

## 2100: Post-HCT Follow-Up

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


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

### Subsequent HCT:

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

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

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

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

### Lost to Follow Up:

Occasionally, centers may lose contact with recipients for a variety of reasons, including the recipient's moving, changing physicians, or death. If contact with a recipient appears lost, please consider calling the recipient at home or work, sending a letter, communicating with the treating or referring physician, or

contacting the hospital billing department. If your center receives documented information that a recipient is alive or dead, the form should be filled out with the recipient survival status. If no documentation exists and several unsuccessful attempts have been made to contact the recipient, they are considered lost to follow-up and the form may be marked as such using the [Lost to Follow-Up Tool](#) in FormsNet3 for each reporting period in which no contact exists.

#### Links to Sections of the Form:

[Q1-5: Vital Status](#)

[Q6-12: Granulopoiesis / Neutrophil Recovery](#)

[Q13-18: Megakaryopoiesis / Platelet Recovery](#)

[Q19-58: Growth Factor and Cytokine Therapy](#)

[Q49-63: Current Hematologic Findings](#)

[Q64-88: Immune Reconstitution](#)

[Q89-107: Chimerism Studies](#)

[Q108-130: Engraftment Syndrome](#)

[Q131-233: Acute Graft vs. Host Disease](#)

[Q234-406: Chronic Graft vs. Host Disease](#)

[Q407-427: Infection Prophylaxis](#)

[Q428-440: Infection](#)

[Q441-645: Organ Function](#)

[Q616-639: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder](#)

[Q640-660: Functional Status](#)

[Q661-668: Subsequent HCT](#)

#### Manual Updates:

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

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

Date	Manual Section	Add/Remove/Modify	Description
5/10/18	2100: Post-HCT Follow-Up	Add	Added <b>Fecal Microbiota Transplant</b> note box to acute (questions 185-233) and chronic (questions 328-399) GVHD treatment instructions.

3/ 27/ 18	2100: Post-HCT Follow- Up	Add	Added HHV-6 to Definitions for Same Infection Table included in the instructions for questions 428-436.
2/ 20/ 18	2100: Post-HCT Follow- Up	Add	Added text (in red below) to the instructions for question 304. This instruction was / is available on the form. <i>Report the date of maximum chronic GVHD involvement <b>since the date of last report</b>, based on clinical grade.</i>
2/ 20/ 18	2100: Post-HCT Follow- Up	Add	Added the following instruction for question 303. This instruction was / is available on the form. <i>Report the extent of chronic GVHD since the date of last report.</i>
2/ 20/ 18	2100: Post-HCT Follow- Up	Add	Added text (in red below) to the instructions for question 302. This instruction was / is available on the form. <i>Report the maximum chronic GVHD involvement <b>since the date of last report</b>, based on clinical grade, as documented by the recipient's primary care provider.</i>
2/ 13/ 18	2100: Post-HCT Follow- Up	Add	Added <b>Liver Toxicity Prophylaxis</b> note box above the instructions for question 490.
11/ 20/ 17	2100: Post-HCT Follow- Up	Modify	Added (in red) and removed (struck out) text from description of IPn / ARDS provided in the instructions for questions 441-485. <i><u>Interstitial pneumonitis / Acute respiratory distress syndrome (IPn/ARDS): IPn refers to inflammation of the alveolar walls. Acute respiratory distress syndrome typically refers to fluid build-up within the alveoli. In either case, gas exchange is impaired resulting in oxygen deprivation. Both conditions can result from infectious or non-infectious causes. <del>Infectious causes may be bacterial, viral (CMV, adenovirus, RSV, influenza, etc.), or fungal.</del> Only report IPn / ARDS resulting from non-infectious causes in questions 441-485.</u></i>
11/ 20/ 17	2100: Post-HCT Follow- Up	Add	Added instructions below for question 158.
11/ 15/ 17	2100: Post-HCT Follow- Up	Add	Added the fungal infection codes below to the list of infections which will prompt the Fungal Infection Post-HCT Form to come due. The list is provided in the instructions for questions 428-436. <ul style="list-style-type: none"> <li>• 270 Blastomyces (dermatitidis)</li> <li>• 201 Candida albicans</li> <li>• 208 Candida non-albicans</li> <li>• 222 Cryptococcus gattii</li> <li>• 221 Cryptococcus neoformans</li> <li>• 261 Histoplasma (capsulatum)</li> <li>• 272 Scedosporium (all species)</li> </ul>

			<ul style="list-style-type: none"> <li>• 503 Suspected fungal infection</li> </ul>
9/26/17	2100: Post-HCT Follow-Up	Add	Added Pneumocystis jiroveci warning box above the instructions for questions 428-436.
9/26/17	2100: Post-HCT Follow-Up	Remove	Removed Pneumocystis jiroveci from the list of scenarios not to report included in the instructions for questions 428-436.
9/15/17	2100: Post-HCT Follow-Up	Add	Added Pregnancy Questions warning box above the instructions for question 654.
8/31/17	2100: Post-HCT Follow-Up	Add	Added text (in red below) to the description of stage 4 gut GVHD provided in the Acute GVHD Grading and Staging Table located below the instructions for question 169. <i>Severe abdominal pain, with or without ileus, and / or grossly bloody stool</i>
8/1/17	2100: Post-HCT Follow-Up	Add	Added the text below to the instructions for question 169. <i>For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic).</i>
8/1/17	2100: Post-HCT Follow-Up	Add	Added the text below to the instructions for questions 170-175. <i>Report the stage of each organ at diagnosis. For reporting purposes, “at diagnosis” is defined as the period between onset of signs / symptoms and the initiation of therapy to treat GVHD (topical or systemic).</i>
7/11/17	2100: Post-HCT Follow-Up	Add	Added the following text to the description of lower GI GVHD provided in the instructions for questions 170-175: <i>Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.</i>
6/8/17	2100: Post-HCT Follow-Up	Remove	Removed incorrect instruction from instructions for questions 185-233. <i>When reporting the date started, report the first day the drug as given on or after the GVHD diagnosis date (reported in question 158). <del>If acute GVHD persisted since the date of the last report, report the first day the drug was given during the current reporting period.</del> For <b>prophylaxis medications</b> continued after the date of diagnosis of acute GVHD, report the date of diagnosis as the date started. If an acute GVHD treatment has continued from a previous reporting period, report the original start date and override the error in FormsNet3<sup>SM</sup> using the code “verified correct.”</i>
6/8/17	2100: Post-HCT Follow-Up	Remove	Removed unnecessary text from the following instruction for question 234 to clarify instructions. <i>Report “no” if chronic GVHD was not clinically diagnosed – initially or as a flare – in the reporting period; this includes instances where chronic GVHD persists from a prior reporting period. <del>without flare in the current reporting period.</del></i>

5/31/17	2100: Post-HCT Follow-Up	Add	Added two additional bullets to the instructions for Questions 428-436 under “Do not report the following scenarios:” <ul style="list-style-type: none"> <li>• Yeast infection in the groin, vagina, or under the breasts</li> <li>• Pneumocystis jiroveci</li> </ul>
5/24/17	2100: Post-HCT Follow-Up	Modify	Corrected an error on multiple pages of the 2100 manual. The manual incorrectly instructed centers to skip the engraftment section of the form (Q108-130). This instruction has been removed. Centers should complete the engraftment section of the form for autologous and allogeneic HCTs.
5/24/17	2100: Post-HCT Follow-Up	Add	Added text (in red below) to description of graft failure included in the instructions for questions 664 and 665. <b><i>Graft failure / insufficient hematopoietic recovery: Additional hematopoietic stem cells are required because the hematopoietic recovery indefinitely declined after the initial hematopoietic recovery (ANC was greater than or equal to <math>0.5 \times 10^9/L</math> for three consecutive days, and then declined to below <math>0.5 \times 10^9/L</math> for at least three consecutive days). This option also includes primary graft failure (no ANC recovery following HCT).</i></b>
5/24/17	2100: Post-HCT Follow-Up	Add	Added <b>Therapy Over Multiple Reporting Periods</b> note box to the instructions for question 4.
5/23/17	2100: Post-HCT Follow-Up	Add	Added scenarios of when to use “Not Applicable” to the instructions for questions 401.
5/23/17	2100: Post-HCT Follow-Up	Remove	Removed references to “Previously Reported” from the instructions for questions 402-403 and 405-406.
5/23/17	2100: Post-HCT Follow-Up	Add	Added <b>Previously Reported</b> warning box to instructions for questions 402-403 and 405-406.
5/23/17	2100: Post-HCT Follow-Up	Add	Added <b>Previously Reported</b> warning box to instructions for questions 402-403 and 405-406.
5/23/17	2100: Post-HCT Follow-Up	Add	Added <b>Corticosteroids</b> note box to instructions for question 401.
4/7/17	2100: Post-HCT Follow-Up	Add	Added the following clarification, in red below, regarding the enabling / disabling of questions 645-647: <b><i>Questions 645-647 will only be enabled / answered for pediatric patients (<math>\leq 16</math></i></b>

			<i>years old) when the form visit ID is 6 months or greater. These questions will be disabled / not answered for all recipients on the day 100 follow-up form.</i>
4/7/17	2100: Post-HCT Follow-Up	Add	<p>Added instructions to questions 170-175 to clarify how to report transaminitis under “other site” for acute GVHD.</p> <p><b>Other site(s) involved with acute GVHD:</b> <i>Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 28. If reporting transaminitis under “other site,” write in “transaminitis” rather than “liver” when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under “other site.”</i></p>
4/6/17	2100: Post-HCT Follow-Up	Add	<p>Added instruction to report site of bone marrow infections as <b>Blood</b> in the instructions for questions 428-436.</p> <p><b>Blood:</b> <i>includes blood or serum obtained from a central IV line, catheter tip, or from a direct needle stick (Peripheral draw). Blood should be the reported site for infections identified in the bone marrow.</i></p>
4/6/17	2100: Post-HCT Follow-Up	Remove	<p>Removed incorrect instruction from Organism description in the instructions for questions 428-436. Suspected bacterial or viral infections should not be reported. <i>Select the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. If the specific organism is not listed, use the code “777 – Other organism” and report the name of the organism in the space provided. If a fungal infection is suspected, but not identified, report using code “503 – Suspected fungal infection.” If a bacterial or viral infection is suspected, but not identified, report using code “777 – Other organism” and specify “suspected bacterial infection” or “suspected viral infection” as applicable. As noted above, only report infections which are clinically significant.</i></p>
4/6/17	2100: Post-HCT Follow-Up	Modify	<p>Updated instructions for question 159 to clarify reporting questions. The wording has changed, but the intent of the instructions is the same.</p> <p><i>Question 159 will only be enabled in FormsNet3<sup>SM</sup> if the center has reported “no” for question 157 and, therefore, has not reported a date of diagnosis in question 158. If prompted to answer question 159, report “yes” if acute GVHD was diagnosed in a prior reporting period <u>and any of the following conditions are met:</u></i></p> <ul style="list-style-type: none"> <li><i>• The recipient’s acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).</i></li> <li><i>• The recipient’s acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred <b>within 30 days</b> of symptom resolution / quiescence.</i></li> <li><i>• The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 157).</i></li> </ul> <p><i>Report “no” for questions 157 and 159 if the recipient had no active</i></p>

			<p><i>acute GVHD symptoms during the reporting period <b>OR</b> all acute GVHD signs / symptoms during the reporting period occurred <u>after</u> a diagnosis of chronic GVHD (see note above question 157).</i></p> <p><del>Indicate whether acute GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive acute GVHD, or a prior history of GVHD. If “yes,” continue with question 176; questions concerning acute GVHD at the time of diagnosis will be skipped. See question 157 for instructions on reporting an acute GVHD flare or acute GVHD occurring after the onset of chronic GVHD. If the recipient has no active symptoms during the reporting period, report “no” and continue with question 234.</del></p>
4/6/17	2100: Post-HCT Follow-Up	Modify	<p>Updated instructions for question 157 to clarify reporting questions. The wording has changed, but the intent of the instructions is the same.</p> <p><i>Questions 157 and 159 on the Post-HCT Follow-Up Data Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 157 or question 158 must be answered “yes” unless there has been a prior / concurrent diagnosis of chronic GVHD (refer to the note above question 157). There will not be a situation where “yes” is reported for both question 157 and question 159. If question 157 is answered yes and a diagnosis date has been reported in question 158, question 159 will be disabled in FormsNet3<sup>SM</sup>. Centers should report “yes” for question 157 to indicate the recipient developed acute GVHD in the following scenarios:</i></p> <ul style="list-style-type: none"> <li>• <i>Acute GVHD is diagnosed for the first time during the reporting period.</i></li> <li>• <i>An acute GVHD flare is diagnosed during the current reporting period <u>and all of the following conditions are met:</u></i> <ul style="list-style-type: none"> <li>◦ <i>The recipient’s prior acute GVHD symptoms did <b>not</b> persist from the prior reporting period into the beginning of the current reporting period.</i></li> <li>◦ <i>The flare is diagnosed after <b>at least 30 days</b> without any active acute GVHD symptoms.</i></li> <li>◦ <i>The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 157).</i></li> </ul> </li> </ul> <p><i>If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report “no” for question 157 and “yes” for question 159. Question 159 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to</i></p>

