCT for which this form is being completed?

Indicate whether the recipient received a second (or third, etc.) stem cell infusion. Stem cells are defined as mobilized peripheral blood stem cells, bone marrow, or cord blood. The source of the stem cells may be allogeneic unrelated, allogeneic related, or autologous. For more information on how to distinguish infusion types (example: HCT versus DCI), see Appendix O.

If "yes," the answers to the subsequent questions should reflect the clinical status of the recipient immediately prior to the start of the preparative regimen for subsequent HCT. If no preparative regimen is given, the answers to the subsequent questions should reflect the clinical status of the recipient immediately prior to the subsequent HCT. Also, complete Subsequent HCT section (questions 454-461). **Some data regarding the subsequent HCT (questions 454-461) are reported on this form even though this data fall outside of the reporting period for this form.**

> **Reporting Subsequent HCTs**
> It is important to note that the date of the actual contact for the Form 2100 being completed should be *before* the date of a subsequent HCT. Also, even if the subsequent transplant date *falls outside of the reporting period for this form*, the answer to "did the recipient receive a subsequent HCT" must be "yes." Answering "yes" to this question triggers a subsequent Pre-TED form (2400) to be made due in FormsNet.

Question 6: Specify the recipient's survival status at the date of last contact

Indicate the clinical status of the recipient on the date of actual contact for follow-up evaluation.

If the recipient is alive, answers to subsequent questions should reflect the recipient's clinical status from the start of the preparative regimen to the day of actual contact for this follow-up evaluation (question 1).

If the recipient has died, answers to subsequent questions should reflect the recipient's clinical status between HCT and their death. You will also need to complete a Recipient Death Data Form (2900).

Question 7: Has the recipient received a donor cellular infusion (DCI)?

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.

A DCI should be reported for a recipient who received cells from the original donor without a preparative regimen. However, **if the recipient received an additional infusion due to engraftment problems** (e.g., no engraftment, partial or poor engraftment, loss of graft, or late graft failure), **or if cells from a different donor are used, report this as a subsequent HCT, *not* a DCI.**

Indicate whether the recipient received a DCI prior to 100 days post-HCT. If "yes," also complete the DCI information in questions 462-560.

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

Additional information regarding DCIs is available on the CIBMTR website: http://www.cibmtr.org/Meetings/Materials/CRPDMC/index.html

Q8-33: Hematopoietic Reconstitution Post-HCT

Question 8: Did the recipient receive hematopoietic, lymphoid growth factors or cytokines after the start of the preparatory regimen?

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.

Indicate whether the recipient received hematopoietic growth factors, lymphoid growth factors, or cytokines between the start of the preparative regimen and 100 days post-HCT. If “yes,” continue with question 9. If “no,” continue with question 34.

Questions 9-33: Specify agents and provide dates for the first course of each agent given in this reporting period

Specify if each agent listed was given to the recipient and report the date the first course of therapy was started. If a specific agent is not listed, select “other agent,” and specify the agent in question 31.

Using the “Codes for Indication of Therapy” table, enter the indication for the therapy. If G-CSF or Erythropoietin is selected, further specify the drug given to the recipient.

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

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.

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.

Velafermin (recombinant human fibroblast growth factor [rhFGF]): Velafermin 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 Velafermin 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.

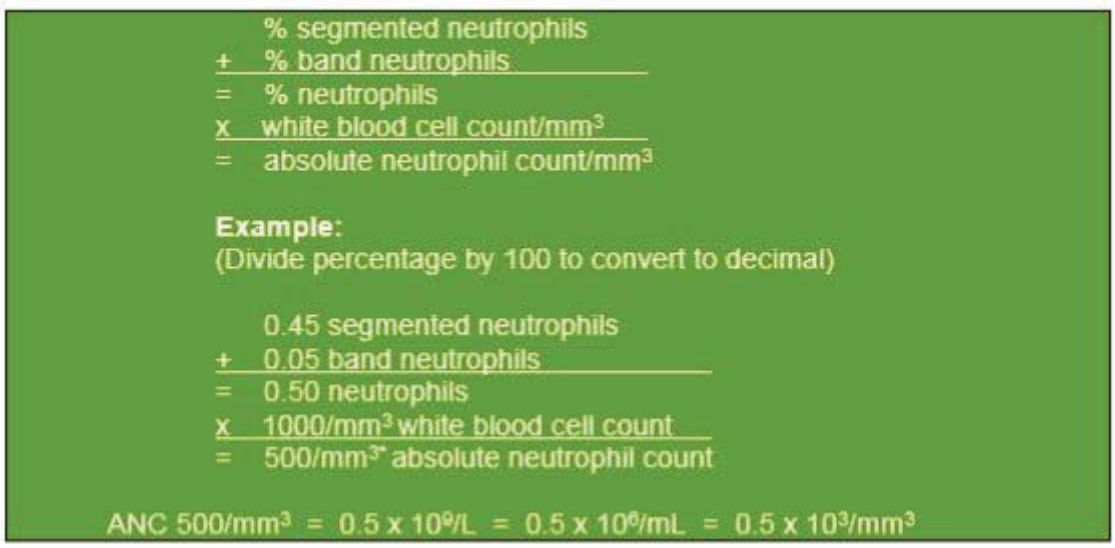
Codes for Indication of Therapy

Code	Desciption
0	Planned therapy per protocol (note: for mucositis prophylaxis, use code 10)
1	Intervention for delay / decline in absolute neutrophil count (ANC)
2	Intervention for delay / decline in platelets
3	Intervention for delay / decline in both ANC and platelets
4	Intervention for delay/ decline in red blood cell counts
5	Anti-leukemic or tumor agent to prevent relapse
6	Anti-leukemic or tumor agent to treat relapse
10	Planned therapy to prevent mucositis
90	Other Indication

Q34-43: Granulopoiesis / Neutrophil Recovery

Granulopoiesis/neutrophil recovery is defined as an absolute neutrophil count (ANC) of ≥ 0.5 × 10^9/L (500/mm^3) for three consecutive laboratory values obtained on different days. Date of ANC recovery is the date of the first of three consecutive laboratory values where the ANC is ≥ 500/mm^3. At some institutions, the laboratory reports display the ANC value once there are sufficient white blood cells to perform a differential count. If the laboratory reports do not display the ANC value, 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, the actual ANC value should be calculated from the manual differential if available. The calculated value from the manual differential will determine ANC recovery. If your institution's laboratory reports do not display the ANC value, use the following calculation to determine the ANC:

Example 1. Calculating Absolute Neutrophil Count (ANC)



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

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 (question 36), the first decline (question 37), and the last recovery (question 41).

Tracking the date of ANC recovery may not always be straightforward. In some cases the ANC may fluctuate for a period of time before the recipient fully recovers. In other cases the ANC may remain above 0.5×10^9/L for several days immediately post-HCT and then fall below 0.5×10^9/L. Do not begin counting ANC values of $\geq 0.5 \times 10^9$/L towards recovery until the ANC has dropped to the lowest level (nadir) post-HCT. If the recipient was transplanted using a non-myeloablative (NST) or reduced intensity (RIC) regimen, or was transplanted for an immunodeficiency (e.g., SCID, WAS), the recipient's ANC may never drop below 0.5×10^9/L. If this is the case, an ANC recovery date will not be reported, and the "never below" option should be chosen. However, if the recipient's ANC drops below 0.5×10^9/L for even one day, this should be considered the nadir and "never below" should not be chosen. See the following example for more information regarding tracking the date of ANC recovery.

Example 2: Tracking ANC Recovery – Initial Recovery without Subsequent Decline

Transplant Date = May 6
Contact Date = August 15

Date	WBC	%Neutrophils	ANC	
May 7	900	0.6	540	
May 8	850	0.59	502	
May 9	720	0.7	504	
May 10	300	0.45	135	
May 11	15	No differential	—	
May 12	30	No differential	—	
May 13	50	No differential	—	
May 14	250	0.4	100	
May 15	800	0.7	560	*Date of initial recovery: ANC ≥ 500/mm^3 (report this date in question 35)*
May 16	1050	0.8	840	

May 17	1000	0.7	700	
May 18	1800	0.6	1080	
May 19	2000	0.55	1100	
May 20	2500	0.53	1325	
May 21-August 14	—	—	—	ANC ≥ 500/mm^3) for timeframe
August 15 (contact date)	2250	0.43	968	

Example 3: Tracking ANC Recovery – Initial Recovery with Subsequent Decline and Recovery

Transplant Date = May 6
Contact Date = August 15

Date	WBC	%Neutrophils	ANC	
May 7	900	0.6	540	
May 8	850	0.59	502	
May 9	720	0.7	504	
May 10	300	0.45	135	
May 11	15	No differential	—	
May 12	30	No differential	—	
May 13	50	No differential	—	
May 14	250	0.4	100	
May 15	800	0.7	560	*Date of initial recovery: ANC ≥ 500/mm^3 (report this date in question 36)*
May 16	1050	0.8	840	
May 17	1000	0.7	700	
May 18	1800	0.6	1080	
May 19	2000	0.55	1100	
May 20	2500	0.53	1325	
May 21	2250	0.43	968	
May 22	1500	0.45	675	

May 23	800	0.6	480	*Date of first decline: ANC ≤ 500/mm3 (report this date in question 37, report WBC count in question 38, report neutrophil count in question 39)*
May 24	850	0.41	349	
May 25	720	0.53	382	
May 26	500	0.45	225	
May 27	490	0.3	147	
May 28	650	0.7	455	
May 29	800	0.8	640	*Date of recovery: ANC ≥ 500/mm3 (report this date in question 41, report WBC count in question 42, report neutrophil count in question 43)*
May 30-August 14	—	—	—	ANC ≥ 500/mm^3 for timeframe
August 15 (contact date)	2245	0.72	1616	

Question 34: Is (was) there evidence of hematopoietic recovery following the initial HCT? *(check only one)*

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

Check only **one** response:

- If “yes, ANC ≥ 500/mm^3 achieved and sustained for 3 laboratory values with no subsequent decline,” continue with question 35.
- If “yes, ANC ≥ 500/mm^3 for 3 laboratory values with subsequent decline in ANC to < 500/mm^3 for ≥3 days,” continue with question 36.
- If “no, ANC ≥ 500/mm^3 was not achieved and there was no evidence of recurrent disease in the bone marrow,” continue with question 44.
- If “no, ANC ≥ 500/mm^3 was not achieved and there was documented persistent disease in the bone marrow post-HCT,” continue with question 44.
- If “ANC never dropped below 500/mm^3 at any time after the start of the preparative regimen,” continue with question 44.

Question 35: Date ANC ≥ 500/mm^3 (first of 3 lab values)

Enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm^3 without a subsequent decline. For an example of tracking ANC, see Example 2 above.

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

Question 36: Date ANC ≥ 500/mm^3 (first of 3 lab values)

Enter the first date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm^3 followed by a subsequent decline. See Example 3 above.

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

Question 37: Date of decline in ANC to < 500/mm^3 for ≥ 3 days (first of 3 days that the ANC declined):

Enter the first date of the three consecutive laboratory values obtained on different days where the ANC declined to < 500/mm^3.

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

Question 38: Actual CBC on first day of decline – WBC

Enter the white blood cell count on the first day of decline. Specify the unit of measure. See Example 3 above.

Question 39: Actual CBC on first day of decline – Neutrophils

Enter the percent of neutrophils on the first day of decline. Include both segmented and band neutrophils. See Example 3 above.

Question 40: Did recipient recover and maintain ANC ≥ 500/mm^3 following the decline?

Indicate whether or not there was evidence of ANC recovery following the decline (three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm^3). If “yes,” continue with question 41. If “no,” continue with question 44.

Question 41: Date of ANC recovery

Enter the first date of the three consecutive laboratory values obtained on different days where the ANC recovered to ≥ 500/mm^3 following the decline. See Example 3.

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

Question 42: CBC on first day of recovery – WBC

Enter the white blood cell count and specify the unit of measure on the first day of recovery. See Example 3 above.

Question 43: CBC on first day of recovery – Neutrophils

Enter the percent of neutrophils on the first day of recovery. Include both segmented and band neutrophils. See Example 3 above.

Q44-47: Megakaryopoiesis / Platelet Recovery

Platelet Recovery
Currently there is an issue on the Form 2100 (versions 1 and 2) regarding platelet recovery requiring clarification. The word "previous" will be removed from the text box above question 44 in future versions of the form. Platelet recovery is reported when the recipient's platelet count is ≥ 20 × 10^9/L seven days after platelet transfusion and is maintained for three consecutive lab values obtained on different days. Carefully review the example below.

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

The following questions refer to **initial** platelet recovery following the HCT for which this form is being completed. When determining the recovery date, ensure that **no platelet transfusions were administered for seven consecutive days**. Report the recovery date as the first of three consecutive laboratory values ≥ 20 × 10^9/L and ≥ 50 × 10^9/L and obtained on different days. When determining the recovery date, include day seven as shown in Example 4 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.

Example 1: Reporting Platelet Recovery

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

June 18	5	19,000	
June 19	6	23,000	
June 20	7	25,000	*1st of 3 consecutive laboratory values ≥ 20 × 10^9/L (report this date in question 45)*
June 21	8	40,000	
June 22	9	50,000	*1st of 3 consecutive laboratory values ≥ 50 × 10^9/L (report this date in question 47)*
June 23	10	56,000	
June 24	11	65,000	
June 25	12	72,000	

Question 44: Was an initial platelet count ≥ 20 × 10^9/L achieved?

Indicate whether or not there was evidence of **initial** platelet recovery following this HCT. Check only **one** response:

- If “yes,” continue with question 45.
- If “no,” continue with question 48.
- Check “platelet count never dropped below 20 × 10^9/L” if the recipient’s platelets **never** dropped below 20 × 10^9/L at any time post-HCT and a platelet transfusion was never required. If the recipient’s platelet count drops below 20 × 10^9/L or the recipient received a platelet transfusion even once (including if the platelet count does not drop below 20 × 10^9/L), do not use this option.

Question 45: Date platelets ≥ 20 × 10^9/L

Enter the **first** date of three consecutive laboratory values, obtained on different days, where the platelet count was ≥ 20 × 10^9/L. Ensure that no platelet transfusions were administered for seven consecutive days. Include day seven, as shown in Example 4 above, when determining the recovery date.

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

Example 2:
The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1st. The platelet count is ≥ 20 × 10^9/L on January 2nd, January 3rd, and January 4th. The recipient does not come into the clinic for evaluation until one month later. The recipient has not received any more platelet transfusions and their platelet count is well above 20 × 10^9/L. Report January 8th (day seven post platelet transfusion) and check "date estimated."

Example 3:
The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1st. The platelet count is ≥ 20 × 10^9/L on January 2nd, January 3rd, and January 4th. The recipient is then discharged back to their primary care physician. The transplant center receives a follow-up note from the primary care physician that states "recipient recovered their platelets in January of 2011." Report the day of the month as the 15th. If the 15th does not make logical sense in relation to the dates of the platelet counts obtained, use either the 1st or 30th. Report month and year as documented. Also, check "date estimated."

Check "date unknown" if there is no documentation of platelet recovery and/or laboratory reports cannot be obtained.

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

Question 46: Was an initial platelet count ≥ 50 × 10^9/L achieved?

Indicate whether or not a platelet count of ≥ 50 × 10^9/L was achieved following this HCT.

Check only **one** response:

- If "yes," continue with question 47.
- If "no," continue with question 48.
- Check "platelet count never dropped below 50 × 10^9/L," if the recipient's platelets never dropped below 50 × 10^9/L at any time post-HCT. If the recipient's platelet count drops below 50 × 10^9/L even once, do not use this option.

Question 47: Date platelets ≥ 50 × 10^9/L

Enter the first date of three consecutive laboratory values obtained on different days where the platelet count was ≥ 50 × 10^9/L. Ensure that no platelet transfusions were administered for seven consecutive days. Include day seven, as shown in Example 1 above, when determining the recovery date.

If three laboratory values were not obtained on consecutive days, but a sequential rise of ≥ 50 × 10^9/L is demonstrated, follow examples 2 and 3 above to determine an estimated date.

Check “date unknown” if there is no documentation of platelet recovery and/or laboratory reports cannot be obtained.

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

Q48-54: Current Hematologic Findings

Transfusions
Currently there is an error on the Form 2100 regarding transfusion history. The form should read: “transfused RBC less than **or equal to** 30 days from date of most current testing” and “transfused platelets less than **or equal to** 7 days from date of most current testing.”

Questions 48-54: Provide the most recent laboratory values recorded

These questions are intended to determine the hematological status of the recipient after the HCT. 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 laboratory value and unit (if applicable) for each listed hematologic finding. If a value was not tested, select “not tested” and continue with the next laboratory value.

For hemoglobin and hematocrit, check the box if red blood cells were transfused less than or equal to 30 days prior to the testing.

For platelets, check the box if platelets were transfused less than or equal to seven days prior to the testing.

Q55-76: Immune Reconstitution

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

Questions 55-60: Specify the immunoglobulin values from the most recent testing

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.
- 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.
- 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.

Report the value, unit, and date tested for each immunoglobulin (antibody). If the immunoglobulin was not tested, select “not tested” and continue with the next immunoglobulin value.

Question 61: Did the recipient receive supplemental intravenous immunoglobulins (IVIG)?

IVIG is a product made from pooled human plasma that primarily contains IgG. It is used to provide immune-deficient recipients with antibody function to prevent infection. Indicate whether the recipient received IVIG during the reporting period. If “yes,” continue with question 62. If “no,” continue with question 70.

IVIG Given without Immunoglobulin Testing
In some cases, IVIG may be given for low immune function without immunoglobulin testing. In these cases, answer questions 55 through 60 “not tested.” Question 61 should be answered “yes.” Question 62 should be answered “no.” (Even though in this case there wasn’t any testing done, the question can still be answered “no”.) Answer question 63 “yes” because the recipient is receiving IVIG for decreased immune function even though there is not a laboratory value to document a low IgG level. The transplant center should verify that Ig levels were not tested at another facility, as it is unusual for IVIG to be given without knowing what the IgG level is.

Question 62: Was therapy ongoing within one month of immunoglobulin testing?

Indicate whether the recipient received IVIG ≤30 days prior to the immunoglobulin testing reported in questions 55-60. If IVIG is given within 30 days of immunoglobulin testing, the IgG level would not represent the recipient's native IgG.

Questions 63-69: Indication(s) for use

Specify the indication(s) for which IVIG was given to the recipient. If the indication is unclear, consult with the transplant physician. If "other indication" is selected, specify the indication for use of IVIG in question 69.

Question 70: Were lymphocyte analyses performed?

Lymphocyte analyses are often performed post-HCT to evaluate the reconstitution of the immune system. Certain lymphocyte groups repopulate earlier than others post-HCT. Indicate whether lymphocyte analyses were performed. If "yes," continue with question 71. If "no," continue with question 77.

Question 71: Date of most recent testing performed

Enter the date that the most recent lymphocyte analysis was performed.

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

Questions 72-76: Lymphocyte analyses – value

Report the value and specify the unit for each lymphocyte. If the lymphocyte was not tested, select "not tested" and continue with the next lymphocyte value.

If the results show the absolute lymphocyte count, but only percentages of lymphocyte subsets, 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:

Absolute Lymphocyte Count: 4.8 × 10^9/L

Phenotype	Lab Report Percentage	Calculation (Percentage x ALC)	Absolute Value
CD3	74%	0.74 × 4.8	**CD3:** 3.55× 10^9/L
CD3CD4	40%	0.40 × 4.8	**CD4:** 1.92 × 10^9/L
CD3CD8	34%	0.34 × 4.8	**CD8:** 1.63 × 10^9/L

CD20	NT	—	**CD20:** Not Tested
CD56	NT	—	**CD56:** Not Tested

The CD20+ data field can capture CD19+ or CD20+ cells. The CD56+ data field can capture CD56+ or CD16+ cells.

Q77-102: Chimerism Studies

> **Autologous or SyngeneicTransplants**
> If this was an autologous or syngeneic HCT, continue with the Infection section at question 260. The next three sections relate to chimerisms and graft-versus-host disease for allogeneic HCTs only.

Chimerism studies are performed to determine the percent of blood cells post transplant that are produced from donor stem cells and the percent that are produced from host (recipient) stem cells. Different types of blood cells and a variety of laboratory tests can be used to determine if a chimera (presence of both donor- and host-derived cells) exists. If cytogenetic testing was performed to look for disease markers, and the donor and recipient are different sexes, the test may also be used to determine if a chimera exists. If the donor and recipient are of the same sex, cytogenetic testing using the common staining technique, known as giemsa banding (G-banding), cannot be used to determine if there is a chimera. However, quinicrine banding (Q-banding) can be used to identify if the cells are of donor origin or not in a same-sex transplant, as this staining technique highlights inherited chromosome polymorphisms on certain human chromosomes including 3, 4, 13, 15, 21, 22, and Y. This is not a commonly used staining technique and is only helpful when the polymorphism is documented pre-HCT. If chimerism studies were attempted, but no evaluable results were obtained, do not report the test.

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

Question 77: *Allogeneic HCTs only:* Were chimerism studies performed post-HCT?

Indicate whether chimerism studies were performed within the reporting period. If “yes,” continue with question 78. If “no,” continue with question 103.

Question 78: Are chimerism laboratory reports attached to this form?

Indicate whether the chimerism laboratory report(s) was(were) submitted using the Log of Appended Documents (Form 2800). For more information regarding the Form 2800, see the Log of Appended Documents manual section.

Question 79: Were infusions from more than one donor given?

Indicate whether this HCT included product(s) from multiple donors. If “yes,” continue with question 91 (Chimerism Studies for multiple donors). If “no,” continue with question 80 (Chimerism Studies for single donor). When a multi-donor chimerism exists and includes a donor or donors from a previous HCT, report as a multi-donor chimerism though there may only be one donor for the current transplant.

Question 80: Specify donor gender

Indicate the donor’s biological gender (sex) as male or female.

Questions 81-90: Provide date(s), method(s) and other information for all chimerism studies performed prior to the date of contact (question 1)

Reporting Chimerisms
If the chimerism study is performed on peripheral blood, but no cell subtype is specified in the results, select “Other, specify” and report “Peripheral blood, NOS.”
Centers may test chimerisms frequently, and not every test needs to be reported.
Chimerisms that should be reported, if assessed, are:
- Day 28
- Most recent prior to the 100 day date of contact
- Most recent prior to and after an intervention (such as a donor cellular infusion)
- The first result to show 100% donor chimerism

Table 1. Chimerism – Single Donor

Data Field	Description
Date	Enter the date the sample was collected for the chimerism test.
Method	From the “Valid Method Codes” table on Form 2100, select the code that corresponds to the test method that was used. If more than one method was used, complete a separate line in the table for each method.
Cell Type	From the “Valid Cell Types” table on Form 2100, select the code that corresponds to the cell type that was used to perform the test. If more than one cell type was used, complete a separate line in the table for each cell type. See Table 3 below for descriptions of cell types.
Cytogenetics – Total Cells Examined	Quantitative tests include standard cytogenetics and fluorescent *in situ* hybridization (FISH). If a quantitative method was used, enter the total number of cells that were examined. If a non-quantitative test was used, leave these boxes blank.
Cytogenetics – Number of Donor Cells	If a quantitative method was used, enter the total number of cells of donor origin that were detected. If a non-quantitative test was used, leave these boxes blank.

Cytogenetics – Number of Host Cells	If a quantitative method was used, enter the total number of cells of host origin that were detected. If a non-quantitative test was used, leave these boxes blank.
Molecular Studies – Percent Donor Cells, Quantitative Method	If a quantitative method was used, enter the percent of cells of donor origin that were detected. Calculate the percent of donor cells by dividing the number of cells of donor origin by the total number of cells examined, and then multiplying by 100. If a non-quantitative method was used, leave these boxes blank.
Molecular Studies – Percent Donor Cells, Non-Quantitative Method	If a non-quantitative method was used, check the box if donor cells were detected.
Molecular Studies – Percent Host Cells, Quantitative Method	If a quantitative method was used, enter the percent of cells of host origin that were detected. Calculate the percent of host cells by dividing the number of cells of host origin by the total number of cells examined, and multiplying by 100. If a non-quantitative method was used, leave these boxes blank.
Molecular Studies – Percent Host Cells, Non-Quantitative Method	If a non-quantitative method was used, check the box if host/recipient cells were detected.