			<p><i>avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer questions 157 and 159.</i></p> <p><i>Report “no” for questions 157 and 159 if the recipient had no active acute GVHD symptoms during the reporting period <b>OR</b> all acute GVHD signs / symptoms during the reporting period occurred <u>after</u> a diagnosis of chronic GVHD (see note above question 157).</i></p> <p><del>Indicate whether a new clinical diagnosis of acute GVHD was documented during the reporting period. If acute GVHD was diagnosed during the reporting period, report “yes” and continue with question 158.</del></p> <p><del>If the recipient had a flare of acute GVHD occurring after at least a 30 day period of symptom quiescence, report “yes” and continue with question 158. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent acute GVHD which is captured in question 159.</del></p> <p><del>Indicate “no” if acute GVHD was not clinically diagnosed—initially or as a flare—in the reporting period; this includes instances where acute GVHD persists from a prior reporting period without flare in the current reporting period.</del></p>
4/4/17	2100: Post-HCT Follow-Up	Modify	<p>Instruction change for questions 239-241 and 651-653: Age range for Lansky Scale has been updated from recipients less than 16 years old to recipients one year old to less than 16 years old. If the recipient is less than one year old, questions 239-241 and 651-653 should be left blank.</p>
3/29/17	2100: Post-HCT Follow-Up Data	Add	<p>Added the following text (in red) to the instructions for question 325: Indicate whether systemic therapy was given to treat chronic GVHD during the reporting period. If systemic therapy was given as treatment for chronic GVHD, report “yes” and continue with question 326. If systemic therapy was not given for treatment of chronic GVHD, report “no” and continue with question 399. See questions 328-399 for Chronic GVHD Treatment Reporting Scenarios.</p>
3/29/17	2100: Post-HCT Follow-Up Data	Add	<p>Added the following instruction to question 326: If treatment is started for a flare of chronic GVHD (see question 234 for definition of flare), report “no” for question 326 and report the date treatment was started for the flare in question 327.</p>
3/29/17	2100: Post-HCT Follow-Up Data	Add	<p>Added the following text (in red) to the instructions for question 327: Report the first date when therapy was started for chronic GVHD if the date has not been previously reported. If the recipient continued GVHD prophylaxis drugs after the onset of chronic GVHD, report the date of diagnosis of chronic GVHD as</p>



			the treatment start date. If the recipient starts treatment multiple times during the same reporting period, report the earliest treatment start date.
3/ 29/ 17	2100: Post-HCT Follow- Up Data	Modify	Modified the instructions for questions 328-399 to correct an error (deleted text) and provide further clarification (in red): <del>For each agent listed, indicate whether or not it was used to treat chronic GVHD during the reporting period.</del> If a therapy was started or escalated for chronic GVHD during the reporting period, report “yes” and answer any additional questions (if applicable). If a dose is required, report the total ordered dose planned to be given at the time treatment was initiated. This may include doses which are planned to be given after the date of contact. % Report %(marker-red)“yes” for prophylactic drugs if they were continued after the onset of chronic GVHD. Report the date of diagnosis of chronic GVHD as the treatment start date for any prophylactic medications which were continued. See Chronic GVHD Treatment Reporting Scenarios below.
3/ 29/ 17	2100: Post-HCT Follow- Up Data	Add	Added the following text (in red) to the instructions for question 327: If treatment is started and subsequently escalated during the same reporting period, report the earliest date treatment was actually given during the reporting period. If a dose is required, contact your center’s liaison to determine how to complete the data field. Additionally, report the earliest start date if a drug is started multiple times during the same reporting period.
3/ 29/ 17	2100: Post-HCT Follow- Up Data	Add	Added Chronic GVHD Treatment Scenarios A, B, and C.
3/ 27/ 17	2100: Post-HCT Follow- Up Data	Add	Added another example to questions 169 and 176 regarding when to report “Not Applicable” for the grade of acute GVHD. This instruction was previously available in the description of staging acute lower intestinal tract GVHD. * Lower intestinal tract involvement where the stage cannot be determined in select scenarios <a href="#">lower intestinal tract</a> involvement description above
3/ 27/ 17	2100: Post-HCT Follow- Up Data	Add	Added instruction to question 177: If “not applicable” was reported for question 176, question 177 must be left blank.
3/ 15/ 17	2100: Post-HCT Follow- Up Data	Add	Clarification was added regarding the intent of questions 658-660. The intent of this question is to determine the recipient’s history of smoking cigarettes only. Do not report the use of cigars, pipe tobacco, chewing tobacco, or other drugs. Indicate whether the recipient has smoked tobacco cigarettes since the date of the last report. If “yes,” complete questions 659-660. If the recipient has not smoked tobacco cigarettes since the date of the last report, or their smoking history is not known, report “no” or “unknown” respectively and continue with question 661.
3/ 15/ 17	2100: Post-HCT Follow- Up Data	Add	The following instruction has been added to questions 645-647. <i>Questions 645-647 will only be enabled / answered for pediatric patients (≤ 16 years old).</i>

3/ 14/ 17	2100: Post-HCT Follow- Up Data	Modify	<p>Modified instructions for Q252-301 to address questions received. The instructions have not changed, but the question now refers to instructions for question 157 which provide greater detail. Examples C and D, which were previously available, are also reference.</p> <p><i>If a recipient has signs / symptoms of both acute and chronic GVHD on or after the date chronic GVHD is diagnosed, report all signs / symptoms in the chronic GVHD section of the form. If acute GVHD signs / symptoms are identified prior to the diagnosis of chronic GVHD, they should also be reported in the acute GVHD section of the form (questions 157-183) during the reporting period, refer to question 157 for additional instructions. Scenarios C and D below have also been provided for further clarification.</i></p>
3/ 14/ 17	2100: Post-HCT Follow- Up Data	Modify	<p>Modified instructions for Q238 to address questions received. The instructions have not changed, but the question now refers to instructions for question 157 which provide greater detail.</p> <p><i>Chronic GVHD can be separated into two different categories; classical chronic GVHD and overlap syndrome. Overlap syndrome is a condition where there are features of both acute and chronic GVHD at the time of diagnosis. Indicate whether signs of acute GVHD were present at the time of diagnosis of chronic GVHD (overlap syndrome). Ensure any features of acute GVHD are reported in questions 169-183. Report all GVHD signs / symptoms (acute and chronic) occurring on or after the diagnosis of chronic GVHD in the chronic GVHD section of the form. See questions 252-301 below for further instructions on reporting acute and chronic GVHD signs / symptoms. Refer to question 157 for instructions on how to complete acute and chronic GVHD sections for recipients with overlap syndrome.</i></p>
3/ 14/ 17	2100: Post-HCT Follow- Up Data	Add	Added Scenario D to Acute GVHD Grading Scenarios under question 176.
3/ 14/ 17	2100: Post-HCT Follow- Up Data	Add	<p>Added the following instruction below to question 176. This instruction was previously provided under question 157, but has been added to question 176 for further clarification.</p> <p><i>If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. See question 157 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.</i></p>
3/ 14/ 17	2100: Post-HCT Follow- Up Data	Add	Added scenario B to Acute GVHD Diagnosis Scenarios under question 157.
3/ 14/ 17	2100: Post-HCT Follow- Up Data	Modify	<p>Modified the note above question 157 to address questions received. The instructions have not changed, but the wording has been updated to be clearer.</p> <p><i>If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 157-233). Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section.</i></p>

			<p>Report any <b>new or persistent acute</b> GVHD symptoms (<del>persistent or newly diagnosed</del>) occurring on or after the date of diagnosis onset of chronic GVHD <b>only</b> in the chronic GVHD section. <del>of the form (questions 234-323). See the examples included in the instructions for questions 252-301.</del> If chronic GVHD was diagnosed in a prior reporting period, <del>the center should report “no” for questions 157 and 159 in each subsequent reporting period.</del> Any GVHD symptoms occurring in each subsequent reporting period must be reported in the chronic GVHD section of the form and should not be re-reported in the acute GVHD data fields. See reporting scenarios included in question 157.</p>
3/13/17	2100: Post-HCT Follow-Up Data	Add	<p>Added the following instruction to <b>Lower Intestinal Tract</b> description beneath questions 170-175: If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, report “stage 0” for lower intestinal tract involvement. In this case, report “Not Applicable” for the overall grade unless stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status was also documented at the time point being reported (at diagnosis or maximum grade during the reporting period). Report an overall grade of IV if stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status is documented at the time point being reported (see GVHD Staging and Grading Table).</p>
3/10/17	2100: Post-HCT Follow-Up Data	Add	<p>Added “stool” to the definition of GI, lower infection site. This instruction is included for questions 428-326.</p>
3/8/17	2100: Post-HCT Follow-Up Data	Add	<p>Added instruction to Questions 185-233: If an acute GVHD treatment has continued from a previous reporting period, report the original start date and override the error in FormsNet3<sup>SM</sup> using the code “verified correct.”</p>
3/1/17	2100: Post-HCT Follow-Up Data	Modify	<p>Updated liver scoring criteria on <a href="#">Chronic GVHD Organ Scoring</a> table included under questions 252-301. The criteria were documented incorrectly and have been updated to match the <a href="#">2014 NIH Consensus Criteria</a>.</p>
1/31/17	2100: Post-HCT Follow-Up Data	Modify	<p>Version 3 of the 2100: Post-HCT Follow-Up Data Form (Form 2100) (formerly 100 Day Post-HSCT Data Form) section of the Forms Instructions Manual released. Version 3 corresponds to revision 4 of the Form 2100.</p>

## Q1-5: Vital Status

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

If the Post-HCT Follow-Up Form reports a subsequent transplant, report the date of latest follow-up as the day prior to the start of the preparative regimen. If no preparative regimen or conditioning was given, report the day prior to infusion as the date of contact.



### Reporting Latest Follow-up

When reporting the date of latest follow-up prior to a subsequent HCT, report the date specified above regardless whether there is actual patient contact on the date. This is an exception to standard date of follow-up reporting to ensure all dates are captured within the sequence of forms.

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

Enter the date of actual contact with recipient to determine medical status for this follow-up report. Acceptable evaluations include those from the transplant center, referring physician, or other physician currently assuming responsibility for the recipient's care. If an evaluation was not performed at Day+100, at 6 months, or on the HCT anniversary, choose the date of the visit closest to the actual time point.

If the recipient has not been seen by a clinician during the reporting period but the survival status is known, submit the Post-HCT Data Form reporting only the survival status.

In general, the date of contact should be reported as close to the 100 day, 6 month, or annual anniversary to transplant as possible. Report the date of actual contact with the recipient to evaluate medical status for the reporting period. In the absence of contact with a clinician, other types of contact may include a documented phone call with the recipient, a laboratory evaluation, or any other documented recipient interaction on the date reported. If there was no contact on the exact time point, choose the date of contact closest to the actual time point. Below, the guidelines show an ideal approximate range for reporting each post-transplant time point:

Time Point	Approximate Range
100 days	+/- 15 days (Day 85-115)
6 months	+/- 30 days (Day 150-210)
Annual	+/- 30 days (Months 11-13, 23-25, 35-37, etc)

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

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

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

What to report:

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

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

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

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

What to report:

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

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

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

#### Additional Information

- A date of contact should never be used multiple times for the same recipient's forms.
  - For example, 6/1/13 should not be reported for both the 6 month and 1 year form. Instead, determine the best possible date of contact for each reporting period; if there is not a suitable date of contact for a reporting period, this may indicate that the recipient was lost to follow-up.