Questions 91-102: Provide date(s), method(s) and other information for all chimerism studies performed prior to date of contact (question 1)

Table 2. Chimerism – Multiple Donors

Data Field	Description
Donor or Cord Blood identification number or Donor/ Infant date of birth	Select the donor or cord blood type and enter the identification number assigned to the donor or cord blood unit, or the donor/infant date of birth in the appropriate field.
Donor/Infant gender	Indicate the donor's or infant's (cord blood) biological gender (sex) as male or female.
Date	Enter the date the sample was collected for the chimerism test.
Method	From the "Valid Method Codes" table on Form 2100, select the code that corresponds to the test method that was used. If more than one method was used, complete a separate line in the table for each method.
Cell Type	From the "Valid Cell Types" table on Form 2100, select the code that corresponds to the cell type that was used to perform the test. If more than one cell type was used, complete a separate line in the table for each cell type. See Table 3 below for descriptions of cell types.

Cytogenetics – Total Cells Examined	Quantitative tests include standard cytogenetics and fluorescent *in situ* hybridization (FISH). If a quantitative method was used, enter the total number of cells that were examined. If a non-quantitative test was used, leave these boxes blank.
Cytogenetics – Number of Donor Cells	If a quantitative method was used, enter the total number of cells of donor origin that were detected. If a non-quantitative test was used, leave these boxes blank.
Cytogenetics – Number of Host Cells	If a quantitative method was used, enter the total number of cells of host origin that were detected. If a non-quantitative test was used, leave these boxes blank.
Molecular Studies – Percent Donor Cells, Quantitative Method	If a quantitative method was used, enter the percent of cells of donor origin that were detected. Calculate the percent of donor cells by dividing the number of cells of donor origin by the total number of cells examined, and multiplying by 100. If a non-quantitative method was used, leave these boxes blank.
Molecular Studies – Percent Donor Cells, Non-Quantitative Method	If a non-quantitative method was used, check the box if donor cells were detected.
Molecular Studies – Percent Host Cells, Quantitative Method	If a quantitative method was used, enter the percent of cells of host origin that were detected. Calculate the percent of host cells by dividing the number of cells of host origin by the total number of cells examined, and multiplying by 100. If a non-quantitative method was used, leave these boxes blank.
Molecular Studies – Percent Host Cells, Non-Quantitative Method	If a non-quantitative method was used, check the box if host/recipient cells were detected.

Table 3. Chimerism Cell Types

Cell Type	Description
1- Bone Marrow	Sample consists of unsorted cells from the bone marrow. If a sorted marrow sample was tested (e.g., T-cells from bone marrow), reported this under “Other, Specify.”
2- Peripheral Blood Mononuclear Cells (PBMCs)	Have round nuclei, including lymphocytes, monocytes, and macrophages which are isolated from whole blood samples
3- T-cells	Includes CD3+ or CD4+ cells
4- B-cells	Includes CD19+ or CD20+ cells
5- Red Blood Cells	Also called RBCs or erythrocytes

6- Monocytes	Includes CD14+ cells
7- PMNs (neutrophils)	Also called polymorphonuclear leukocytes. Neutrophils (including CD15+ cells) are the most numerous subtype, but eosinophils and basophils are also present.
8- Lymphocytes, not otherwise specified	Includes lymphocytes that are not further divided into subsets
9- Myeloid cells, not otherwise specified	Includes CD33+ cells
90- Other, specify	Use this option to report cell types that do not fit in a category above. Chimerisms on peripheral or whole blood that are not specified on the report or by the laboratory should be reported using this option as “peripheral blood, not otherwise specified.” If testing was performed on sorted cells from a bone marrow sample, report “{cell type} from bone marrow” (e.g., T-cells from bone marrow).

Q103-109: Engraftment Syndrome

Question 103: 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 “yes,” continue with question 104. If “no,” continue with question 110.

Question 104: Date of onset

Report the date of onset of engraftment syndrome.

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

Questions 105-108: Specify symptoms of engraftment syndrome

Indicate whether the recipient developed the symptoms listed. If “skin rash” is selected, also specify the body surface percentage affected.

Question 109: Was engraftment syndrome treated with corticosteroids?

Indicate whether the recipient’s engraftment syndrome was treated with corticosteroids.

Q110-187: Acute Graft vs. Host Disease (GVHD)

Autologous or SyngeneicTransplants
If this was an autologous or syngeneic HCT, continue with the Infection section at question 260.

Graft vs. Host Disease

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. Autologous GVHD will only be reported in cases where specific therapy was used to induce it.

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

In the past, GVHD was classified as acute or chronic based on its time to diagnosis following transplant, and other clinical and histological (biopsy or post-mortem) features. Today, there has been increased recognition that acute and chronic GVHD are not dependent upon 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.

GVHD Therapy
Do not include agents, such as hematopoietic growth factors, lymphoid growth factors, or cytokines (question 8), unless given for hematopoietic reconstitution **and** continued for the purpose of GVHD prophylaxis.

ATG
For ATG, Campath, and Cyclophosphamide: If these agents are given for GVHD prophylaxis both prior to and after Day 0, they must be reported in separate sections of the Pre-TED form, and Recipient Baseline Forms. Report doses given prior to Day 0 in the preparative regimen section of the Pre-TED (questions 168-315) and Recipient Baseline (107-242). If given after Day 0 as planned GVHD prophylaxis, report in the GVHD prophylaxis section of the Pre-TED (questions 316-341) and below.

Ex vivo T-Cell Depletion
Report ex vivo T-cell depletion on the HCT Infusion Form (2006).

Question 110: Was specific therapy used after the start of the preparative regimen to prevent acute GVHD or graft rejection or for autologous HCT to induce acute GVHD?

Following an allogeneic HCT, specific immunosuppressive therapy may be administered to prevent GVHD or to immunosuppress the host marrow, thereby promoting engraftment of the donor stem cells. 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 prophylactic drug options listed on the form are intended to be **systemic** (IV or oral administration). If the recipient received one of the listed drugs in a topical form, report the drug in the "other, specify" category.

The 100 Day Post-HCT 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.

If GVHD prophylaxis is used for a syngeneic (monozygotic or identical twin) or autologous HCT, fax or e-mail an explanation to your center's CIBMTR CRC, and request it be scanned as part of the form documentation.

If "yes," continue with question 111. If "no," continue with question 140 for allogeneic transplants, or question 260 for autologous transplants.

Questions 111-139:

For each agent listed, indicate whether it was used to prevent acute GVHD or graft rejection, and answer any additional question(s) for each prophylactic therapy used.

ALS (Anti-Lymphocyte Serum), ALG (Anti-Lymphocyte Globulin), ATS (Anti-Thymocyte Serum), ATG (Anti-Thymocyte Globulin): Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes. Also report the animal source. If "other" is selected, specify the source.

Corticosteroids: Examples: dexamethasone, hydrocortisone, methylprednisolone, prednisone/ prednisolone. Corticosteroids are usually combined with cyclosporine when used for prophylaxis. Only report systemic steroids in this section. If topical steroids are used prophylactically, report in questions 138-139 and provide an explanation regarding how the site for topical application was selected.

Cyclosporine (CSA, CYA): Examples: sandimmune, Neoral. Cyclosporine is usually given for ≥ 3 months.

ECP (extra-corporeal photopheresis): The recipient's blood is exposed to ultraviolet light outside of their body, and re-infused.

FK 506: Alternate names: Tacrolimus, Prograf. FK 506 inhibits the production of interleukin-2 by T-cells.

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 be given to prevent oral mucositis. Verify whether the recipient is receiving KGF as prevention for mucositis (if yes, report in question 20), or as GVHD prophylaxis.

Velafermin: a recombinant human fibroblast growth factor (rhFGF). Velafermin may be given to prevent oral mucositis. Verify whether the recipient is receiving Velafermin as prevention for mucositis (if yes, report in question 23), or as GVHD prophylaxis.

In vivo anti T-lymphocyte monoclonal antibody: Antibody preparations that are infused in the recipient following HCT. Specify the antibody used as: Anti CD25 (Zenapax, Daclizumab, AntiTAC), Campath, Entanercept (Enbrel), and/or Infliximab (Remicade).

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

Methotrexate (MTX): Example: Amethopterin. MTX 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): Alternate name: CellCept. MMF inhibits the de novo pathway used for lymphocyte proliferation and activation.

Sirolimus: Alternate names: Rapamycin, Rapamune. Sirolimus inhibits the response to interleukin-2, blocking the activation of T-cells.

Ursodiol: Supresses synthesis and secretion of cholesterol from the liver and absorption in the intestines.

Blinded randomized trial: If the recipient is on a blinded randomized trial, specify agent being studied in the trial. Additionally, update the 100 Day Post-HCT Form (2100) once the trial is over to specify whether the recipient received the trial drug or placebo.

Other agent: 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 (2006).
- Do not include agents used to prevent infection. Report infection prophylaxis agents in the infection section, questions 260-289.

Question 140: Did acute GVHD occur?

Indicate whether acute GVHD occurred during the reporting period in response to transplant or donor cellular infusion.

If “yes,” continue with question 141. If “acute GVHD persists from prior HCT/DCI,” continue with question 142. If “no” or “unknown,” continue with question 188.

Question 141: Date of acute GVHD diagnosis

Report the date of clinical diagnosis of acute GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed a rash one week prior to the physician documenting it as acute GVHD versus a drug reaction). If the clinical diagnosis date is not documented, then report the date of histological confirmation.

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

If the date of diagnosis is greater than 100 days Post-HCT, verify the symptoms are related to acute GVHD versus chronic GVHD and check the “date is greater than 100 days, date is correct” box.

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

Question 142: Was the diagnosis based on evidence from a biopsy (histology)?

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 whether a biopsy was used to diagnose acute GVHD. If “yes,” continue with question 143. If “no,” continue with question 150.

Questions 143-148: Specify result(s)

For each organ listed, indicate the test result documented on the laboratory report as either “positive,” “negative,” or “inconclusive.” If a biopsy was not completed, select “not tested.” If “other site” is selected, specify the site biopsied in question 148.

Question 149: Is a copy of the pathology report attached?

Attaching a copy of the diagnostic pathology report for acute GVHD reduces the need for later data queries.

If “yes,” complete the Log of Appended Documents (Form 2800) and attach the pathology report. For more information regarding the Form 2800, see the Log of Appended Documents manual section.

Question 150: Was the diagnosis based on clinical evidence?

Acute GVHD may damage the skin, gut, liver, or other organs. Clinical evidence of acute GVHD may include maculopapular rash, nausea, vomiting, diarrhea, and/or jaundice (elevated total bilirubin). Indicate whether clinical evidence was used to diagnose acute GVHD.

Question 151: Maximum overall grade of acute GVHD

The acute GVHD grading scale is based on **clinical evidence** (physician observation), not histology. If there is a difference in the clinical grade recorded by the physician and a histological report, use the data from the clinical documentation. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, **overall grading remains** clinical and is based on the criteria published by Przepiorka et al., *Bone Marrow Transplant* 1995; 15(6):825-8, see Table 4 below.

Table 4. GVHD Grading and Staging

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

			Pediatric: 280-555 ml/m^2/day or 10-19.9 mL/kg/day
2	Rash on 25-50% of skin	Bilirubin 3-6 mg/dl	Diarrhea >1000 ml/day *Pediatric*: 556-833 ml/m^2/day or 20-30 mL/kg/day
3	Rash on >50% of skin	Bilirubin 6-15 mg/dl	Diarrhea >1500 ml/day *Pediatric*: >833 ml/m^2/day or > 30 mL/kg/day
4	Generalized erythroderma with bullous formation	Bilirubin >15 mg/dl	Severe abdominal pain with or without ileus
Grade[5]			
I	Stage 1-2	None	None
II	Stage 3 or	Stage 1 or	Stage 1
III	—	Stage 2-3 or	Stages 2-4
IV[6]	Stage 4	Stage 4	—

[1] Use “Rule of Nines” (Table 5) or burn chart to determine extent of rash.