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

### **Date of Contact & Death**

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

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

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

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

What to report:

100 Day Date of Contact: 4/8/13 (note the latest disease assessment would likely be reported as 4/4/13)

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

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

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

What to report:

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

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

### **Date of Contact & Subsequent Transplant**

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

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

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

What to report:

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

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

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

What to report:

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

6 Month Date of Contact: 5/30/13

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

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

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

**Question 3: Did the recipient receive a subsequent HCT since the date of last report?**

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

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

**Questions 4: Has the recipient received a cellular therapy since the date of last report? (e.g., DCI)****Therapy Over Multiple Reporting Periods**

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

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

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

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



**Question 5: Date of cellular therapy:**

Report the date of cellular therapy infusion. If multiple infusions were received in the reporting period, report the earliest. If infusions are continuing from a previous instance of DCI, only report in the period during which the first infusion was received.

## Q6-12: Granulopoiesis / Neutrophil Recovery

**! Questions 6-12 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.**

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

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

$$\begin{array}{r}
 \text{\% segmented neutrophils} \\
 + \text{\% band neutrophils} \\
 \hline
 = \text{\% neutrophils} \\
 \times \text{white blood cell count}/\text{mm}^3 \\
 \hline
 = \text{absolute neutrophil count}/\text{mm}^3
 \end{array}$$

**Example:**  
(Divide percentage by 100 to convert to decimal)

$$\begin{array}{r}
 0.45 \text{ segmented neutrophils} \\
 + 0.05 \text{ band neutrophils} \\
 \hline
 = 0.50 \text{ neutrophils} \\
 \times 1000/\text{mm}^3 \text{ white blood cell count} \\
 \hline
 = 500/\text{mm}^3 \text{ absolute neutrophil count}
 \end{array}$$

ANC  $500/\text{mm}^3 = 0.5 \times 10^9/\text{L} = 0.5 \times 10^6/\text{mL} = 0.5 \times 10^3/\text{mm}^3$

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

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

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

### Example 2: Tracking ANC Recovery

*Transplant Date = May 6*

*Contact Date = August 15*

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

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

### Example 3: Initial Recovery with Subsequent Decline and Recovery

*Transplant Date = May 6*

*Contact Date = August 15*

Date	WBC	%Neutrophils	ANC	
May 7	900	0.6	540	
May 8	850	0.59	502	
May 9	720	0.7	504	
May 10	300	0.45	135	
May 11	15	No differential	—	
May 12	30	No differential	—	
May 13	50	No differential	—	
May 14	250	0.4	100	
May 15	800	0.7	560	<i>Date of initial recovery: ANC <math>\geq</math> 500/mm<sup>3</sup> (report this date in question 7)</i>
May 16	1050	0.8	840	
May 17	1000	0.7	700	
May 18	1800	0.6	1080	
May 19	2000	0.55	1100	
May 20	2500	0.53	1325	
May 21	2250	0.43	968	
May 22	1500	0.45	675	
May 23	800	0.6	480	<i>Date of first decline: ANC <math>\leq</math> 500/mm<sup>3</sup> (report this date in question 9)</i>

May 24	850	0.41	349	
May 25	720	0.53	382	
May 26	500	0.45	225	
May 27	490	0.3	147	
May 28	650	0.7	455	
May 29	800	0.8	640	<i>Date of recovery: ANC <math>\geq</math> 500/mm<sup>3</sup> (report this date in question 12)</i>
May 30-August 14	—	—	—	ANC $\geq$ 500/mm <sup>3</sup> for timeframe
August 15 (contact date)	2245	0.72	1616	

### Question 6: Was there evidence of initial hematopoietic recovery?

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

Check only **one** response:

- If “yes, ANC  $\geq$  500/mm<sup>3</sup> (or  $\geq$  0.5  $\times$  10<sup>9</sup>/L) achieved and sustained for 3 laboratory values,” continue with question 7.
- If “no, ANC  $\geq$  500/mm<sup>3</sup> (or  $\geq$  0.5  $\times$  10<sup>9</sup>/L) was not achieved,” continue with question 13.
- Check “not applicable” if the recipient’s ANC never dropped below 500/mm<sup>3</sup> (or  $\geq$  0.5  $\times$  10<sup>9</sup>/L) at any time after the start of the preparative regimen. Continue with question 8.
- Check “previously reported,” if the recipient’s initial hematopoietic recovery was recorded on a previous report. Continue with question 13.

### Question 7: Date ANC $\geq$ 500/mm<sup>3</sup> (first of 3 lab values):

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

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

**Question 8: Following the initial hematopoietic recovery, was there subsequent decline in ANC to  $< 500/\text{mm}^3$  for  $\geq 3$  days since the date of last report?**

Report if there was subsequent decline in ANC  $< 500/\text{mm}^3$  (or  $< 0.5 \times 10^9/\text{L}$ ) (three consecutive laboratory values obtained on different days where the ANC declined to  $< 500/\text{mm}^3$ ). If “yes,” continue with question 9. If “no,” continue with question 13.

 **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 7), the first decline (question 9), and the last recovery (question 12).

**Question 9: Date of decline in ANC  $< 500/\text{mm}^3$  for  $\geq 3$  days (first of 3 days that the ANC declined):**

Enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC declined to  $< 500/\text{mm}^3$  (or  $< 0.5 \times 10^9/\text{L}$ ).

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

**Question 10: Did recipient recover and maintain ANC  $\geq 500/\text{mm}^3$  following the decline?**

Indicate whether there was evidence of ANC recovery following the decline (three consecutive laboratory values obtained on different days where the ANC was  $\geq 500/\text{mm}^3$  (or  $\geq 0.5 \times 10^9/\text{L}$ ). If “yes,” continue with question 11. If “no,” continue with question 13.

**Question 11-12: Date of ANC recovery:**

Report if the date of ANC recovery following the decline is “known” or “unknown.” If the date of recovery is “known,” continue with question 12 and enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC recovered to  $\geq 500/\text{mm}^3$  (or  $\geq 0.5 \times 10^9/\text{L}$ ) following the decline. See [Example 3](#) above. If the date of recovery following decline is “unknown,” continue with question 13.

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

## Q13-18: Megakaryopoiesis / Platelet Recovery

**!** Questions 13-18 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.

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

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

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

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

### Example 1: Reporting Platelet Recovery

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

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

Date	Day	Platelet Count	
June 13	0	10,000	<i>Date of last platelet transfusion</i>

June 14	1	30,000	
June 15	2	25,000	
June 16	3	10,000	
June 17	4	15,000	
June 18	5	19,000	
June 19	6	23,000	
June 20	7	25,000	<i>1st of 3 consecutive laboratory values <math>\geq 20 \times 10^9/L</math> (report this date in question 15)</i>
June 21	8	40,000	
June 22	9	50,000	<i>1st of 3 consecutive laboratory values <math>\geq 50 \times 10^9/L</math> (report this date in question 18)</i>
June 23	10	56,000	
June 24	11	65,000	
June 25	12	72,000	

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

**Question 13: Was an initial platelet count  $\geq 20 \times 10^9/L$  achieved?**

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

Check only **one** response:

- If “yes,” continue with question 14.
- If “no,” continue with question 19.
- Check “not applicable,” if the recipient’s platelets never dropped below  $20 \times 10^9/L$  at any time post-HCT and a platelet transfusion was never required. If the recipient’s platelet count drops below



$20 \times 10^9/L$  and/or the recipient received a platelet transfusion even once, do not use this option. This option is only applicable in the 100-day reporting period. Continue with question 16.

- Check “previously reported” if this is the 6 month or annual follow-up, and initial platelet recovery has already been reported on a previous form. Continue with question 16.

#### Question 14-15: Date platelet $\geq 20 \times 10^9/L$

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

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

#### Reporting Scenarios:

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

**B.** The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is  $\geq 20 \times 10^9/L$  on January 2, January 3, and January 4. The recipient is then discharged back to their primary care physician. The transplant center receives a follow-up note from the primary care physician that states “recipient recovered their platelets in January of 2011.” Report an estimated date of recovery using the guidelines available in General Instructions, [General Guidelines for Completing Forms](#).

#### Question 16: Was an initial platelet count $\geq 50 \times 10^9/L$ achieved?

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

Check only **one** response:

- If “yes,” continue with question 17.
- If “no,” continue with question 19.

- Check “not applicable,” if the platelet count never dropped below  $50 \times 10^9/L$  at any time post-HCT. Continue with question 19.
- Check “previously reported,” if a platelet count of  $\geq 50 \times 10^9/L$  was achieved and reported previously. Continue with question 19.

**Question 17-18: Date platelets  $\geq 50 \times 10^9/L$ :**

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

If three laboratory values were not obtained on consecutive days, but a sequential rise of  $\geq 50 \times 10^9/L$  is demonstrated, follow the examples included in the instructions for questions 14-15 above.

## Q19-48: Growth Factor and Cytokine Therapy



Questions 19-48 can only be completed on the 100 day follow-up form. These questions will be skipped for all subsequent reporting periods.

### Question 19: 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 20. If “no,” continue with question 49.

### Questions 20-48: Specify agents and provide dates for the first course of each agent given in this reporting period.

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

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

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

**Erythropoietin (EPO):** Alternate names: Epogen, Procrit, darbepoietin alfa (Aranesp). EPO stimulates red blood cell production.

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

**Blinded growth factor or cytokine trial:** If the recipient is on a blinded randomized trial, specify the trial agent administered. Additionally, update this form (2100) once the trial is over to specify whether the recipient received the trial drug or placebo.

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

## Q49-63: Current Hematologic Findings

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**Questions 49-63 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.**

### Questions 49-63: 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 hematologic finding. If a value is not known, select “unknown” and continue with the next laboratory value.

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

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

## Q64-88: Immune Reconstitution

**! Questions 64-88 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.**

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

### Questions 64: Date sample collected:

Report the date when the most recent immunoglobulin sample was collected. If no immunoglobulin testing was performed during the reporting period, leave question 64 blank and override the validation error using the “Not Tested” option.

### Question 65: Did the recipient receive supplemental intravenous immunoglobulins (IVIG)?

IVIG is a product made from pooled human plasma and primarily contains IgG. It is used to provide immune-deficient recipients with antibody function to prevent infection. It may be administered intravenously or subcutaneously and IVIG given via either route should be reported in this section of the form.

Indicate whether the recipient received IVIG during the reporting period. If “yes,” continue with question 66. If “no,” continue with question 69.

#### **IVIG Given without Immunoglobulin Testing**

In some cases, IVIG may be given for low immune function without immunoglobulin testing. The transplant center should verify that Ig levels were not tested at another facility, as it is unusual for IVIG to be given without knowing what the IgG level is. In these cases, question 65 should be answered “yes” and question 66 should be answered “no” (even though testing was not done). Answer question 67 as “prophylaxis for low IgG...” because the recipient is receiving IVIG for decreased immune function even though there is not a laboratory value to document a low IgG level. Report “unknown” for questions 69, 71, and 73.

**Question 66: Was supplemental IVIG received in the 30 days prior to the date the sample was collected?**

Indicate whether the recipient received IVIG  $\leq 30$  days prior to the immunoglobulin testing reported in questions 69-74. If IVIG is given within 30 days of immunoglobulin testing, the IgG level would not represent the recipient's native IgG.

**Question 67-68: Specify the indication for which IVIG was given:**

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 68.

**Question 69-74: 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 if the value for each immunoglobulin (antibody) is "known" or "unknown." If "known," specify the value and unit from the most recent test performed during the reporting period. Report "unknown" if testing was not performed during the reporting period or the results cannot be obtained.

**Question 75-76: 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," report the date the sample was collected in question 76. If "no," continue with question 89.

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

## Questions 77-88: Results of Lymphocyte Analysis



### Testing for CD16+ Cells

If testing is not performed for CD56+ cells, but is performed for CD16+ cells, report the CD16+ result in questions 87-88.

Report the value and specify the unit for each lymphocyte subset if known. If the subset was not tested on the date specified in question 76 or the result is not known, select “unknown” and continue with the next subset.

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:

#### Example 1: Calculating lymphocyte counts

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

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



## Q89-107: Chimerism Studies

### \* Autologous Transplants

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

### \* Syngeneic Transplants

If this was a syngeneic HCT, continue with the [Engraftment Syndrome section](#) starting with question 108. Chimerism testing is not collected for syngeneic HCTs.



**Questions 89-107 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.**

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

### \* Chimerism Studies

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

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

**Question 89-90: Were chimerism studies performed post-HCT? (Allogeneic HCTs only)**

Indicate whether chimerism studies were performed within the reporting period. If “yes,” continue with question 90 and indicate whether documentation was submitted to CIBMTR (e.g., chimerism laboratory reports).

If chimerism studies were not performed within the reporting period, select “no,” and continue with question 108.

**Question 91: Were chimerism studies assessed for more than one donor / multiple donors?**

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

**Questions 92-107: Provide date(s), method(s) and other information for all chimerism studies performed prior to the date of contact (question 1)****Reporting Multiple Chimerism Studies**

FormsNet3 application: Complete questions 92-107 for each chimerism study by adding additional instance(s) in the FormsNet application.

Paper form submission: Copy question 92-107 and complete for each chimerism study being reported.

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

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

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

**Chimerism – Single Donor**

Data Field	Description
92. NMDP donor ID	If the donor or one of the donors was an NMDP PBSC or marrow donor, enter the 9 digit NMDP donor ID.

93. NMDP cord blood unit ID	If the donor or one of the donors was an NMDP cord blood unit, enter the 9 digit NMDP cord blood unit ID.
94. Non-NMDP unrelated donor ID	If the donor or one of the donors was a non-NMDP unrelated PBSC or marrow donor, enter the non-NMDP registry donor ID.
95. Non-NMDP cord blood unit ID	If the donor or one of the donors was a non-NMDP cord blood unit, enter the non-NMDP registry donor ID.
96. Date of birth or age	If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry, provide the date of birth, if known; if date of birth is not known, provide the donor's age at donation.
97. Sex	If the donor was related or the cord blood unit was related or supplied by a non-NMDP registry, provide the biological sex.
98. Date sample collected	Enter the date the sample was collected for the chimerism test.
99-100. Method	Report the test method used for the reported chimerism study. Cytogenetic testing methods include karyotyping and fluorescent in situ hybridization (FISH). Cytogenetic methods are only valid for sex mismatched transplants with the exception of quinicine banding. VNTR / STR is one of the most common molecular methods for assessing chimerism. See the <a href="#">Chimerism Methods table</a> below for additional details on chimerism testing methods.
101. Cell source	Report whether the specimen taken for chimerism testing was from a marrow or peripheral blood source.
102-103. Cell type	Indicate the cell type tested. If the specimen was not sorted for a specific cell line, indicate "unsorted / whole." See the <a href="#">Chimerism Cell Types table</a> below for additional details on cell markers unique to certain cell lines.
104. Total cells examined	Cytogenetic testing methods include karyotyping and fluorescent in situ hybridization (FISH), each of which examines a specific and relatively low number of cells – generally 15 to 200, depending on specimen and test method. If a cytogenetic method was used, enter the total number of cells that were examined. If a non-cytogenetic test was used, leave these boxes blank.
105. Number of donor cells	Cytogenetic methods, karyotyping and FISH, examine a specific and relatively low number of cells – generally 15 to 200, depending on specimen and test method. If a cytogenetic method was used, enter the total number of cells that were examined and found to be of donor origin. If a non-cytogenetic test was used, leave these boxes blank.
106. Were donor cells detected?	Molecular testing methods include RFLP and VNTR / STR. If a molecular method was used, indicate whether donor cells were detected. Report "yes," if the testing identified any percentage of cells as being of donor origin.
107. Percent donor cells	Molecular testing methods include VNTR / STR, RFLP, and AFLP. Report the percentage of donor cells identified by molecular testing. If the test result did not detect any recipient cell population within the sensitivity of the assay, report 100% donor cells. If the test detected recipient

cells, but indicated donor cells “> n%,” report “n + 1” percent donor cells. If the test detected donor cells but indicated donor cells “< n%,” report “n – 1” percent donor cells.

## Chimerism Methods

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

## Chimerism Cell Types

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

## Q108-130: Engraftment Syndrome

**! Questions 108-130 can only be completed on the 100 day follow-up form. These questions will be skipped for all subsequent reporting periods.**

### Question 108-109: Did engraftment syndrome occur?

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

Indicate whether the recipient developed engraftment syndrome.

If the recipient developed engraftment syndrome during the reporting period, report “yes” and indicate the date of diagnosis in question 109. If the recipient did not develop engraft syndrome, report “no” and continue with question 131.

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

### Question 110-119: Specify symptoms of engraftment syndrome

Indicate whether the recipient developed the symptoms listed. If “other symptom” is selected, specify symptom in question 119.

### Question 120: Was a biopsy performed?

If a biopsy was performed to evaluate engraftment syndrome, report “yes” and specify the site(s) in questions 121-125. If no biopsies were done to evaluate for engraftment syndrome, report “no” and continue with question 126.

### Question 121-125: Specify site:

From the options listed, report the biopsy site. If “other site” is selected, specify the location of the biopsy in question 124. Indicate whether documentation (pathology report) was attached to the form in FormsNet3 or

otherwise submitted to the CIBTMR in question 125. For further instructions on how to attach documents in FormsNet3, refer to the [training guide](#).

**Question 126: Was therapy given for engraftment syndrome?**

Report if therapy was given for engraftment syndrome. If therapy was given for engraftment syndrome, report “yes” and continue with question 127. If therapy was not given, report “no” and continue with question 130.

**Question 127-129: Specify therapy given for engraftment syndrome (systemic corticosteroids, other therapy)**

Report any treatment given for engraftment syndrome. If “other therapy” is chosen, specify the treatment(s) in question 129.

**Question 130: Did engraftment syndrome resolve?**

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

# Q131-233: Acute Graft vs. Host Disease (GVHD)

## \* Autologous Transplants

If this was an autologous HCT, continue with the [Infection Prophylaxis section](#) of the form starting with question 407. Chimerism testing and graft-versus-host disease sections should only be completed for allogeneic HCTs.



**Questions 131-156 can only be completed on the 100 day follow-up form. These questions will be skipped for all subsequent reporting periods.**

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

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

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

## \* GVHD Prophylaxis

ATG, cyclophosphamide, and alemtuzumab given *prior to and including* Day 0 as GVHD prophylaxis should be reported in the **preparative regimen** section on the [Baseline Form](#) and on the [Pre-TED Form](#).



Report ATG, cyclophosphamide, and alemtuzumab given **after** Day 0 as **GVHD prophylaxis** in the GVHD prophylaxis section on the 100 day Post-HCT Data Form and the Pre-TED Form.

Please note, ATG, cyclophosphamide, and alemtuzumab 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.

Report ex vivo T-cell depletion in the product manipulation sections of the Pre-TED Form and HCT Infusion Form. Do not report this method of product manipulation in GVHD prophylaxis data fields.

**Question 131: Was specific therapy used after the start of the preparative regimen to prevent acute GVHD? (Note: do not include growth factors reported in questions 19-48, or ex vivo T-cell depletion reported on the Product Insert. Do not include drugs given as part of the preparative regimen)**

Following an allogeneic HCT, specific immunosuppressive therapy may be administered to prevent GVHD or to immunosuppress the host marrow, thereby promoting engraftment of the donor hematopoietic 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.

Do not include growth factors reported in question 19, or ex vivo T-cell depletion reported on the Product Insert. Do not include drugs given as part of the preparative regimen.

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

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

If specific therapy was given after the start of the preparative regimen to prevent acute GVHD, report “yes” and continue with question 132. See the GVHD Prophylaxis note above for additional instructions on how to report **ATG, cyclophosphamide, and alemtuzumab**. If specific therapy to prevent acute GVHD was not given after the start of the preparative regimen, report “no” and continue with question 157.

**Questions 132-156:**

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.

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

**Bortezomib (Velcade):** A proteasome inhibitor.

**Corticosteroids (systemic) (e.g., prednisone, dexamethasone):** Usually combined with cyclosporine when used for prophylaxis. Only report systemic steroids in this section. If topical steroids are used prophylactically, report in questions 155-156 and provide an explanation regarding how the site for topical application was selected.

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

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

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

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

**In vivo monoclonal antibody:** Antibody preparations that are infused in the recipient following HSCT. Specify the antibody used as: anti CD25 (Zenapax, Daclizumab, AntiTAC), alemtuzumab (Campath), entanercept (Enbrel), infliximab (Remicade), and / or rituximab (Rituxan).

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

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

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

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

**Blinded randomized trial:** If the recipient is on a blinded randomized trial, specify agent being studied in the trial. Additionally, update the Post-HCT Data Form (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 (Form 2006).
- Do not include agents used to prevent infection. Report infection prophylaxis agents in the infection section, questions 407-427.

#### Acute / Chronic GVHD

If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 157-233). Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section.

Report any **new or persistent** acute GVHD symptoms occurring on or after the onset of chronic GVHD only in the chronic GVHD section. If chronic GVHD was diagnosed in a prior reporting period, report “no” for questions 157 and 159 in each subsequent reporting period. See Acute GVHD Diagnosis Scenarios included in the instructions for question 157.

#### **Question 157: Did acute GVHD develop since the date of the last report?**

Questions 157 and 159 on the Post-HCT Follow-Up Data Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 157 or question 158 must be answered “yes” unless there has been a prior / concurrent diagnosis of chronic GVHD (refer to the note above question 157). There will not be a situation where “yes” is reported for both question 157 and question 159. If question 157 is answered yes and a diagnosis date has been reported in question 158, question 159 will be disabled in FormsNet3<sup>SM</sup>. Centers should report “yes” for question 157 to indicate the recipient developed acute GVHD in the following scenarios:

- Acute GVHD is diagnosed for the first time during the reporting period.
- An acute GVHD flare is diagnosed during the current reporting period and all of the following conditions are met:
  - The recipient's prior acute GVHD symptoms did **not** persist from the prior reporting period into the beginning of the current reporting period.
  - The flare is diagnosed after **at least 30 days** without any active acute GVHD symptoms.
  - The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 157).

If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report "no" for question 157 and "yes" for question 159. Question 159 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer questions 157 and 159.

Report "no" for questions 157 and 159 if the recipient had no active acute GVHD symptoms during the reporting period **OR** all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 157).

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

### **Acute GVHD Diagnosis Scenarios:**

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

#### *100 Day Post-Infusion Data Form:*

Question 157: Report "yes" to indicate a new clinical diagnosis of acute GVHD.

Question 158: Report the initial date of diagnosis (2/1/2015).

Question 159: Leave blank. This question will be skipped whenever a diagnosis date has been entered

in question 158.

Questions 160-175: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

*Six Month Post-Infusion Data Form:*

Question 157: Report “no” to indicate acute GVHD persists from a previous report. Note, the flare of acute GVHD was < 30 days from symptoms resolution so it doesn’t count as a new reportable episode.

Question 158: Leave blank. This question will be skipped whenever question 157 is answered “no.”

Question 159: Report “yes” to indicate GVHD persists from a previous report.

Questions 160-175: Leave blank. Answering “yes” for question 159 prevents the center from re-reporting diagnosis information already captured on the 100 day form.

*One Year Post-Infusion Data Form:*

Question 157: Report “yes” to indicate a flare of acute GVHD occurred at least 30 days after resolving during a prior reporting period.

Question 158: Report the diagnosis date of the flare occurring during the reporting period (8/15/2015).

Question 159: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 158.

Questions 160-175: Answer these questions based on the assessments performed at the time of diagnosis of the flare of acute GVHD (8/15/2015).

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

100 Day Post-Infusion Data Form:

Question 157: Report “yes” to indicate a new clinical diagnosis of acute GVHD.

Question 158: Report the initial date of diagnosis (2/1/2015).

Question 159: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 158.

Questions 160-175: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

Questions 176-233: Answer these questions based on any symptoms and treatment documented from the onset of acute GVHD (2/1/2015) up to the diagnosis of chronic GVHD (3/1/2015). This instruction is provided in the note box above question 157.

### Six Month Post-Infusion Data Form:

Question 157: Report “no” to indicate acute GVHD did not develop during the reporting period.