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

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

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

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

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

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

If acute GVHD was present, but the maximum grade was not documented nor is it able to be determined from the grading and staging table, leave the maximum overall grade blank and override the error as “Unknown.”

Example 1: A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging/grading can be determined using Table 4.

Example 2: A recipient developed acute liver GVHD with elevated LFTs with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in Table 4; "present, grade unknown" would be the best option to report.

Question 152: Is acute GVHD still present at the date of contact for this report (question 1)?

Indicate whether the recipient has active clinical signs/symptoms of acute GVHD at the date of contact. Select "yes," "no," "progressed to chronic GVHD," or "unknown."

Questions 153-160: List the maximum severity of organ involvement

Skin: Select the stage that reflects the body surface area involved with a maculopapular rash. See Table 5 below to determine the percent of body surface area involved with a rash. If the recipient has acute GVHD but does not have skin rash, report "stage 0 – no rash." If the recipient has a skin rash that is not attributed to acute GVHD (i.e., due to a drug reaction, infection, or some other reason), report "no skin acute GVHD / rash not attributable to acute GVHD."

Table 5: Percent Body Surfaces

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

Pediatric Recipients

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

Lower intestinal tract: Select the stage that reflects the volume of diarrhea. Use mL/day for adult recipients and mL/m^2/day for pediatric recipients. Input and output records may be useful in determining the volume of diarrhea. If the recipient has acute GVHD but does not have diarrhea, report "stage 0 – no diarrhea." If the recipient has diarrhea, but it is not attributed to acute GVHD (i.e., due to a drug reaction, infection, or some other reason) report "no gut acute GVHD / diarrhea not attributable to acute GVHD."

Upper intestinal tract: Select the stage that reflects the presence of persistent nausea or vomiting.

Liver: Select the stage that reflects the bilirubin level. If a recipient has evidence of acute GVHD but has a bilirubin level less than 2.0 mg/dL, select "stage 0 – bilirubin < 2.0 mg/dL." If the recipient has hyperbilirubinemia, but it is not attributed to acute GVHD (i.e., due to liver dysfunction not related to acute GVHD), select "no liver acute GVHD / bilirubin level not attributable to acute GVHD."

For recipients who have a normal bilirubin level with elevated transaminase levels and a liver biopsy documenting GVHD, report this in "Other clinical organ involvement."

Other clinical organ involvement: Indicate whether acute GVHD affected another organ. If "yes," continue with question 158. If "no," continue with question 161. If "other site" is selected (question 159), specify the site in question 160.

Questions 161-187: Was specific therapy used to treat acute GVHD?

Indicate whether therapy was used to treat acute GVHD. If "yes," continue with question 162. If "no," continue with question 188.

For each agent listed, indicate whether or not it was used to treat acute GVHD. If "yes," answer any additional questions if applicable.

Report prophylactic drugs if they were continued after the onset of acute GVHD.

Refer to questions 111-139 for a description of each agent listed. "Systemic" refers to drugs given by mouth, intramuscularly (IM), or intravenously (IV). "Topical" refers to drugs applied to the skin, eye drops, or inhalation therapy. An exception to this guidance would be the drugs budesonide and oral beclomethasone. They are drugs given by mouth for treatment of gut GVHD, but considered a "topical" since they're not absorbed.

Alternate methods of treatment (example: PUVA) may be used in combination with drug therapy. If alternate methods were used, report in "other agent" (questions 186-187).

Q188-259: Chronic Graft vs. Host Disease (GVHD)

Autologous or SyngeneicTransplants
If this was an autologous or syngeneic HCT, continue with the Infection section at question 260.

Question 188: Has the recipient developed clinical chronic GVHD?

Chronic GVHD affects 25-50% of long-term survivors of allogeneic transplants and usually develops after day 100. However, it has been documented as occurring as early as day 60 and as late as day 400 post-HCT. In chronic GVHD, the mechanism of tissue damage differs from acute GVHD and a greater variety of organs may be affected.

Indicate whether the recipient developed chronic GVHD during the reporting period. If “yes,” continue with question 189. If “chronic GVHD persists from prior HCT/DCI,” continue with question 193. If “no” or “unknown,” continue with question 258.

Question 189: 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 dry eyes one week prior to the physician documenting the dry eyes as a manifestation of chronic GVHD). If the clinical diagnosis date is not documented, then report the date of histological confirmation.

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

If the date of diagnosis is less than 100 days Post-HCT, verify the symptoms are related to chronic GVHD versus acute GVHD and check the “date is less than 100 days, date is correct” box.

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

Question 190: Onset of chronic GVHD was:

Indicate whether the onset of chronic GVHD was:

- Progressive – acute GVHD progressed directly to chronic GVHD
- Interrupted – acute GVHD resolved for greater than 7 days, then chronic GVHD developed
- de novo – acute GVHD never developed
- chronic GVHD flare – symptoms reactivated within 30 days of drug tapering or discontinuation

Question 191: Karnofsky/Lansky score at diagnosis of chronic GVHD

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 less than 16 years old.

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 healthcare provider rather than make an assignment themselves, based on inadequate information. The score determined by this discussion must be documented in the recipient record. 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.

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.

Question 192: Platelet count 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.

Question 193: Diagnosis was based on

Select the method used to diagnose chronic GVHD.

Question 194: Maximum grade of chronic GVHD

The grading system for chronic GVHD is divided into two categories: limited and extensive.

Reporting Grade of Chronic GVHD (Sullivan KM, *Blood* 1981; 57:267)
Limited: Localized skin involvement resembling localized scleroderma with or without liver involvement; no other organ involvement.
Extensive: Generalized skin and/or multiple organ involvement.

Indicate the maximum grade of chronic GVHD present during this reporting period.

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
- Involvement of the salivary glands or oral mucous membranes
- Involvement of any other target organ

Question 195: Overall severity of chronic GVHD

Currently there are no specific criteria for the severity of chronic GVHD. This subjective assessment should be reported as documented by the physician using the guidelines 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 (corticosteroids and/or cyclosporine or FK 506).
- Moderate – signs and symptoms of chronic GVHD interfere somewhat with function despite appropriate therapy or are progressive through first line systemic therapy (corticosteroids and/or cyclosporine or FK 506).
- Severe – signs and symptoms of chronic GVHD limit function substantially despite appropriate therapy or are progressive through second line therapy.

Select the overall severity of chronic GVHD.

Questions 196-225: Indicate if there was organ involvement with chronic GVHD from the list below

Indicate whether chronic GVHD affected each organ/system listed. If “yes,” also indicate if the involvement was proven by histological evidence (biopsy).

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
- Rash
- Ulcers
- Pruritus: itching of the skin
- Dyspigmentation: change in color of the skin. Usually erythema (redness) or vitiligo (loss of skin color)
- Alopecia: scalp hair loss
- Lichenoid skin changes: whitish lacy patches

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

- Xerophthalmia: dry eyes
- Schirmer’s test: a measure of tear production, decreased wetting <5 mm
- Slit lamp: The binocular slit lamp examination provides stereoscopic magnified view of the eye structures in detail
- Corneal erosion/conjunctivitis: ulcers on the cornea, usually quite painful, or inflammation of thin membrane covering the eye and inner lids

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

- Lichenoid changes: whitish lacy patches that usually appear first on inner cheeks, but can involve roof of mouth, gums, and/or tongue
- Mucositis/ulcers: similar to cold sores but they can involve any part of the mouth, important not to confuse with herpes simplex infections
- Erythema: redness

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

- Bronchiolitis Obliterans (BO): literally, scarring of the small airways. Usually diagnosed by lung biopsy or pulmonary function tests (showing obstruction of airflow). Symptoms include shortness of breath

(dyspnea), dry cough, and wheezing. **If bronchiolitis obliterans was a manifestation of chronic GVHD, also complete the bronchiolitis obliterans section, questions 322-330.**

- Other pulmonary involvement: include related pulmonary disorders here. Do not report interstitial pneumonitis (IPn). Report IPn in the Pulmonary Function section, questions 298-320.

Gastrointestinal tract (GI):

- Esophageal: may have difficulty swallowing (dysphagia), pain when swallowing (odynophagia), narrowing of esophagus (esophageal web), poor motility (food does not move down esophagus normally).
- Chronic nausea/vomiting: either nausea or vomiting that occurs on at least 25% of days (1 out of 4 weeks) or occurs frequently enough to interfere with functioning and lifestyle.
- Chronic diarrhea: occurs on at least 25% of days (1 out of 4 weeks) or occurs frequently enough to interfere with functioning and lifestyle. This may occur due to thickening of the intestinal wall.
- Malabsorption: inability to digest or absorb the nutrients from food. Diagnosed with specific tests measuring fecal fat, xylose uptake, or vitamin level.
- Abdominal pain or cramping.

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

- Liver involvement may be manifested by elevation of any of the liver function tests (bilirubin, particularly the direct component; alkaline phosphatase; GGT; SGOT [AST]; SGPT [ALT]).
- A liver biopsy may show obliteration of bile ducts (canaliculi) or cirrhosis.

Genitourinary tract (GU):

- Vaginitis/stricture: pain, ulceration, inflammation, eventually scarring/narrowing of the vaginal opening.

Musculoskeletal: Refers to pain, contractures, and/or joint deformities.

- Arthritis: inflammation of joints
- Contractures: loss of joint mobility due to skin changes
- Myositis: inflammation of muscles
- Myasthenia: weakness of muscles

Hematologic: Involving the blood system

- Thrombocytopenia: decreased platelet count (<100,000)
- Eosinophilia: elevation in percent eosinophils in blood (>5% of upper limit normal for your institution).
- Autoantibodies: any abnormal antibody against the patient's normal bodily tissue (for example, antinuclear antibody [ANA], red cell autoantibodies [if directed against patient's own blood type]).
- Other hematologic involvement: not classifiable above, specify the involvement.

Other:

- Serositis: inflammation of a serous membrane, specify the site.
- Weight loss.
- Other organ involvement from chronic GVHD: specify the additional site in question 224.

Questions 226: Was specific therapy used to treat chronic GVHD?

Indicate whether therapy was used to treat chronic GVHD. If "yes," continue with question 227. If "no," continue with question 257.

For each agent listed, indicate whether or not it was used to treat chronic GVHD. If "yes," answer any additional questions if applicable.

Report prophylactic drugs if they were continued after the onset of chronic GVHD.

Refer to questions 111-139 for a description of most agents listed. "Systemic" refers to drugs given by mouth, intramuscularly (IM), or intravenously (IV). "Topical" refers to drugs applied to the skin, eye drops, or inhalation therapy. An exception to this would be the drug budesonide; it is a drug given by mouth for treatment of gut GVHD, but it is considered a "topical" drug since it is not absorbed.

Additional Agents:

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

Etretinate: A synthetic derivative of vitamin A.

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

Lamprene: Example: Clofazimine. Lamprene acts as an anti-inflammatory agent.

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

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

Thalidomide: Was once used as an anti-nausea medication in pregnant women, but was found to cause severe birth defects. Currently, thalidomide is used for its anti-inflammatory properties, as well as in combination with dexamethasone for the treatment of multiple myeloma.

Alternative treatments may be used in combination with drug therapy (example: low dose cyclophosphamide). If alternative treatments were used, report in “other agent” (questions 255-256).

Question 257: Are symptoms of chronic GVHD still present on the date of actual contact (or present at the time of death)?

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

Only report “no” if the recipient has no symptoms.

Question 258: Is the recipient still taking immunosuppressive agents (including PUVA) to treat or prevent GVHD?

Indicate whether the recipient is still taking immunosuppressive agents to treat or prevent GVHD on the date of contact. If “no,” continue with question 259. If “yes” or “unknown,” continue with question 260.

Do not include local or topical therapies.