Question 158: Leave blank. This question will be skipped whenever question 157 is answered “no.”

Question 159: Report “no” to indicate acute GVHD did not persist from a previous report.

*If chronic GVHD has been diagnosed in a prior reporting period, report “no” for questions 157 and 159. Any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD must be reported in the chronic GVHD section of the form. Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section. This instruction has been provided in the note above question 157.*

### **Question 158: Date of acute GVHD diagnosis**

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

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

If the date of diagnosis is **unknown**, leave question 158 blank and override the validation error using the code “Unknown.” However, question 158 may **not** be left blank if treatment for acute GVHD (question 185) is reported “Yes.” If the exact clinical diagnosis date is unknown, but the treatment start date is known, report the date treatment started as the date of acute GVHD diagnosis.

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

### **Question 159: Did acute GVHD persist since the date of the last report?**

Question 159 will only be enabled in FormsNet3<sup>SM</sup> if the center has reported “no” for question 157 and, therefore, has not reported a date of diagnosis in question 158. If prompted to answer question 159, report “yes” if acute GVHD was diagnosed in a prior reporting period and **any** of the following conditions are met:

- The recipient’s acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).
- The recipient’s acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred **within 30 days** of symptom resolution / quiescence.

- The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 157).

Report “no” for questions 157 and 159 if the recipient had no active acute GVHD symptoms during the reporting period **OR** all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 157).

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

#### **Question 160: Was acute GVHD evaluated by biopsy (histology)? (at diagnosis)**

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

Indicate whether a biopsy was used to diagnose acute GVHD. If “yes,” specify the site(s) / result(s) in questions 161-168. If “no,” continue with question 169.

#### **Questions 161-168: Specify result(s)**

For each organ listed, indicate the test result documented on the pathology report as either “positive,” “suggestive,” “negative,” or “inconclusive / equivocal.” “Suggestive” or “inconclusive / equivocal” should be reported if in the final diagnosis or comments section of the pathology report those words are used. If a biopsy was not completed for a specific organ, select “not done” and continue with the next organ. If “other site” is selected, specify the site biopsied in question 167.

Indicate whether documentation was submitted to the CIBMTR (e.g., pathology report) in question 168. For further instructions on how to attach documents in FormsNet3, refer to the training guide.

#### **Question 169: Overall grade of acute GVHD at diagnosis:**

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

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

- Only elevated liver function tests without increased bilirubin
- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios [lower intestinal tract](#) involvement description below



### Upper GI GVHD

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

## GVHD Grading and Staging

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

<sup>1</sup> Use “Rule of Nines” (see Percent Body Surfaces table below) or burn chart to determine extent of rash.

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



<sup>3</sup> 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.

<sup>4</sup> Persistent nausea with or without histologic evidence of GVHD in the stomach or duodenum.

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

<sup>6</sup> Grade IV may also include lesser organ involvement with an extreme decrease in performance status

### Question 170-175: Indicate the stage for each organ involvement at time of diagnosis of acute GVHD

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

**Skin:** Select the stage that reflects the body surface area involved with a maculopapular rash attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. See Table 5 below to determine the percent of body surface area involved with a rash. Do not report ongoing rash not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

#### Percent Body Surfaces

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

#### Lower intestinal tract (use mL/day for adult recipients and mL/m<sup>2</sup>/day for pediatric recipients):

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

If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, report “stage 0” for lower intestinal tract involvement. In this case, report “Not Applicable” for the overall grade unless stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in

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

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

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

For recipients who have a normal bilirubin level with elevated transaminase levels attributed to acute GVHD, report this in "Other clinical organ involvement."

**Other site(s) involved with acute GVHD:** Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 175. If reporting transaminitis under "other site," write in "transaminitis" rather than "liver" when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under "other site."

#### Question 176: Maximum overall grade of acute GVHD

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

If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. See question 157 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.

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

Examples may include:

- Only elevated liver function tests without increased bilirubin
- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios [lower intestinal tract](#) involvement description above



### Upper GI GVHD

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

#### Acute GVHD Grading Scenarios:

- A.** A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging / grading can be determined based on the skin involvement alone.
- B.** A recipient developed acute liver GVHD with elevated LFTs (i.e., transaminases) with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in the GVHD Grading and Staging Table; "not applicable" would be the best option to report.
- C.** A recipient developed stage 2 skin involvement, which showed improvement in response to topical steroids. However, the recipient then developed hyperbilirubinemia attributed to stage 1 liver involvement; the skin involvement at that time was stage 1. In this case, grade II would be reported (assuming this was the extent of the recipient's acute GVHD in the reporting period).
- D.** A recipient developed stage 2 skin involvement which resolved in response to topical steroids. Later in the reporting period, the recipient was diagnosed with mild chronic eye GVHD. Shortly thereafter, they were diagnosed with a stage 3 flare of acute skin GVHD. In this case, grade I would be reported. Do not consider any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD when completing the acute GVHD section of the form.

**Question 177: Date maximum overall grade of acute GVHD**

Report the date of maximum acute GVHD involvement, based on clinical grade. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date. If “not applicable” was reported for question 176, question 177 must be left blank. |

**Question 178-183: Specify organ involvement at time of maximum grade**

Report the stage of involvement for each organ on the date reported in question 177. Refer to the GVHD Grading and Staging Table above for staging guidelines. Also, see additional information included for each organ in the instructions for questions 170-175 above.

 **Corticosteroids**

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

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

Other Topical Treatments: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. If these treatments are given for acute GI GVHD during the reporting period, report “Yes” for question 184. If these treatments were given for other organ involvement of GVHD, contact your liaison to determine the best option for reporting this therapy.

Systemic Treatments: Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in questions 197-198).

**Question 184: Were corticosteroids (topical GI) used to treat acute GVHD?**

Report “yes” if topical corticosteroids were used to **treat GI GVHD**. Do not report topical therapies used for skin or lung GVHD in this question. Also, do not report systemic corticosteroids such as prednisone or dexamethasone. Systemic therapies are captured in questions 185-233.

**Question 185-233: Was specific therapy given for acute GVHD?** **Fecal Microbiota Transplant**

Fecal microbiota transplant (FMT) is under investigation as a viable therapy to treat acute or chronic steroid-refractory gastrointestinal GVHD. This procedure involves collecting fecal matter from a pre-screened donor and transferring it to a recipient by the oral or rectal route (for example by nasogastric tube or enema) in order to restore intestinal microbial flora. If an FMT was performed to treat acute GVHD, report “Yes” for “Other agent” and specify

“Fecal Microbiota Transplant.” The date started will be the date of the FMT. If multiple FMTs were performed during reporting period, report the earliest date.

Indicate whether systemic therapy was used to treat acute GVHD during the reporting period. If “yes,” continue with question 186. Report any prophylactic drugs as therapy for acute GVHD if they were continued after the date of diagnosis. If no therapy was given, indicate “no” and continue with question 233. If systemic therapy was given to treat acute GVHD during the reporting period, specify the drugs given in questions 186-233.

When reporting the total dose, report the total delivered dose of each drug during the reporting period. **Do not report the prescribed doses or daily doses.** For example, if 50 mg/kg of ATGAM was given for 5 days, the center should report a total dose of 250 mg/kg. Drug doses must be reported in whole numbers. If the total dose includes a decimal, round to the nearest whole number.

When reporting the date started, report the first day the drug as given on or after the GVHD diagnosis date (reported in question 158). For **prophylaxis medications** continued after the date of diagnosis of acute GVHD, report the date of diagnosis as the date started. If an acute GVHD treatment has continued from a previous reporting period, report the original start date and override the error in FormsNet3<sup>SM</sup> using the code “verified correct.”

# Q234-406: Chronic Graft vs. Host Disease (GVHD)

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## ✿ Autologous Transplants

If this was an autologous HCT, continue with the [Infection Prophylaxis section](#) of the form starting with question 407. Chimerism testing and graft-versus-host disease sections should only be completed for allogeneic HCTs.

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

### Question 234: Did chronic GVHD develop since the date of the last report?

Indicate whether a new clinical diagnosis of chronic GVHD was documented during the reporting period. If chronic GVHD was diagnosed during the reporting period, report “yes” and continue with question 235.

If the recipient had a flare of chronic GVHD occurring after *at least* a 30 day period of symptom quiescence, report “yes” and continue with question 235. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent chronic GVHD which is captured in question 236.

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

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

### Question 235: Date of chronic GVHD diagnosis

Report the date of clinical diagnosis of chronic GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed shortness of breath one month prior to the

clinical diagnosis of pulmonary chronic GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

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

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

#### **Question 236: Did chronic GVHD persist since the date of last report?**

Indicate whether chronic GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive chronic GVHD, or a prior history of GVHD. If “yes,” continue with question 302; questions concerning chronic GVHD at the time of diagnosis will be skipped. See question 234 for instructions on reporting a chronic GVHD flare.

If the recipient has no active symptoms during the reporting period, report “no” continue with question 400.

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

#### **Question 237: Onset of chronic GVHD was:**

Indicate whether the onset of chronic GVHD was:

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

#### **Question 238: Were signs of acute GVHD present at the time of chronic GVHD diagnosis (overlap syndrome)?**

Chronic GVHD can be separated into two different categories; classical chronic GVHD and overlap syndrome. Overlap syndrome is a condition where there are features of both acute and chronic GVHD at the time of diagnosis. Indicate whether signs of acute GVHD were present at the time of diagnosis of chronic GVHD (overlap syndrome). Refer to question [157](#) for instructions on how to complete the acute and chronic GVHD sections for recipients with overlap syndrome.

**Question 239-241: Karnofsky/Lansky score at time of chronic GVHD diagnosis**

The Karnofsky Scale is designed for recipients aged 16 years and older, and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. If the recipient is less than one year old, leave questions 239-241 blank.

Indicate the score (10-100) that best represents the recipient's activity status at diagnosis of chronic GVHD. The only valid scores are 10-100, zero is not a valid response for this scale, nor are values not ending in zero, such as "85." The Karnofsky/Lansky scale can be found in [Appendix L, Karnofsky/Lansky Performance Staus](#).

For further information on reporting Karnofsky / Lansky Scores refer to the instructions for Questions 651-653 below.

**Question 242: Platelets (at diagnosis of chronic GVHD):**

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

**Question 243: Total serum bilirubin (at diagnosis of GVHD):**

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

**Question 244: Was chronic GVHD evaluated by biopsy (histology)? (at diagnosis)**

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

Indicate whether a biopsy was used to diagnose chronic GVHD. If "yes," specify the site(s) / result(s) in questions 245-251. If "no," continue with question 252.

**Question 245-251: Specify result(s):**

For each organ listed, indicate the result documented on the laboratory report as either "positive," "suggestive," "negative," or "inconclusive / equivocal." If a biopsy was not completed for a specific organ, select "not done" and continue with the next organ. If "other site" is selected, specify the site biopsied in question 251.



**Question 252-301: Organ involvement and NIH scoring at diagnosis of chronic GVHD**

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

Signs or symptoms occurring at the time of diagnosis may be partially or entirely attributed to GVHD. Alternatively, reportable features may be observed at diagnosis, but attributed entirely to non-GVHD causes. In any case, report “yes” for organ involvement if any reportable signs / symptoms are documented during the reporting period regardless of whether those features are attributed to GVHD. Features **entirely** explained by non-GVHD causes will be excluded when determining the overall severity of chronic GVHD, but are still collected on the form. Spaces have been provided to document non-GVHD causes.

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

If a recipient has signs / symptoms of both acute and chronic GVHD during the reporting period, refer to question 157 for additional instructions. Scenarios C and D below have also been provided for further clarification.

**GVHD Reporting Scenarios:**

**A.** A recipient developed a maculopapular rash covering 25% BSA as well as deep sclerotic features. Both features are attributed to chronic GVHD. In this case, report “yes” and “score 3” for skin involvement (based on findings of deep sclerotic features).

**B.** A recipient developed a maculopapular rash covering 25% BSA as well as diarrhea without significant weight loss. Both findings were identified and diagnosed at the same time. The skin rash was attributed to acute GVHD while diarrhea was entirely attributed to chronic GVHD. In this case, report “yes” and “Score 2” for skin involvement. Report “yes” and “score 1” for GI involvement. Any acute findings identified on or after the date of chronic GVHD diagnosis must be reported in the chronic GVHD section. The skin rash would not be reported in the acute GVHD section of the form unless identified and diagnosed prior to any findings of chronic GVHD.