If the recipient has died prior to the discontinuation of immunosuppressive agents used to treat or prevent GHVD, select “yes.”

> ! This question must be answered for all allogeneic transplants, whether or not the recipient developed GHVD.

Question 259: Date final treatment administered

Report the date the final treatment or prophylaxis dose was administered.

If only the month and year that the immunosuppressive agents were discontinued are known, enter this information. Do not select “unknown” in this situation.

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

Q260-297: Infection

Infection Prophylaxis
It is important to look at the Medication Administration Record (MAR) throughout the entire reporting period, as one prophylactic drug may be stopped due to a reaction and another started in its place. Also, the use of some infection prophylactic drugs may not start immediately post-HCT (example: Pentamidine).

Questions 260-289: Did the recipient receive any of the following agents for infection prophylaxis after the start of the preparative regimen?

Indicate whether specific antimicrobial therapy was administered after the start of the preparative regimen to prevent infections. Most transplant centers have specific infection prophylaxis protocols that may include: antiviral, antifungal, antibacterial, and/or anti-*PCP* drugs. Any agents a recipient received as a result of these protocols should be included in this section.

Report prophylactic immunoglobulins in the Immune Reconstitution section (questions 63-64).

Do not report agents used as treatment for documented or suspected infections.

If “yes,” continue with question 261. If “no” or “unknown,” continue with question 290. For each agent listed, indicate whether it was used to prevent infection.

Systemic antibacterial antibiotics: These agents may be given IV (example: ceftazidime) or orally (example: ciprofloxacin).

Non-absorbable oral antibiotics: The main purpose of these agents is to sterilize the gastrointestinal tract. Examples include: Coly-Mycin S, colistin sulfate, polymixin E, Mycifradin, Neobiotic, neomycin, Aerosporin, polymixin B.

If “other systemic antifungal agent,” “other antiviral agent,” “other pneumocystis prophylaxis,” or “other prophylaxis agent” is selected, specify the agent given.

Question 290: Did the recipient receive irradiated granulocyte infusions after the start of the preparative regimen to 60 days post-HCT?

Indications for irradiated granulocyte infusions may include:

- Prophylactic administration post-transplant for patients deemed to be at high risk of fungal infection or severe/resistant bacterial infection.
- Therapeutic administration for clinically significant bacterial or fungal infection.
- Administration due to an inability to control infections with antibiotics and the persistence of neutropenia.

For allogeneic transplants, report infused granulocytes that are **not irradiated** in the DCI Section (questions 462-560).

Indicate whether irradiated granulocytes were infused between the start of the preparative regimen and 60 days post-HCT.

Questions 291-295: Did the recipient develop a clinically significant infection after the start of the preparative regimen?

Indicate if 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 (exceptions: oral thrush, toe nail fungus, etc.). Surveillance cultures in which normal flora is present and the recipient is asymptomatic do not need to be reported.

Report Interstitial Pneumonitis (IPn) that developed from an infection (e.g., CMV, adenovirus) in the Pulmonary Function section (questions 298-318).

If “yes,” continue with question 292. If “no,” continue with question 298.

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

Organism: From the drop down menu, select the code corresponding to the identified or suspected organism as reported on the microbiology, laboratory report, or other physician documentation. Report the code in the boxes provided. If the specific organism is not listed, use the “other, specify” code (198 – bacteria, 209 – candida, 219 – aspergillus, 259 – fungus, 329 – virus, 409 – parasite) and report the name of the organism in the space provided. If an organism is suspected, but not identified, report using codes 501-505, as applicable. If the source of the infection is not identified, use code 509.

Bacterial infections: *Atypical bacteria* (codes 101-119 and 501) are collected separately from other more common types of bacteria. *Typical bacteria* are codes 120-198 and 502. If more than one typical bacterial organism is found in a single site, include all the organisms in one listing; do not record each separately. Either write the code in the margin or use Report “Notes.”

Fungal infections: Note the inclusion of Pneumocystis (formerly found under parasites). The most commonly found fungal infections are Candida (*C. albicans, C. tropicalis, C. glabrata* [also known as *Torulopsis glabrata*], *C. parapsilosis, C. krusei*), *Aspergillus (A. fumigatus), Fusarium sp*., and *Zygomycetes*.

- For fungal species marked with a section symbol (§), also complete a Fungal Infection Form (2146).

Viral infections: Caused by exposure to a new virus or reactivation of a dormant virus already present in the body. The most common viral infections are due to HSV (Herpes simplex), VZV (Varicella zoster, shingles), and CMV (Cytomegalovirus). If the site of CMV is the lung, confirm whether the patient had interstitial pneumonitis rather than CMV pneumonia.

- For hepatitis infections marked with a dagger symbol (†), also complete a Hepatitis Form (2147).
- For HIV infections marked with a currency symbol (¤), also complete an HIV Infection Form (2148).

Parasitic infections: These are fairly rare. Toxoplasma gondii is often transmitted through the handling of cat litter. Giardia and Cryptosporidium can be found in contaminated water.

Fever of undetermined origin: Defined as any fever (> 38°C) not associated with documented/suspected infection in a specific site, these are not collected by the CIBMTR because the occurrence is too common for analysis.

Site: From the drop down menu, select the code corresponding to the site of the infection. If three or more sites are infected with the same organism, enter code 2 (Disseminated- generalized, isolated at 3 or more distinct sites).

Disseminated Infections
The CIBMTR acknowledges that a discrepancy exists between the CIBMTR definition (3 or more sites) and the BMT CTN definition (2 or more sites) for disseminated infections.

Date of Diagnosis: Report the date of diagnosis of the infection as the collection date for the positive microbiology culture. For suspected infections, enter the date of a radiological test or the date treatment was started as the date of diagnosis.

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

Questions 296-297: Did the recipient develop more than 7 infections post-HCT

Indicate whether the recipient developed more than seven infections post-HCT.

If “yes,” use the multiple feature to report the organism, site, and date of diagnosis for each infection in the FormsNet3^{SM} application. For paper form submission, make a copy of the infection section to report multiple infections and indicate that extra pages are attached.

If “no,” continue with question 298.

Bacterial Infections: If the infection is due to bacteria (except for Clostridium difficile), and recurs in less than or equal to 7 days off antimicrobial therapy, it is considered a single incident and should *not* be reported multiple times.

- **Example:** In the case of VRE, where antibiotic (i.e., Linezolid) therapy can last 14-28 days, the recipient would have to be off antibiotics for more than 7 days to report a new VRE infection of the same site again.

If the infection is due to Clostridium difficile, and recurs in less than or equal to 30 days, it is considered a single incident and should *not* be reported multiple times.

If the infection is due to Helicobacter pylori, and recurs in less than or equal to 365 days, it is considered a single incident and should *not* be reported multiple times.

Viral Infections: If the infection is due to VZV, HZV, Adenovirus, Enterovirus, Influenza, Parainfluenza or Rhinovirus, and recurs in less than or equal to 14 days, it is considered a single incident and should *not* be reported multiple times.

If the infection is due to CMV, HSV, EBV, HHV-6 or Polyomavirus (BK virus), and recurs in ≤ 60 days, it is considered a single incident and should *not* be reported multiple times.

Fungal Infections: If the infection is due to yeast (e.g., Candida), and recurs in ≤ 14 days, it is considered a single incident and should *not* be reported multiple times.

If the infection is due to mold (e.g., aspergillus), and recurs in ≤ 90 days, it is considered a single incident and should *not* be reported multiple times.

Q298-449: Organ Function

Pulmonary Function

Bacterial and Fungal Pneumonia
Report bacterial and fungal pneumonia in the Infection section (questions 291-295).

Question 298: Did the recipient develop interstitial pneumonitis (IPn or ARDS) / idiopathic pneumonia syndrome (IPS) after the start of the preparative regimen to the date of last contact (question 1)?

Interstitial pneumonitis or ARDS can result from infectious or non-infectious causes. Infectious causes may be bacterial, viral (CMV, adenovirus, RSV, influenza, etc.), or fungal. Interstitial pneumonitis may also be idiopathic (no organism was isolated).

Idiopathic pneumonia syndrome defines **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).

Diagnostic methods for IPn, ARDS, and/or IPS include x-ray, bronchoscopy (including bronchoalveolar lavage), biopsies, arterial blood gas assessments, CBC, blood chemistries, and cultures.

If “yes,” continue with question 299. If “no,” continue with question 321.

Question 299: Date of diagnosis of IPn / IPS

Report the date of diagnosis of IPn / IPS. 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.

Question 300: Were diagnostic tests done (other than radiographic studies)?

In addition to radiographic studies used to determine evidence of IPn / IPS, indicate whether diagnostic tests were performed. If “yes,” continue with question 301. If “no,” continue with question 307.

Questions 301-306: Diagnosis was evaluated by

Select the method used for diagnosis of IPn / IPS. If “other test” is selected, specify the test method used in question 306.

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.
Other: report other evaluations for IPn/ARDs or IPS in question 306, excluding radiographic assessment.

Question 307: Was an organism isolated

If an organism was isolated, check “yes,” and continue with question 308. If an organism was not isolated, the cause was non-infectious or idiopathic, or the organism isolated was thought to be a contaminant, check “no,” and continue with question 319.

Questions 308-318: Etiology

Indicate “yes” or “no” for each organism isolated. If “other virus” is selected, specify the virus isolated in question 316. If “other organism” is selected, specify the organism isolated in question 318.

Questions 319-320: Did the recipient experience two or more episodes of IPn / IPS after the start of the preparative regimen to the date of last contact (question 1)?

Indicate whether the recipient developed two or more episodes of IPn / IPS between the start of the preparative regimen and the date of last contact. If the etiology of IPn is infectious, use the timelines provided for infections under question 296 of the *Infection* section above to determine if multiple episodes of infectious IPn occurred. If the etiology is non-infectious, a recipient must have completed steroid treatment or been weaned from prednisone to adrenal level dosing (less than or equal to 20 mg/day) before reporting the development of a subsequent episode of IPS. If “yes,” complete questions 299-318 for each infection in the FormsNet3^{SM} application. For paper form submission, make a copy of the pulmonary function section to report multiple infections and indicate that extra pages are attached.

Question 321: Did the recipient develop non-infectious pulmonary abnormalities (other than IPn / IPS / ARDS) after the start of the preparative regimen to the date of the last contact (question 1)?

Indicate whether the recipient developed a non-infectious pulmonary abnormality between the start of the preparative regimen and the date of last contact (question 1). If “yes,” continue with question 322. If “no,” continue with question 351.

Non-infectious pulmonary abnormalities include but are not limited to: Diffuse Alveolar Hemorrhage (DAH), Bronchiolitis Obliterans (BO/BOS), and Bronchiolitis Obliterans with Organizing Pneumonia (BOOP) / Cryptogenic Organizing Pneumonia (COP).

Bronchiolitis Obliterans (BO) and Bronchiolitis Obliterans with Organizing Pneumonia (BOOP)
Both BO and BOOP are pulmonary complications that occur late after HCT (in contrast to IPS, which occurs early post-HCT). BO is an obstructive complication which affects the small airways. BOOP is a restrictive complication which affects the alveoli ducts and alveoli (air sacs). Idiopathic BOOP is also known as cryptogenic organizing pneumonia (COP).

Question 322: Did the recipient develop bronchiolitis obliterans after the start of the preparative regimen to the date of the last contact (question 1)?

Bronchiolitis obliterans is often a manifestation of chronic GVHD. Confirm if the recipient has either histological or clinical evidence of chronic GVHD of the lung. If bronchiolitis obliterans is a result of chronic GVHD, confirm that bronchiolitis obliterans was also reported in the chronic GVHD section of this form (question 204).

Indicate whether the recipient developed bronchiolitis obliterans. If “yes,” continue with question 323. If “no,” continue with question 331.

Question 323: Date of diagnosis

Report the date of diagnosis of bronchiolitis obliterans. If the diagnosis was determined at an outside center and no documentation of 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.

Question 324: Were diagnostic tests done?

Bronchiolitis obliterans is mainly diagnosed by Pulmonary Function Testing (PFT), radiographic studies, and/or lung biopsy.

Indicate whether diagnostic tests were performed. If “yes,” continue with question 325. If “no,” continue with question 331.

Questions 325-330: Diagnosis was evaluated by

Select the method used for diagnosis of bronchiolitis obliterans. If “other test” is selected, specify the test method used in question 330.

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 in 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.
Other: report other evaluations for BO in question 330.

If PFT and/or radiographic imaging are used to diagnose BO in the absence of lung biopsy, select “other test” and specify PFT and/or radiographic imaging in question 330.

Question 331: Did the recipient develop pulmonary hemorrhage?

Indicate whether the recipient developed a pulmonary hemorrhage, including diffuse alveolar hemorrhage (DAH). If “yes,” continue with question 332. If “no,” continue with question 340.

Question 332: Date of diagnosis

Report the date of diagnosis of pulmonary hemorrhage. 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.

Question 333: Were diagnostic tests done?

Indicate whether diagnostic tests were performed. If “yes,” continue with question 334. If “no,” continue with question 340.

Questions 334-339: Diagnosis was evaluated by

Select the method used for diagnosis of pulmonary hemorrhage. If “other test” is selected, specify the test method used in question 339.

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: 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 in 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.
Other: report other evaluations for pulmonary hemorrhage in question 339.

Question 340: Did the recipient develop cryptogenic organizing pneumonia (COP)?

Cryptogenic organizing pneumonia is also known as bronchiolitis obliterans with organizing pneumonia (BOOP). Indicate whether the recipient developed cryptogenic organizing pneumonia or BOOP. If “yes,” continue with question 341. If “no,” continue with question 349.

Question 341: Date of diagnosis

Report the date of diagnosis of cryptogenic organizing pneumonia. 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.

Question 342: Were diagnostic tests done?

Indicate whether diagnostic tests were performed. If “yes,” continue with question 343. If “no,” continue with question 349.

Questions 343-348: Diagnosis was evaluated by

Select the method used for diagnosis of cryptogenic organizing pneumonia. If “other test” is selected, specify the test method used in question 348.

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: 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 in 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.
Other: report other evaluations for COP in question 348.

Questions 349-350: Did the recipient develop any other non-infectious pulmonary abnormalities?

Indicate whether the recipient developed any other non-infectious pulmonary abnormalities. If “yes,” specify the other pulmonary abnormality in question 350. If “no,” continue with question 351.

Question 351: Did the recipient receive endotracheal intubation or mechanical ventilation post-HCT?

Endotracheal intubation or mechanical ventilation may be used post-HCT 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.

Liver Function

Liver Toxicity
Questions 352-374 are 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 352: Did the recipient develop non-infectious liver toxicity (excluding GVHD) after the start of the preparative regimen to the date of last contact (question 1)?

Cirrhosis: 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.

Hepatic veno-occlusive disease (VOD): can be caused by systemic chemotherapy or radiation therapy. VOD consists of endothelial damage, micro thrombosis of the hepatic venules and sinusoidal fibrosis. It is more common in allogeneic transplants than autologous and typically occurs within three weeks of transplant. In the absence of a histological diagnosis, recipients must fulfill the following criteria for a diagnosis of VOD (McDonald GB, et al. *Hepatology* 1984; 4:116-22. Jones RJ, et al. *Transplantation* 1987; 44:778-83):

- Jaundice (bilirubin ≥ 2 mg/dL or > 34 µmol/L)
- Hepatomegaly with right upper quadrant pain
- Ascites and/or weight gain

Other: report liver abnormalities not listed above. Do not include hepatic infections or GVHD. Report infections in the Infection Section (questions 291-295) and GVHD in the acute (questions 140-187) and/or chronic (questions 188-259) GHVD sections.

Indicate whether the recipient developed a non-infectious liver toxicity between the start of the preparative regimen and the date of last contact (question 1). If “yes,” continue with question 353. If “no,” continue with question 375.

Question 353: Date of diagnosis

Report the date of diagnosis of non-infectious liver toxicity. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed ascites prior to the physician documenting clinical evidence of veno-occlusive disease). If the diagnosis is based on histological, radiological, hematologic, or other methods, report the date of specimen collection. 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.

Questions 354-362: Etiology

For each option listed, indicate whether it was the cause of the recipient's liver toxicity and, if applicable, answer any additional questions. If "other" is selected, specify the cause in question 361.

Questions 363-374: Specify diagnosis of liver toxicity by clinical signs and symptoms / evaluation

For each sign, symptom, or evaluation listed, indicate whether it was used to diagnose the recipient's liver toxicity. If "other" is selected, specify the evaluation in question 374.

Ascites: the accumulation of fluid in the abdomen that ranges from mild to severe. Diagnosis may be made by clinical evaluation, laboratory tests, and/or radiological imaging.
Autopsy: a post-mortem procedure used to determine the cause of death and to evaluate other disease present at the time of death.
Bilirubin > 2.0 mg: elevated bilirubin may be a sign of liver toxicity, but clinical correlation is necessary to determine if elevated bilirubin is the result of non-GVHD-related liver toxicity. Do not report liver GVHD in this section.
Biopsy: a liver biopsy is a procedure in which a sample of liver tissue is taken percutaneously, transvenously, or laparoscopically.
Elevated hepatic venous pressure gradient: hepatic venous pressure gradient (HVPG) is a method used to detect portal hypertension. The procedure includes measuring the venous pressure before and after inflation of a fluid-filled balloon in the portal vein.
Elevated liver enzymes (e.g., alkaline phosphatase, ALT, AST, LDH, GGT): elevated liver enzymes may be a sign of liver toxicity, but clinical correlation is necessary to determine if elevated liver enzymes are the result of non-GVHD-related liver toxicity. Do not report GVHD in this section. Generally, elevated liver enzymes should be reported if they are two times the upper limit of normal at your center.
Hepatomegaly: hepatomegaly is the enlargement of the liver. Hepatomegaly is often detected upon physical examination, but may be detected using radiological techniques.
Right upper quadrant pain or tenderness: right upper quadrant (RUQ) pain or tenderness is often detected upon physical examination and is a general symptom that should be clinically correlated with other examinations for liver toxicity.
Ultrasonography / doppler (abnormal portal vein flow): Ultrasound can be used to determine if the flow through the hepatic portal vein is abnormal.
Weight gain > 5%: weight gain of greater than 5% is detected upon physical examination, but is a general symptom that should be clinically correlated with other assessment for liver toxicity.
Other: report other evaluations or signs/symptoms of liver toxicity in question 374.

Other Organ Impairment / Disorder

Question 375: Has the recipient developed any other clinically significant organ impairment or disorder after the start of preparative regimen to the date of last contact (question 1)?

The intent of this question is to identify *serious* conditions that have an effect on the outcome of the HCT. For the purposes of this manual, the term "clinically significant" refers to conditions that are being treated post-HCT, or have caused complications post-HCT. Do not report complications that are expected for most transplant recipients (e.g., mild-moderate mucositis).

Indicate whether the recipient developed any other clinically significant organ impairment or disorder between the start of the preparative regimen and the date of last contact (question 1). If "yes," continue with question 376. If "no," continue with question 407.

Questions 376-406: Specify impairment / disorder and the date of diagnosis

Avascular necrosis: localized tissue death due to inadequate oxygen to the cells. Also known as coagulation necrosis or ischemic necrosis.
Cataracts: loss of transparency in the lens of the eye.
Congestive heart failure (CHF): inability of the heart to supply oxygenated blood to meet the body's needs. Ejection fraction < 40%.
Diabetes / hyperglycemia: 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.
Gonadal dysfunction / infertility requiring hormone replacement: 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.
Growth hormone deficiency: a condition in which the body does not produce enough growth hormone.
Growth disturbance: a reduced overall rate of growth.
Hemorrhagic cystitis / hematuria requiring medical intervention: 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 (questions 291-295). Examples of medical intervention include catheterization of bladder, extra transfusions, or a urology consult.
Hypothyroidism: 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.
Myocardial infarction (MI): an obstruction in the coronary artery resulting in damage/necrosis to the

cardiac muscle.
Pancreatitis: inflammation of the pancreas.
Post-transplant thrombotic microangiopathy, thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), or similar syndrome:
Features include:

- microangiopathic hemolysis
- thrombocytopenia (< 50 × 10^9/L)
- LDH greater than the center-specific upper limit of normal
- serum creatinine > 2 mg/dL or > 50% rise over baseline
- neurological changes
- bilirubin greater than twice the center-specific upper limit of normal
- pulmonary involvement.

Renal failure severe enough to warrant 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.
Stroke: loss of brain function due to a disturbance in the blood supply to the brain.
Seizure: sudden, involuntary muscle contractions due to the hyperexcitation of neurons.

For each organ impairment and/or disorder listed, check “yes” or “no.” If “yes,” enter the date of diagnosis of the corresponding 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.

The “other impairment or disorder, specify” category should be used to report any clinically significant impairment(s)/disorder(s) not listed on the form. Examples may include but are not limited to:

- Non-infectious eye complications (retinopathy due to radiation therapy)
- Bone abnormalities (aseptic necrosis, osteoporosis)
- Grade 4 mucositis (including anywhere along the digestive tract), reporting the first instance of grade 4 disease (e.g., the date of initiation of total parenteral nutrition (TPN))

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

New Malignancy

Question 407: Did a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder appear that is different from the disease for which the HCT was performed?

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.

Report relapse of the recipient's primary disease on the appropriate post-HCT Disease 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
- PTLD (post-transplant lymphoproliferative disorder) report as lymphoma or lymphoproliferative disease

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

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

Skin Cancers
For most malignancies, one does not report recurrence, progression or transformation of the recipient's primary disease (disease for which the transplant was performed) or relapse of a prior malignancy in the "New Malignancy" section. However, in the case of a basal cell or squamous cell skin cancer, one needs to report each discrete episode. For example, a recipient had a basal cell skin cancer diagnosed on the neck four months post-HCT and six months later had another basal cell located on the nose. The lesion on the nose is not considered a metastasis from the neck, but a new discrete lesion. These discrete episodes

should be reported in the “Other skin malignancy” questions on the 100 Day forms (revision 3, questions 435-437).

If a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder has occurred following the HCT, check “yes” and continue with question 408. If not, check “no” and continue with question 450.

Question 408: For all new malignancies except for “other skin malignancy (basal cell, squamous),” was testing performed to determine the cell of origin?

Indicate whether testing was performed on the malignant tumor cells to determine the cell origin of the new malignancy. If “yes,” continue with question 409. If “no,” continue with question 411.

Select “the only new malignancy in this reporting period was ‘other skin malignancy (basal cell, squamous)’” if the skin malignancy (basal cell, squamous) was the only new malignancy identified.

Question 409: Specify the cell of origin of the new malignancy

Indicate whether the new malignancy originated from the recipient (host), the donor, or an unknown cell origin.

Question 410: Is a copy of the cell origin evaluation (VNTR, cytogenetics, FISH) attached?

Attaching a copy of the evaluation for the cell origin assists in disease confirmation and **reduces the need for later data queries.**

If “yes,” complete the Log of Appended Documents (Form 2800) and attach the laboratory report. For more information regarding the Form 2800, see the Log of Appended Documents manual section.

Questions 411-448: Specify which new disease(s) occurred and if applicable, the date of diagnosis.

For each malignancy, lymphoproliferative disorder, or myeloproliferative disorder listed, check “yes” or “no.” If “yes,” enter the date of diagnosis of the corresponding malignancy, lymphoproliferative disorder, or myeloproliferative disorder and answer any applicable additional questions.

The “other malignancy, specify” category should be used to report any subcategories of new malignancies that are not listed on the form.

Question 449: Is a pathology / autopsy report or other documentation attached?

Attaching a copy of the diagnostic pathology or autopsy report for the new malignancy assists in disease confirmation and **reduces the need for later data queries.** Include information regarding the histological diagnosis, site(s) of disease, and any applicable ancillary information available.

If “yes,” complete the Log of Appended Documents (Form 2800) and attach the pathology report. For more information regarding the Form 2800, see the Log of Appended Documents manual section.