**C.** A recipient developed a maculopapular rash covering 25% BSA. This was diagnosed as acute GVHD, treated, and completely resolved during the 100 day reporting period. During the six month reporting

period, the recipient developed mild dry eyes which was diagnosed as chronic GVHD. Shortly thereafter, the recipient was also diagnosed with an acute flare of skin GVHD.

**100 Day Post-HCT Data Form:** Report the acute GVHD findings (maculopapular rash) in the acute GVHD section of the form. Report “no” for questions 234 and 235 to indicate chronic GVHD was not diagnosed during the 100 day reporting period.

**6 Month Post-HCT Data Form:** Report acute and chronic GVHD findings in the chronic GVHD section of the form. Report “no” for questions 157 and 159 to indicate no acute GVHD symptoms were identified during the reporting period. Even though acute skin GVHD was diagnosed, it is not necessary to report these symptoms in both acute and chronic sections of the form. Once a chronic GVHD diagnosis is made, report all signs / symptoms of GVHD (acute and chronic) in the chronic GVHD section of the form.

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

**Acute GVHD data fields:** Report any signs or symptoms of acute GVHD documented prior to the diagnosis of chronic GVHD in the acute GVHD section of the form (Questions 157-183). In this case, the initial diagnosis of skin GVHD as well as any treatments initiated prior to the diagnosis of chronic GVHD will be reported in acute GVHD data fields.

**Chronic GVHD data fields:** Report any signs or symptoms of GVHD (acute or chronic) documented on or after the diagnosis of chronic GVHD in the chronic GVHD section of the form (Questions 234-323). In this case, the initial diagnosis of gut GVHD as well as the subsequent flare of skin GVHD will be reported in chronic GVHD data fields. Any treatments continued or initiated on or after the date of diagnosis of chronic GVHD will be reported in chronic GVHD data fields.

**E.** A recipient developed a maculopapular rash covering 25% BSA as well as diarrhea without significant weight loss. The skin rash was entirely attributed to a drug reaction while the diarrhea was attributed to chronic GVHD and an ongoing CMV infection. In this case, report “yes” and “score 2” for skin involvement. The center should also specify the observed rash was entirely attributed to a drug reaction in questions 259-260. Report “yes” and “score 1” for GI involvement. Do not specify CMV as a non-GVHD cause in questions 273-274 because the observed symptoms were not entirely explained by this diagnosis.

**F.** A recipient developed maculopapular rash covering 55% BSA as well as superficial sclerotic features of the skin. The rash is attributed to a drug reaction and the sclerotic findings are entirely attributed to chronic GVHD. In this case, report “yes” and “score 3” as well as “superficial sclerotic features” for skin

involvement. The center should also specify the observed rash was entirely attributed to a drug reaction in questions 259-260.

### Organ Scoring of Chronic GVHD

Organ	Score 0	Score 1	Score 2	Score 3
<b>Skin % BSA<sup>1</sup></b>	No BSA involved	1-18% BSA	19-50% BSA	>50% BSA
<b>Skin Features</b>	No sclerotic features	N/A	Superficial sclerotic features, but not "hidebound"	Deep sclerotic features; "hidebound;" impaired mobility; ulceration
<b>Mouth</b>	No symptoms	Mild symptoms <b>with</b> disease signs but not limiting oral intake significantly	Moderate symptoms with disease signs <b>with</b> partial limitation of oral intake	Severe symptoms with disease signs <b>with</b> major limitation of oral intake
<b>Eyes</b>	No symptoms	Mild dry eye symptoms not affecting ADL (requirement of lubricant drops $\leq$ 3x/day)	Moderate dry eye symptoms partially affecting ADL (requiring lubricant drops > 3x/day or punctal plugs) <b>WITHOUT</b> new vision impairment due to keratoconjunctivitis sicca (KCS)	Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) <b>OR</b> unable to work because of ocular symptoms <b>OR</b> loss of vision due to keratoconjunctivitis sicca (KCS)
<b>GI Tract</b>	No symptoms	Symptoms without significant weight loss (< 5%)	Symptoms associated with mild to moderate weight loss (5-15%) within 3 months <b>OR</b> moderate diarrhea without significant interference with daily living	Symptoms associated with significant weight loss (> 15%) within 3 months, requires nutritional supplement for most calorie needs <b>OR</b> esophageal dilation <b>OR</b> severe diarrhea with significant interference with daily living.
<b>Liver</b>	Normal total bilirubin and ALT or AP < 3 x ULN	Normal total bilirubin with ALT $\geq$ 3 to 5 x ULN or AP $\geq$ 3 x ULN	Elevated total bilirubin but $\leq$ 3 mg / dL or ALT > 5 x ULN	Elevated total bilirubin > 3 mg / dL
<b>Lungs <u>Symptom Score:</u></b>	No symptoms	Mild symptoms (SOB after climbing one flight of steps)	Moderate symptoms (SOB after walking on flat ground)	Severe symptoms (SOB at rests; requires O2)

<b>Lungs Lung Score:</b>	FEV1 ≥ 80%	FEV1 60-79%	FEV1 40-59%	FEV1 ≤ 39%
<b>Joints and Fascia</b>	No symptoms	Mild tightness of arms or legs, normal or mild decreased range of motion <b>AND</b> not affecting ADL	Tightness of arms or legs <b>OR</b> joint contractures, erythema thought to be due to fasciitis, moderate decrease of range of motion <b>AND</b> mild to moderate limitation of ADL	Contractures <b>WITH</b> significant decrease of range of motion <b>AND</b> significant limitation of ADL (unable to tie shoes, button shirts, dress self, etc.)
<b>Genital Tract<sup>2</sup></b>	No signs	Mild signs and females with or without discomfort on exam	Moderate signs and may have signs of discomfort on exam	Severe signs with or without symptoms
<b>Other Features<sup>3</sup></b>	No GVHD	Mild	Moderate	Severe

[NIH Consensus Criteria, 2014](#)

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

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

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

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

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

If any skin abnormalities were present, but explained entirely by non-GVHD causes, specify any documented causes in question 260.

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

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

If any mouth abnormalities were present, but explained entirely by non-GVHD causes, specify any documented causes in question 265.

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

- Keratoconjunctivitis sicca (KCS): dry eye syndrome

If any eye abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes in question 270.

**Gastrointestinal tract (GI):**

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

If any GI abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes in question 274.

**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]).

If any liver abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes in question 286.

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

If pulmonary function tests were performed, specify FEV1 percent in question 290.

If any lung abnormalities were present, but explained entirely by non-GVHD documented causes, specify causes in question 292.

**Joints and fascia:**

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

If any joint or fascia abnormalities were present, but explained entirely by non-GVHD causes, specify causes in question 296.

**Genital tract:**

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

If any genital tract abnormalities were present, but explained entirely by non-GVHD causes, specify documented causes in question 301.

**Question 302: Maximum grade of chronic GVHD: (according to best clinical judgment)**

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

Indicate "unknown" if there is no information about the recipient's GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period. Please note, questions 303 and 304 must still be answered if question 302 is reported as "unknown."

**Question 303: Specify if chronic GVHD was limited or extensive:**

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

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

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

**Question 304: Date of maximum grade of chronic GVHD:**

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

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

**Question 305-323: Indicate whether there was organ specific manifestations with chronic GVHD since the date of last report:**

Report if there were any organ specific manifestations associated with chronic GVHD. If “yes,” answer any additional questions. If “no,” continue with the next option.

**Sclerosis of skin:**

- Scleroderma: thickening of the skin, which may cause loss of suppleness
- Fasciitis: inflammation of the fascia of a muscle or organ
- Morphea: thickening or hardening patches of the skin which are discolored

**Erythematous skin rash:** skin rash characterized by redness.

**Join contractures:** loss of joint mobility due to skin or fascia changes.

**Other skin or hair involvement:** other skin or hair involvement, includes, but is not limited to:

- 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: purplish rash

**Eyes:** Dry eyes and corneal ulcers due to keratoconjunctivitis sicca.

- Xerophthalmia: dry eyes
- Abnormal Schirmer's test: a measure of tear production, decreased wetting <5 mm
- Abnormal 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, red inflammation, 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

**Bronchiolitis obliterans:** 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 [Pulmonary Function section](#), questions 441-489.**

**Other lung involvement:** includes related pulmonary disorders here. Do not report interstitial pneumonitis (IPn). Report IPn in the [Pulmonary Function section](#), questions 441-489.

**Upper gastrointestinal tract:**

- 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 days) or occurs frequently enough to interfere with functioning and lifestyle.

**Lower gastrointestinal tract:**

- Chronic diarrhea: occurs on at least 25% of days (1 out of 4 days) 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:** Includes, but is not limited to:

- 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
- Myositis: inflammation of muscles
- Myasthenia: weakness of muscles

**Thrombocytopenia:** Decreased platelet count (<100,000).

**Eosinophilia:** Elevation in eosinophils in the peripheral blood (> 500 cells /  $\mu$ L)

**Serositis:** Inflammation of a serous membrane, includes but is not limited to:

- Pleural effusion: Buildup of fluid between the chest and the tissues which line the lungs
- Ascites: Accumulation of fluid in the peritoneal cavity
- Pericardial effusion: Accumulation of fluid in the pericardial cavity

**Other:**

- Weight loss
- Other organ involvement from chronic GVHD: specify the additional site

**Question 324: Were corticosteroids (topical GI) given for chronic GVHD?**

Report if corticosteroids (topical GI) were given for chronic GVHD. Examples include beclomethasone and budesonide. Do not report corticosteroids (topical GI) given as a GVHD prophylaxis.

**Question 325: Was systemic therapy given to treat chronic GVHD?**

Indicate whether systemic therapy was given to treat chronic GVHD during the reporting period. If systemic therapy was given as treatment for chronic GVHD, report “yes” and continue with question 326. If systemic therapy was not given for treatment of chronic GVHD, report “no” and continue with question 399. See questions 328-399 for Chronic GVHD Treatment Reporting Scenarios.

**Question 326: Was the date therapy was first started previously reported?**

Indicate whether the date therapy was first started for chronic GVHD was previously reported. If the therapy start date was previously reported, select “yes” and continue with question 328. If the therapy start date for chronic GVHD has not been reported, select “no” and report the start date in question 327.

If treatment is started for a flare of chronic GVHD (see question 234 for definition of flare), report “no” for question 326 and report the date treatment was started for the flare in question 327.

**Question 327: Date therapy was first started:**

Report the first date when therapy was started for chronic GVHD if the date has not been previously reported. If the recipient continued GVHD prophylaxis drugs after the onset of chronic GVHD, report the date of diagnosis of chronic GVHD as the treatment start date. If the recipient starts treatment multiple times during the same reporting period, report the earliest treatment start date.

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

**Question 328-399: Specify systemic therapy started or escalated for chronic GVHD since the date of last report:****\* Fecal Microbiota Transplant**

Fecal microbiota transplant (FMT) is under investigation as a viable therapy to treat acute or chronic steroid-refractory gastrointestinal GVHD. This procedure involves collecting fecal matter from a pre-screened donor and transferring it to a recipient by the oral or rectal route (for example by nasogastric tube or enema) in order to restore intestinal microbial flora. If an FMT was performed to treat chronic GVHD, report “Yes” for “Other agent” and specify “Fecal Microbiota Transplant.” The date started will be the date of the FMT. If multiple FMTs were performed during reporting period, report the earliest date.

If a therapy was started or escalated for chronic GVHD, report “yes” and answer any additional questions (if applicable). If a dose is required, report the total ordered dose planned to be given at the time treatment was initiated. This may include doses which are planned to be given after the date of contact. Report “yes”

for prophylactic drugs if they were continued after the onset of chronic GVHD. Report the date of diagnosis of chronic GVHD as the treatment start date for any prophylactic medications which were continued. See Chronic GVHD Treatment Reporting Scenarios below.

If treatment is started and subsequently escalated during the same reporting period, report the earliest date treatment was actually given during the reporting period. If a dose is required, contact your center's liaison to determine how to complete the data field. Additionally, report the earliest start date if a drug is started multiple times during the same reporting period.

Refer to [questions 132-156](#) for a description of most agents listed. Agents not described under acute GVHD are described below under [Additional Agents](#). "Systemic" refers to drugs given by mouth, intramuscularly (IM), or intravenously (IV). "Topical" refers to drugs applied to the 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.

### **Chronic GVHD Treatment Reporting Scenarios:**

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

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

Question 324: Report "no" to indicate no topical GI corticosteroids were given. Topical steroids applied to the skin should not be reported here.

Question 325: Report "yes" to indicate systemic therapy was given to treat chronic GVHD.

Question 326: Report "no" to indicate the therapy start date was not previously reported.

Question 327: Report 5/1/2016 as the treatment start date. This is the date cyclosporine was started as treatment for chronic GVHD. Note, topical steroids should not be considered when completing questions 325-399.

Question 328-399: Corticosteroids will be reported as "yes" with a start date of 5/15/2016. Cyclosporine will be reported as "yes" with a start date of 5/1/2016. All other medications will be reported as "no."

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

Question 324: Report "no" to indicate no topical GI corticosteroids were given. Topical steroids applied to the skin should not be reported here.

Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.  
Question 326: Report “yes” to indicate the therapy start date was previously reported.  
Question 327: Leave blank. This question will be skipped when question 326 has been answered “yes.”  
Question 328-399: All medications will be reported as “no.” Prednisone and cyclosporine would only be reported on this form if a dose increase was given to treat chronic GVHD during the reporting period.

**B.** During the one year reporting period, a recipient on sirolimus for GVHD prophylaxis was diagnosed with chronic gut GVHD (7/1/2016). This was initially treated with topical steroids (oral budesonide) in addition to continuing sirolimus at the current dose. Prednisone was started 7/30/2016 due to minimal improvement. The chronic gut GVHD resolved and budesonide as well as prednisone were discontinued. Sirolimus was continued as prophylaxis. Later in the one year reporting period, a severe flare chronic gut GVHD occurred (10/15/2016). This was first treated by restarting prednisone on the date of diagnosis; however, no response was observed. Equine ATG was started on 10/20/2016 with a plan to give 6 total doses of 30 mg / kg. Symptoms resolved following administration of ATG.

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

Question 324: Report “yes” to indicate topical GI corticosteroids were given. Budesonide should be reported here.  
Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.  
Question 326: Report “no” to indicate the therapy start date was not previously reported.  
Question 327: Report 7/1/2016 as the treatment start date. This is the date sirolimus was started as treatment for chronic GVHD. Note, topical steroids, including budesonide, should not be considered when completing questions 325-399.  
Question 328-399:

- ATG will be reported as “yes” with a start date of 10/20/2016 . The total dose will be reported as 180 mg / kg to reflect the total planned dose at the time treatment was initiated (6 \* 30 mg / kg).
- Corticosteroids will be reported as “yes” with a start date of 7/30/2016. Report the earliest start date if a medication is started multiple times during the reporting period.
- Sirolimus will be reported as “yes” with a start date of 7/1/2016.
- All other medications will be reported as “no.”

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

while attempting to taper cyclosporine. This was treated by increasing the dose of cyclosporine on the date of diagnosis of the flare.

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

Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.

Question 326: Report “no” to indicate the therapy start date was not previously reported.

Question 327: Report 9/20/2016 as the treatment start date. This is the date cyclosporine was started as treatment for chronic GVHD. Note, topical steroids, including budesonide, should not be considered when completing questions 325-399.

Question 328-399: Cyclosporine will be reported as “yes” with a start date of 9/20/2016. All other medications will be reported as “no.”

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

Question 325: Report “yes” to indicate systemic therapy was given to treat chronic GVHD.

Question 326: Report “no” to indicate the therapy start date was not previously reported. See question 326 for further instructions.

Question 327: Report 11/15/2016 as the treatment start date.

Question 328-399: Cyclosporine will be reported as “yes” with a start date of 11/15/2016. All other medications will be reported as “no.”

#### **Additional Agents:**

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

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

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

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

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

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

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

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

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

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

Alternative treatments may be used in combination with drug therapy (example: low dose cyclophosphamide). If alternative treatments were used, report in “other agent” (questions 397-399).

**Question 400: Are symptoms of GVHD still present on the date of actual contact (or present at the time of death)?**

Questions 400-406 refer to any symptoms of GVHD (acute and / or chronic) observed during the reporting period. This section of the form must be completed if the center reported yes for question 157, 159, 234, or 236.

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

**Question 401: Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency,  $\leq 10$  mg/day for adults,  $< 0.1$  mg/kg/day for children)**

 **Corticosteroids**

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

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

Other Topical Treatments: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. Do not consider these medications when answering question 401.

**Systemic Treatments:** Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in question 401.

Indicate whether the recipient is still taking systemic steroids to treat or prevent GVHD on the date of contact. If the recipient is no longer taking systemic steroids for GVHD, report “no” and continue with question 402. If the recipient is still receiving systemic steroids during the reporting period to treat or prevent GVHD, report “yes” and continue with question 404. Refer to the guidelines included in the question text if the recipient is taking low dose steroids or steroids for adrenal insufficiency.

If the recipient did not receive systemic steroids for acute and / or chronic GVHD during the reporting period, report “Not applicable” and continue with question 404.

Indicate “Not applicable” in any of the following scenarios:

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

Indicate “unknown” if there is no information to determine if the recipient is still taking systemic steroids and continue with question 404. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD on the date of contact.

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

#### **Question 402-403: Date final treatment administered**



#### **Previously Reported**

Based on the current reporting instructions for GVHD therapy captured in questions 401-406, there is no scenario when it would be appropriate to report “Previously Reported” for questions 402 or 405. In cases where the recipient stopped systemic steroids or non-

steroidal immunosuppression in a prior reporting period and did not restart systemic steroids or non-steroidal immunosuppression during the current reporting period, centers should report “Not Applicable” for questions 401 and / or 404 and skip questions 402 and / or 405. The option choices for questions 402 and 405 will be reviewed and updated the next time this form is revised.

Indicate whether the date when systemic steroids were discontinued is “known” or “unknown.” If the final treatment date is “known,” continue with question 403. If the date is “unknown,” continue with question 404.

For question 403, report the date when the final dose of systemic steroids was administered. For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

**Question 404: Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for GVHD?**

Indicate whether the recipient is still taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent acute and / or chronic GVHD on the date of contact. If the recipient is still taking non-steroid immunosuppressive agents, report “yes” and continue with question 407. If the recipient is no longer receiving non-steroid agents for GVHD, report “no” and continue with question 405.

If the recipient did not receive non-steroidal immunosuppressive agents to treat or prevent acute and / or chronic GVHD during the reporting period, report “Not applicable” and continue with question 407.

Indicate “Not applicable” in any of the following scenarios:

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

Indicate “unknown” if there is no information to determine if the recipient is still taking non-steroidal immunosuppressive agents and continue with question 407. This option should be used sparingly and only



when no judgment can be made about the recipient still receiving treatment for GVHD in the reporting period.

#### Question 405-406: Date final treatment administered



##### **Previously Reported**

Based on the current reporting instructions for GVHD therapy captured in questions 401-406, there is no scenario when it would be appropriate to report “Previously Reported” for questions 402 or 405. In cases where the recipient stopped systemic steroids or non-steroidal immunosuppression in a prior reporting period and did not restart systemic steroids or non-steroidal immunosuppression during the current reporting period, centers should report “Not Applicable” for questions 401 and / or 404 and skip questions 402 and / or 405. The option choices for questions 402 and 405 will be reviewed and updated the next time this form is revised.

Indicate whether the final administration date of non-steroidal immunosuppressive agents (including PUVA) is “known” or “unknown.” If the final treatment date is “known,” continue with question 406. If the date is “unknown,” continue with question 407.

For question 405, report the date when the final treatment or prophylaxis dose of non-steroidal immunosuppressive agents was administered.

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

## Q407-427: Infection Prophylaxis

### \* Infection Prophylaxis

It is important to look at the Medication Administration Record (MAR) throughout the entire reporting period to ensure medications are not missed. Also, the use of some infection prophylactic drugs may not start immediately post-HCT (example: Pentamidine). Do not report agents used as treatment for documented or suspected infections. Report prophylactic immunoglobulins in the Immune Reconstitution section (questions 64-68).

**! Questions 407-427 can only be completed on the 100 day follow-up form. These questions will be skipped for all subsequent reporting periods.**

Antimicrobial therapy is generally given to HCT recipients to help prevent infections. Questions 407-427 are intended to obtain information on the infection prophylaxis regimen actually received by the recipient. In general, most centers have a standard cocktail of drugs used which include an antibacterial agent (or agents), antiviral agent, antifungal agent, and an anti-pneumocystis agent. Sometimes, recipients are on one of these medications prior to starting the preparative regimen and therefore it could be treating an infection or is being used as “secondary prophylaxis.” Information regarding primary and secondary prophylaxis can provide insight into the development of resistant infections.

### **Questions 407-427: Report the first infection prophylaxis drugs administered during the reporting period.**

Indicate whether any antibacterial, antiviral, antifungal, and anti-pneumocystis (PJP) drug(s) were given for infection prophylaxis during the reporting period. Include infection prophylaxis drugs started prior to day 0.

For each category of infection prophylaxis medications, indicate the drug which was administered closest to the start of the preparative regimen (or infusion if no preparative regimen was given) and started no later than day +45. This may include prophylaxis medications started prior to the start of the preparative regimen as long as they were continued at the start of the preparative regimen. Only one drug may be reported for antiviral, antifungal, and anti-pneumocystis categories; however, multiple drugs may be reported under the **antibacterial** category if the drugs were started on the same date (and were administered closest to the start of the preparative regimen and prior to day +45). For example, if both cefepime and vancomycin were started as prophylaxis on the same day the preparative regimen was started, the center should report both medications under the antibacterial category. However, if cefepime was administered at the start of the preparative regimen and vancomycin was started 2 days later, the center should only report cefepime as the first antibacterial infection prophylaxis drug.

Ensure the start date for any medications reported reflects the first date the drug was administered. Refer to the medication administration record to confirm the start date.

## Q428-440: Infection

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Infections occur frequently in transplant patients. Questions 428-440 are intended to capture detailed information on *clinically significant* infections diagnosed during the reporting period. A single infection may be found on multiple cultures or at multiple sites. Infections may recur following resolution of symptoms and negative testing. Use the instructions provided in this section to determine when an infection should be considered clinically significant, and therefore reported, as well as when to report new and / or recurrent infections.

**Questions 428-436: Did the recipient develop a clinically significant infection since the date of last report?**



### **Pneumocystis jiroveci**

Pneumocystis jiroveci was incorrectly listed as a scenario not to report. This error in the manual has been corrected. Centers are instructed to report Pneumocystis jiroveci infections in questions 428-436 if diagnosed during the reporting period.

Indicate whether the recipient developed a clinically significant bacterial, viral, or fungal infection during the reporting period. For the purpose of this manual, the term “clinically significant” refers to any infection requiring treatment. Surveillance cultures in which normal flora is present and the recipient is asymptomatic do not need to be reported. If no clinically significant infections occurred during the reporting period, report “no” for question 428 and skip to question 437.

Do **not** report the following scenarios:

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

Systemic inflammatory response syndrome and septic shock may be diagnosed with or without an organism identified by relevant testing. In either case, a clinical diagnosis of these complications will be reported in questions 437- 440. If an organism is identified by molecular report, laboratory report, or other physician documentation, the infection should be reported in questions 428-436. If no organism is identified, the center should use the following guidelines to determine whether to report an infection:

- If a fungal infection is suspected (per radiology assessments), but no organism is isolated during the reporting period, report the suspected infection in questions 428-436.
- If a bacterial or viral infection is suspected, but not confirmed, do not report an infection in questions 428-436.
- If no particular organism group is identified or suspected, do not report an infection in questions 428-436.