Q450-453: Functional Status

Question 450: Was the recipient discharged from the hospital after HCT?

Indicate whether the recipient was discharged from the hospital after HCT. If the recipient died without ever being discharged from the hospital, answer this question “no.” If “yes,” continue with question 451. If “no” or “not applicable, therapy and HSC infusion given as outpatient,” continue with question 452.

Question 451: Date first discharged from hospital post-HCT

Report the date the recipient was first discharged from the hospital.

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

Number of Inpatient Days
The CIBMTR previously captured the number of inpatient days in the first 60 days post-HCT for autologous transplant recipients and the number of inpatient days in the first 100 days post-HCT for allogeneic transplant recipients. The total number of inpatient days in the first 100 days post-HCT now applies to both autologous and allogeneic recipients.

Question 452: Total number of inpatient days (day 0 to day 100) in first 100 days post-HCT

Enter the total number of inpatient days (starting from 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 HCT prior to day 100, do not include the start date of the preparative regimen for the subsequent HCT (or the date of the subsequent infusion if no preparative regimen was given).

Question 453: Specify the functional status of the recipient on the date of actual contact (question 1).

If the recipient has died, skip this question and continue with the Subsequent HCT section at question 454.

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 less than 16 years old.

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 healthcare provider rather than make an assignment themselves, based on inadequate information.

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.

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.

Q454-461: Subsequent HCT

Complete this section if the recipient received a subsequent HCT (question 5, answered "yes"). If no subsequent HCTs were performed, continue with the DCI section at question 462.

In addition to this section, a new Pre-TED Form (2400) and Recipient Baseline Data Form (Form 2000) must be completed for the subsequent HCT. The exception to this is an *autologous HCT performed for engraftment reasons* (indications 1-3 in question 457). The cells used for this subsequent autologous HCT would have been collected prior to the previous transplant.

For information on how to distinguish infusion types (e.g., HCT versus DCI), see Appendix O.

Question 454: Date of subsequent HCT

Report the date of the subsequent HCT.

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

Question 455: Was the subsequent HCT performed at a different institution?

Indicate if the subsequent HCT was performed at another institution. If "yes" continue with question 456. If "no" continue with question 457.

Question 456: Specify the institution that performed the subsequent HCT

Report the name, city, state, and country of the institution where the recipient's subsequent HCT was performed. These data are used to identify and link the recipient's information in the database.

Questions 457-458: What was the indication for subsequent HCT?

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

- **No hematopoietic recovery.** Additional stem cells are required because neutrophil recovery was not achieved following previous high-dose therapy and HCT (i.e., ANC was never ≥ 0.5×10^9/L for three consecutive days). A subsequent autologous HCT for no hematopoietic recovery does not require an additional Pre-TED (Form 2400) or Baseline (2000) to be completed.
- **Partial hematopoietic recovery.** Additional stem cells are required because hematopoietic recovery was deemed insufficient or too slow for survival following previous high-dose therapy and HCT. A

subsequent autologous HCT for partial hematopoietic recovery does not require an additional Pre-TED (Form 2400) or Baseline (2000) to be completed.

- **Graft failure / rejection after achieving initial hematopoietic recovery.** Additional stem cells are required because the hematopoietic recovery indefinitely declined after the initial hematopoietic recovery (ANC was greater than or equal to 0.5×10^9/L for three consecutive days, and then declined to below 0.5×10^9/L for at least three consecutive days). A subsequent autologous HCT for graft failure or rejection does not require an additional Pre-TED (Form 2400) or Baseline (2000) to be completed.
- **Persistent primary disease.** Additional stem cells are required because of the persistent presence of disease pre- and post-transplant (i.e., complete remission was never achieved following the previous transplant).
- **Recurrent primary disease.** Additional stem cells are required because of relapsed primary disease (i.e., complete remission was achieved pre- or post-transplant, but the disease relapsed following the previous transplant).
- **Planned second HCT, per protocol.** Additional stem cells are given as defined by the protocol for a subsequent transplant/infusion. This transplant is not based upon recovery, disease status, or any other assessment.
- **New malignancy (including PTLD and EBV lymphoma).** Additional stem cells are required because the recipient has developed a new malignancy. This does not include a transformation or progression of the original malignancy for which the recipient was transplanted (refer to question 407 for more information). If “new malignancy” is selected, also complete questions 407-449.
- **Stable, mixed chimerism.** In the case of a stable, mixed donor chimerism, the infusion of additional cells (usually lymphocytes and not mobilized stem cells) is typically classified as a DCI. Verify with the transplant physician that the cells given should be reported as a subsequent transplant and that stable, mixed chimerism is the reason for the transplant.
- **Declining chimerism.** In the case of declining chimerism—when the percentage of donor cells is sequentially decreasing on several studies, indicating possible impending graft failure—additional stem cells are required. Usually the donor chimerism has fallen below 30-50%.
- **Other.** If additional stem cells are given for a reason other than the options listed, select “other” and complete question 458.

Multiple Products

In the FormsNet3^{SM} application, use the multiple feature to complete questions 459-461 for each product infused. For paper form submission, copy and complete questions 459-461 for each product infused.

Question 459: Source of HSCs

Report the stem cell source of the recipient's subsequent HCT.

If "allogeneic, related" is selected, indicate whether the same donor was used in question 460 and complete a new Pre-TED Form (2400) and Recipient Baseline Data Form (Form 2000).

If "allogeneic, unrelated" is selected, specify the product/donor type in question 461 and complete a new Pre-TED Form (2400) and Recipient Baseline Data Form (Form 2000).

If "autologous" is selected, complete a new Pre-TED Form (2400) and Recipient Baseline Data Form (Form 2000), unless the indication for transplant was due to engraftment reasons (indications 1-3 in question 457).

Q462-560: Donor Cellular Infusion (DCI) Information

This section captures information on DCIs (question 7, answered “yes”) from any donor source (unstimulated peripheral blood mononuclear cells, T cells, NK cells, other cells). Complete this DCI section for all infusions given in a 10 week period. If the recipient did not receive any DCIs, continue with the signature lines.

For information on how to distinguish infusion types (e.g., HCT versus DCI), see Appendix O.

Additional information regarding DCIs is available on the CIBMTR website: http://www.cibmtr.org/Meetings/Materials/CRPDMC/index.html

The paper version of the 100 Days Post-HCT Data Form (2100) provides space to report one Donor Cellular Infusion (DCI) event (in a 10-week period). If more than 10 weeks have elapsed between DCIs, copy and complete this section for each 10-week period. The FormsNet3^{SM} application will allow as many DCI entries as needed.

A DCI is a form of immunotherapy that is commonly used to treat infections (e.g., viral) or recurrent disease. In the setting of recurrent disease, the DCI is used to create a graft-versus-leukemia/tumor (GVL/GVT) effect. A DCI may also be utilized to treat GVHD or promote engraftment when chimerism studies reveal less than 100% donor cells. The recipient does not receive a preparative regimen prior to receiving the additional donor cells since replacement of the marrow is not the goal.

A DCI should not be reported if additional donor cells are given for failed ANC recovery, partial or poor ANC recovery, loss of graft, or late graft failure. These would be considered as subsequent HCTs.

The types of cells used for a DCI include, but are not limited to the following:

- Lymphocytes (TC – T Cells): A therapeutic product from any source containing a quantified T-cell population.
- Peripheral blood mononuclear cells (both stimulated and unstimulated) (TC – Whole Blood): Whole blood collected as a source of nucleated cells intended for therapeutic use other than HPCs.
- Dendritic cells from the original donor (TC – DC): A therapeutic cell product containing dendritic cells for therapeutic use.
- Mesenchymal cells (TC – MSC): A therapeutic product containing mesenchymal stromal cells for therapeutic use.

Recipients may receive DCI infusions over several days or weeks. A single DCI section should be completed for all infusions given within a 10-week period.

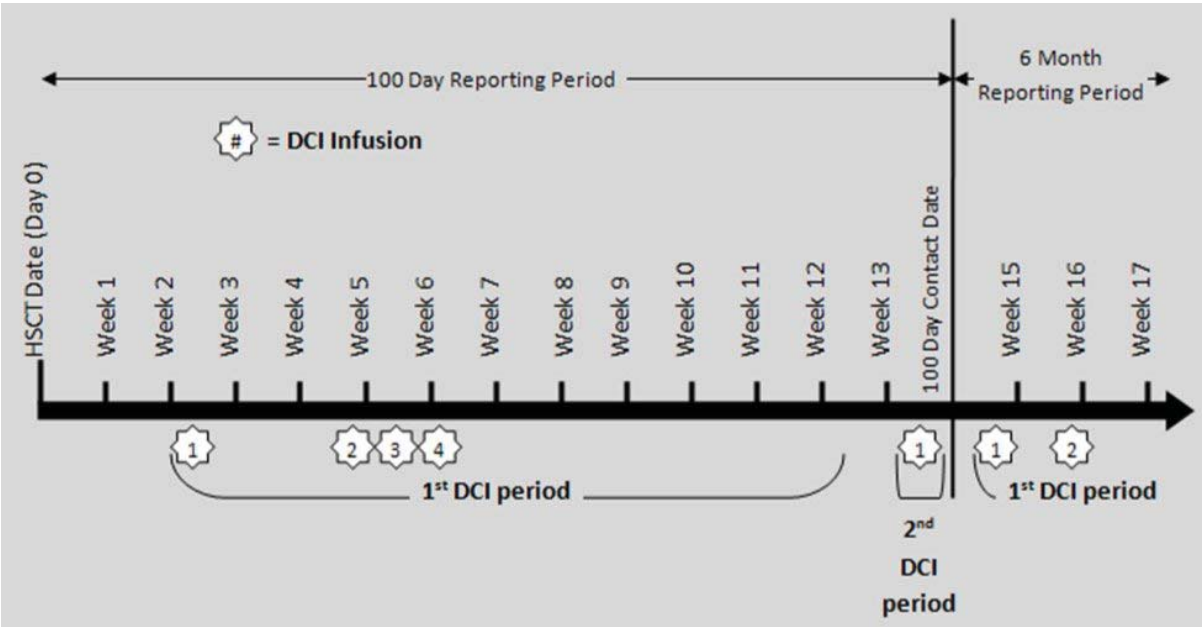
Complete the first DCI section for all infusions given between day 0 (of the DCI) and 10 weeks post initial DCI infusion. If the recipient receives an additional DCI, but it is infused after the initial 10-week period, report this subsequent DCI in a second DCI section. Any additional infusion(s) performed within 10 weeks of DCI should be reported in the subsequent DCI section.

This 10-week period is limited to within a reporting period; if the recipient continues to receive infusions beyond the 100 Day date of contact, report infusions only until the contact date (even if the period has not yet extended 10 weeks since the initial infusion). Report the first DCI in the new reporting period (Form 2200) under the first DCI instance and begin the 10-week reporting period again.

In this example, four DCIs are reported in the first 10-week period and one DCI is reported in the second 10-week period within the 100-day reporting period (which ends at the 100 Day contact date). At least two DCIs would be reported in the first DCI instance in the six-month reporting period.

See the illustration below for an example of a recipient receiving multiple DCIs.

Example: Calculation Timeline



Question 462: Date the first DCI was given

Report the date of the first DCI given in this reporting period.

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

Question 463: Specify the number of cell infusions given within 10 weeks of the first DCI

Indicate the total number of DCIs given in a 10-week period or up to the date of contact, whichever comes first. (In the example above, the total number is four.)

Question 464: Was the DCI infusion performed at a different institution?

If the DCI was performed at another institution, indicate “yes” and continue with question 465. If “no,” continue with question 466.

Question 465: Specify the institution that performed the DCI

Report the name, city, state, and country of the institution where the recipient’s DCI was performed. These data are used to identify and link the recipient’s information in the database.

Question 466: Indication for DCI

Indicate the reason for the DCI. If multiple DCIs were given within the 10-week period, select the most appropriate reason in the FormsNet3SM application. If completing the paper version of the form, check all applicable indications.

- **Planned as part of initial HCT protocol.** Additional cells are given as defined by the protocol for the DCI. This infusion is not based upon hematopoietic recovery, disease status, or any other assessment.
- **Treatment for relapsed, persistent, or progressive disease.** Following the HCT, additional cells are given because:
    - The disease for which the recipient was transplanted relapsed
    - The recipient was transplanted with disease present, and never entered a remission
    - The disease for which the recipient was transplanted has progressed

      If the reason is treatment for relapsed, persistent, or progressive disease, also complete questions 467-474.
- **Treatment for B cell lymphoproliferative disorder (PTLD, EBV lymphoma).** Additional cells are given because the recipient developed a B cell lymphoproliferative disorder such as PTLD or EBV lymphoma.
- **Treatment for GVHD.** Mesenchymal cells are given as treatment for GVHD.
- **Viral Infection.** Additional cells (e.g., T-lymphocytes) are given because the recipient developed a viral infection. If viral infection is indicated, also complete question 475.

- **Stable, mixed chimerism.** Mixed chimerism is the concurrent presence of donor and recipient hematopoietic cells. Stable mixed chimerism indicates the quantity is neither going up nor down. Lymphocytes may be infused to reduce and potentially eliminate the host cells and improve donor cell percentage.
  If the reason is stable, mixed chimerism, also complete question 476. If multiple chimerism tests were performed in the reporting period, document the date the stable, mixed chimerism was first detected.
- **Loss of / decreased donor T-cell chimerism.** In the case of declining chimerism, when the percentage of donor cells is sequentially decreasing on several studies (indicating possible impending graft failure), additional cells are required. Usually the donor chimerism has fallen below 30-50%. The purpose of the infusion of donor T-cells is to restore 100% donor chimerism.
  - If the reason for the DCI is loss of/decreased donor T-cell chimerism, also complete question 476. If multiple chimerism tests were performed in the reporting period, document the date the loss of/decreased T-cell chimerism was first detected.
- **Other.** Additional cells are required and/or given for a reason other than the options listed. If the DCI is given for another reason, select “other” and complete question 477.

Questions 467-472: Specify the method(s) of disease detection below.

If the reason for the DCI is treatment for relapsed, persistent, or progressive disease, indicate the method(s) of disease detection. For each method used, if the result was positive, report the first date the disease was detected. If the result was negative, report the last method date prior to the DCI date (question 462).

Question 473: Was chemotherapy used to attempt to induce disease response prior to the first DCI?

If the reason for the DCI is treatment for relapsed, persistent, or progressive disease, indicate whether chemotherapy was used to attempt to induce disease response prior to the DCI. If “yes,” continue with question 474 and report the date of administration of the final chemotherapy dose.

Question 478: What was the recipient’s disease status immediately prior to the first DCI?

When determining disease status, refer to the Pre-TED Form Instructions for the specific definitions for each disease. Indicate the recipient’s disease status immediately prior to the first DCI. If the recipient’s disease status was not evaluated post-HCT, select “not evaluated post-HCT,” and continue with question 480.

Question 479: Date disease status was established prior to the first DCI

Report the date of the most recent assessment (e.g., pathology, radiology, laboratory, physician assessment) prior to the first DCI. Enter the date the sample was collected for examination, the date radiological examination was performed, or the date the disease was assessed by a physician.

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

Question 480: Specify the functional status of the recipient immediately prior to the first DCI

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 less than 16 years old.

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 healthcare provider rather than make an assignment themselves, based on inadequate information. 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.

Indicate the score (10-100) that best represents the recipient's activity status immediately prior to the first DCI. 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.

Questions 481-487: Specify DCI source

Indicate the source of the cells used for the DCI as:

- Collected at the time of PBSC mobilization and collection.
- Negative fraction of CD34 selected PBSC.

- Negative fraction of CD34 selected bone marrow.
- Apheresis at a different time than collection of PBSC used for allogeneic HCT. If “yes,” specify the date of apheresis in question 485.
- Isolated from a unit(s) of whole blood. If “yes,” specify the number of units in question 487.

Question 488: Were the donor cells collected by leukapheresis?

Leukapheresis is a procedure in which white blood cells are removed from the donor and portions are used for the DCI. Indicate whether the donor cells for the DCI were collected by leukapheresis. If “yes,” continue with question 489. If “no,” continue with question 492.

Question 489: Date of first leukapheresis

Report the date the first leukapheresis.

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

Question 490: Date of last leukapheresis

Report the date the last leukapheresis.

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

Question 491: Number of leukaphereses

Report the number of leukapheresis procedures.

Question 492: Did the donor receive treatment to enhance cell collection prior to donation?

Stem cells do not typically circulate in the blood stream. Therefore, in order to increase the quantity of cells for collection, an agent is frequently given to the allogeneic donor or autologous recipient. The purpose of the agent is to move the stem cells from the bone marrow into the peripheral blood. This practice is often referred to as *mobilization* or *priming*. In general, mobilization or priming is not required to collect a DCI product when it is isolated from whole blood or by apheresis at a different time than collection of PBSCs used for allogeneic HCT. Indicate whether the donor received treatment to enhance cell collection prior to donation. If “yes,” continue with question 493. If “no,” continue with question 500.

Questions 493-499: Specify treatment(s) given:

- G-CSF. Indicate if the donor/autologous recipient received G-CSF (filgrastim, Neupogen) prior to the cell harvest to enhance the product.
- GM-CSF. Indicate if the donor/autologous recipient received GM-CSF (sargramostim, Leukine) prior to the cell harvest to enhance the product.
- Other (growth factor). If the donor/autologous recipient received a growth factor such as AMD3100 (plerixafor, Mozobil) prior to the cell harvest, check “yes” and specify the other growth factor(s) given to the donor/autologous recipient in question 497.
- Other treatment. If the donor/autologous recipient received any other treatment prior to the cell harvest to enhance the product, check “yes,” and specify the other treatment administered to the donor/autologous recipient in question 499.

Questions 500-506: For each DCI given, report the total number of cells infused.

Report the total number of cells infused and specify the exponent for each cell type. If the cells were cryopreserved, report the totals after processing, but before cryopreservation. If multiple cellular infusions were given within the 10-week period, report the cumulative total of all cells infused; submit a log of appended documents showing the product analyses for each individual DCI product.

Question 507: Were dendritic cells infused?

Indicate whether dendritic cells were infused.

Question 508: Were fibroblasts infused?

Indicate whether fibroblasts were infused.

Questions 509-510: Were any other cell types infused (not including cell types reported in questions 500-508)?

Indicate whether any other cell types were infused. If “yes,” specify the cell type in question 510.

Question 511: Were the cells cryopreserved prior to infusion?

Indicate whether the cells were cryopreserved prior to infusion. If “yes,” continue with question 512. If “no,” continue with question 513.

Question 512: Specify portion cryopreserved

Specify whether all of the cells or a portion of the cells were cryopreserved prior to infusion.

Product Manipulation
Cryopreservation is not considered a method of product manipulation. If the product was cryopreserved, but no actual manipulation was performed, report "no" for question 513.

Question 513: Were the cells manipulated prior to infusion?

If any part of the product was manipulated in any way prior to infusion, check "yes," and continue with question 514. Do not report cryopreservation as a method of manipulation. If the product was not manipulated, check "no," and continue with the signature lines.

Question 514: Specify portion manipulated

If all of the cells were manipulated using the same method, select "all cells." If some of the cells were manipulated, select "portion of cells."

Report all methods used to manipulate the product at the transplant facility (i.e., if the product was shipped to your facility, do not report manipulation of the product performed at the collection center).
All bags from one mobilization cycle are considered a single product; report all manipulation methods used on any part of the single product.
Do not report methods of manipulation performed as part of another procedure (e.g., T-cell depletion as part of expansion).

Plasma Removal versus Volume Reduction
Plasma removal for ABO incompatibility (question 519) is performed for ABO or Rh incompatibility between the donor and recipient. Volume reduction as a manipulation method (question 526) is performed for the sole purpose of reducing the total volume of product (not as a result of any incompatibility between the donor and recipient).
If "yes" is reported for both question 519 and 526, the product must be plasma reduced for ABO incompatibility and then further reduced to decrease the total product volume.

Question 515: ABO incompatibility

RBC or plasma depletion is often used in cases where there is ABO incompatibility between donor and recipient. Incompatibility can cause hemolysis and delayed red blood cell recovery.

This option should be used for **allogeneic** products only; report RBC depletion of **autologous** products as "volume reduction" under question 526. Indicate if the product was manipulated for ABO incompatibility. If "yes," continue with question 516. If "no," continue with question 523.

Questions 516-522: Specify method

Indicate the method(s) used for ABO incompatibility manipulation. If “other” is selected, specify the method in question 522.

Question 523: Dextran-albumin wash

A dextran-albumin wash method is used to improve cell recovery and reduce reaction(s) to the infusion.

Indicate if a dextran-albumin wash method was used on the product.

Question 524: Ex-vivo expansion

Ex-vivo expansion is a type of manipulation where the cells have been maintained ex vivo (cultured) to activate, expand, or promote development of a specified cell population in the presence of specified additive(s). The most common method of ex vivo expansion uses hematopoietic growth factors. Ex-vivo expansion is most commonly used with cord blood transplants.

Indicate if ex-vivo expansion was used on the product. Do not report T-cell depletion separately if it was done as a part of this procedure.

Question 525: Genetic manipulation (gene transfer/transduction)

Genetic manipulation (gene transfer/transduction) may be used to lessen the negative effects of DCIs. For example, a DCI may include T cells that have been transduced with HSV-TK (herpes simplex virus) which are susceptible to gancyclovir treatment. A recipient who develops DCI-related GVHD may be treated effectively with gancyclovir.

Indicate if genetic manipulation was used on the product.

Question 526: Volume reduction

The purpose of volume reduction is specifically to reduce the volume in order to prevent volume overload.

Indicate if volume reduction was used to manipulate the product.

Question 527: CD34+ selection

CD34+ selection is a manipulation method also known as “positive selection.” This method identifies and selects stem cells that have a CD34+ marker on the cell surface, and is commonly done with a CliniMACS/ CliniMax or Isolex machine.

Indicate if CD34+ selection was used. If “yes,” continue with question 528. If “no,” continue with question 530.

Questions 528-529: Specify manufacturer of CD34+ selection machine

Indicate the type of machine used for CD34+ selection. If “other” is selected, specify the manufacturer in question 529.

Questions 530-540: T-cell depletion

This method of negative selection manipulation is most commonly used for allogeneic HCT, as it removes some or all of the T-cells in an effort to minimize GVHD. The removed T-cells may be infused at a later date (e.g., DCI). Methods of T-cell depletion may include the use of antibodies.

Indicate if the product was T-cell depleted and the method used. If “yes” is selected for questions 531-536, indicate the specific antibodies used for T-cell depletion in questions 543-560. If “other” is selected, specify the method in question 540.

CD34 Affinity Column Plus Sheep Red Blood Cell Rosetting (Question 538)
CD34 affinity column plus sheep red blood cell rosetting combines two methods (positive and negative selection) to achieve a greater degree of T-cell depletion. Sheep erythrocytes adhere spontaneously to human T-cells forming rosettes. The rosettes are then isolated from the rest of the cells using Ficoll-Hypaque gradient centrifugation.

Questions 541-542: Other cell manipulation

Indicate if the cells were manipulated using any other method, and specify the manipulation type in question 542.

Examples include but are not limited to the following:

- Preparation of T-regulatory cells
- B-cell reduction
- Buffy coat enrichment
- CD133 enrichment
- Monocyte enrichment
- Mononuclear cell enrichment
- PUV treatment

Cryopreservation is NOT considered a method of manipulation. Do not include cryopreservation or freeze media in the “other cell manipulation” category.

Question 543: Were antibodies used during graft manipulation?

If antibodies were used during product manipulation, select “yes” and continue with question 544. If antibodies were not used, select “no” and continue with the signature lines.

Questions 544-560: Specify Antibodies

Specify whether each antibody listed was used for product manipulation. Do not leave any responses blank. If “other CD3” is selected, specify what in question 554. If “anti CD52” is selected, further specify the antibody in questions 556-558. If “other antibody” is selected, specify in question 560.