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

### Definitions for *Same Infection*

Bacteria	Virus	Fungal
<p><u>≤ 7 Days</u></p> <ul style="list-style-type: none"> <li>• Any bacteria</li> </ul>	<p><u>≤ 14 Days</u></p> <ul style="list-style-type: none"> <li>• Adenovirus</li> <li>• Enterovirus</li> <li>• Herpes zoster</li> <li>• Influenza</li> <li>• Parainfluenza</li> <li>• Rhinovirus</li> <li>• Respiratory syncytial</li> <li>• Varicella zoster</li> </ul>	<p><u>≤ 14 Days</u></p> <ul style="list-style-type: none"> <li>• Any yeasts</li> </ul>
<p><u>≤ 30 Days</u></p> <ul style="list-style-type: none"> <li>• Clostridium difficile</li> </ul>		<p><u>≤ 90 Days</u></p> <ul style="list-style-type: none"> <li>• Any molds</li> </ul>
<p><u>≤ 365 Days</u></p> <ul style="list-style-type: none"> <li>• Helicobacter pylori</li> </ul>	<p><u>≤ 30 Days</u></p> <ul style="list-style-type: none"> <li>• Human Herpes Virus - 6</li> </ul> <p><u>≤ 60 Days</u></p> <ul style="list-style-type: none"> <li>• Cytomegalovirus</li> <li>• Epstein-Barr virus</li> <li>• Herpes simplex</li> <li>• Polyomavirus</li> </ul>	

### Organism:

Select the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. If the specific organism is not listed, use the code “777 – Other organism”

and report the name of the organism in the space provided. If a fungal infection is suspected, but not identified, report using code “503 – Suspected fungal infection.” As noted above, only report infections which are *clinically significant*.

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

- 211 Aspergillus flavus
- 212 Aspergillus fumigatus
- 213 Aspergillus niger
- 210 Aspergillus, NOS
- 215 Aspergillus terreus
- 214 Aspergillus ustus
- 270 Blastomyces (dermatitidis)
- 201 Candida albicans
- 208 Candida non-albicans
- 222 Cryptococcus gattii
- 221 Cryptococcus neoformans
- 230 Fusarium (all species)
- 261 Histoplasma (capsulatum)
- 241 Mucorales (all species)
- 242 Rhizopus (all species)
- 272 Scedosporium (all species)
- 240 Zygomycetes, NOS
- 503 Suspected fungal infection

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

- 307 Hepatitis B Virus
- 308 Hepatitis C Virus

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

- 309 Human Immunodeficiency Virus 1 or 2

**Site:**

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

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

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

For clarification, the following site definitions are provided:

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

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

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

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

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

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

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

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

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

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

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

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

**Sinus and/or upper respiratory tract:** all areas from the nose to the throat and sinuses, does not include lungs (report as “Lung”), mouth, or dental infections (report mouth and dental as “GI tract, upper”).

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

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

**Date of Diagnosis:**

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

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



Copy and complete questions 429-436 to report more than one infection. Do not report a single infection occurring at multiple sites under separate instances of questions 439-436 unless the time between positive cultures meets the definition of a new infection according to the [Definitions for the Same Infection table](#) above.

**Infection Reporting Scenarios:**

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

The center should report one instance of questions 429-436 to capture the CMV infection first documented on 1/10/2015. A second instance of questions 429-436 should also be reported to capture a recurrent CMV infection documented on 6/3/2015. This is >60 days after PCR testing reverts to negative and is therefore considered a recurrence and not the same infection per the guidelines in the [Definitions for the Same Infection table](#) above. The recurrent infection would be reported on a subsequent Post-Infusion Data Form if it is diagnosed after the date of contact for the form being completed.

**B.** A recipient with concerning respiratory symptoms undergoes a bronchiolar lavage on 10/1/2014. A culture performed on the sample collected from the procedure revealed a Streptococcus, Group B infection. The recipient received systemic antibacterial antibiotics, but the infection progressed to their



blood as demonstrated by a culture performed on sample collected 11/1/2014. The recipient did not have any repeat cultures performed between their initial diagnosis and testing performed on 11/1/2014.

The center should report one instance of questions 429-436 to capture the Streptococcus, Group B infection. The diagnosis date is the date of the first positive culture performed on the sample collected 10/1/2014.

- If the positive culture from 11/1/2014 was collected during the same reporting period, “lung” and “blood” should both be reported as sites of infection.
- If the positive culture from 11/1/2014 was collected after the date of contact for the current reporting period, do not report “blood” as a second site of infection.

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

As no organism was identified, the only scenario in which the center should report this as an infection in questions 428-436 is if there is documentation confirming a suspected fungal infection. In any case, the clinical diagnosis of septic shock will be reported in questions 439-440.

**Question 437-438: Did the recipient develop Systemic Inflammatory Response Syndrome (SIRS) since the date of last report?**

Systemic inflammatory response syndrome refers to unregulated inflammation which may or may not be related to an infection. If SIRS was clinically diagnosed during the reporting period, report “yes” for question 437 and indicate the diagnosis date in question 438.

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

**Question 439-440: Did the recipient develop septic shock since the date of last report?**

Septic shock refers to the failure to maintain sufficient mean arterial pressure without intervention with vasopressors. It results from vasodilation associated with infection. If septic shock was clinically diagnosed during the reporting period, report “yes” for question 439 and indicate the diagnosis date in question 438.

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

# Q441-615: Organ Function

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Links within section:

[Pulmonary Function](#)

[Liver Toxicity Prophylaxis](#)

[Liver Function](#)

[Thrombotic Microangiopathy](#)

[Other Organ Impairment / Disorder](#)

## Pulmonary Function



### **Bacterial, Viral, and Fungal Pneumonia**

Report pneumonia due to infection in the Infection section (questions 428-440).

**Question 441-485: Indicate any non-infectious pulmonary abnormalities diagnosed since the date of the last report.**

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

### **Non-Infectious Pulmonary Abnormalities:**

Interstitial pneumonitis / Acute respiratory distress syndrome (IPn/ARDS): IPn refers to inflammation of the alveolar walls. Acute respiratory distress syndrome typically refers to fluid build-up within the alveoli. In either case, gas exchange is impaired resulting in oxygen deprivation. Both conditions can result from infectious or non-infectious causes. Only report IPn / ARDS resulting from non-infectious causes in questions 441-485.

Idiopathic pneumonia syndrome (IPS): 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).

Bronchiolitis obliterans (BO): an airway obstruction as a result of inflammation of the bronchioles. This complication typically occurs late after HCT. It is often a manifestation of chronic GVHD. If bronchiolitis obliterans is a result of chronic GVHD, confirm that bronchiolitis obliterans was also reported in the chronic GVHD section of this form (question 311).

Cryptogenic organizing pneumonia (COP) / Bronchiolitis obliterans with organizing pneumonia (BOOP): an idiopathic form of pneumonia which affects different parts of the lungs including the bronchioles and alveoli. This complication typically occurs late after HCT.

Diffuse alveolar hemorrhage (DAH): bleeding into the alveolar space typically resulting from an injury to the pulmonary blood vessels.

Other non-infectious abnormalities: any other non-infectious pulmonary abnormalities not already captured in the above categories. Do not report pleural effusions here.

### **Diagnostic Methods:**

Bronchoalveolar lavage (BAL): a procedure in which a bronchoscope is guided into the lower respiratory system. Fluid is emitted from the bronchoscope and then collected for further examination.

Transbronchial biopsy: a procedure in which forceps on the end of the bronchoscope are used to collect lung tissue samples for further examination.

Open / thorascopic lung biopsy: An open lung biopsy is a procedure in which an incision is made between the ribs to collect a sample of lung tissue for further examination. A thorascopic lung biopsy is a procedure in which an incision is made to the chest and an endoscope is used to collect samples of lung tissue.

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

Other: Specify "other diagnostic test" for IPn / ARDs or IPS in question 449, excluding radiographic assessment.

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

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

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

**Question 486-487: 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. If “yes,” report the date when endotracheal intubation or mechanical ventilation was started in question 487. If “no,” continue with question 490.

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

**Question 488-489: Was the recipient successfully extubated?**

Indicated if the recipient was successfully extubated during the reporting period. If “yes,” report the date of extubation in question 489. If “no,” continue with question 490.

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

## Liver Toxicity Prophylaxis

**Liver Toxicity Prophylaxis**

Questions 490-496 can only be completed on the 100 day and 6 month follow-up forms. These questions will be skipped for all subsequent reporting periods.

**Question 490: Was specific therapy used to prevent liver toxicity?**

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

Indicate whether the recipient received any therapy intended to prevent liver toxicity during the reporting period, including therapy given during the conditioning regimen. Report only agents given to prevent liver

toxicities, not those given to treat a diagnosed liver injury or toxicity. If liver toxicity prophylaxis was given, report “yes” and complete with questions 491-496. If liver toxicity prophylaxis was not given during the reporting period, report “no” and continue with question 497.

**Question 491-496: Specify therapy (Defibrotide, N-acetylcysteine, tissue plasminogen activator (TPA), Ursodiol, Other)**

Report all agents given during the reporting period to prevent liver toxicity, including therapy given during the conditioning regimen. Only report agents given to prevent liver toxicities, not those given to treat a diagnosed liver injury or toxicity. If “other” therapy is reported in question 495, specify agent in question 496.

## Liver Function



### Liver Toxicity

Questions 497-505 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 497: Did the recipient develop non-infectious liver toxicity (excluding GVHD) since the date of last report?**

Indicate whether the recipient developed a non-infectious liver toxicity during the reporting period. Include and toxicities which developed between the start of the preparative regimen and the date of last contact (question 1) when completing the 100 day follow-up form. Do not report liver complications due to GVHD in this section. If “yes,” continue with question 498. If “no,” continue with question 507.

**Question 498-506: Specify the non-infectious liver toxicity etiology (veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS), cirrhosis, other, and unknown etiology)**

Report the etiology of the non-infectious liver toxicity that the recipient developed since the date of the last report in questions 498-506.

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

**Question 498-499: Did veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOD) develop since the date of last report?**

Indicate whether VOD / SOS was diagnosed during the reporting period. If “yes,” report the date of diagnosis in question 499. If VOD / SOS persisted from the prior reporting period, indicate “no” and continue with question 500.

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

**Question 500-501: Cirrhosis**

Cirrhosis is a degenerative disease in which fibrous tissue forms and the lobes become filled with fat. Cirrhosis may be diagnosed using a liver biopsy, but clinical symptoms (enlarged liver), blood tests, laparoscopy, or radiology imaging are often used to determine the diagnosis of cirrhosis when a liver biopsy is not necessary.

Indicate whether cirrhosis was diagnosed during the reporting period. If “yes,” report the date of diagnosis in question 501. If cirrhosis persisted from a prior reporting period, indicate “no” and continue with question 502.

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

**Question 502-504: Other etiology**

Report liver complications not listed above. Do not include hepatic infections or GVHD. Report infections in the [Infection section](#) (questions 428-440); and GVHD in the [Acute GVHD section](#) (questions 157-233) and / or in the [Chronic GVHD section](#) (questions 234-406).

If reporting “yes” for “other etiology,” specify the documented etiology in question 503 and report the date of diagnosis in question 504. If reporting “no,” continue with question 505.

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

**Question 505: Unknown etiology**

Indicate “unknown” if there is no information about the etiology of the non-infectious liver toxicity. This option should be used sparingly and only when no judgment can be made about the etiology in the reporting period.

## Thrombotic Microangiopathy (TMA)

Thrombotic microangiopathy (TMA) is a multifactorial condition where intravascular platelet activation, formation of thrombi, and microangiopathic hemolytic anemia occur due to generalized endothelial dysfunction. Organ injury, specifically the kidney, may occur as a result of these processes.<sup>1</sup> Characteristics of thrombotic microangiopathy includes microangiopathic hemolysis, thrombocytopenia ( $< 50 \times 10^9/L$ ), neurological changes, and pulmonary dysfunction: Other laboratory features include:

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

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

**Question 506: Did the recipient develop post-transplant thrombotic microangiopathy (TMA) (include microangiopathy, thrombotic thrombocytopenia purpura (TTP), hemolytic uremic syndrome (HUS)), or similar syndrome since the date of last report?**

**Microangiopathy:** Disease of the capillaries where the capillaries bleed and slow the flow of blood due to thickening and weakening of capillary walls.

**Thrombotic thrombocytopenia (TTP):** Blood disorder where blood clots form in the small blood vessels of the body.

**Hemolytic uremic syndrome (HUS):** Abnormal destruction of red blood cells which block the kidneys resulting in kidney failure. May be caused by *Escherichia coli*, other infections, and medications.

Indicate whether the recipient developed post-transplant TMA or a similar syndrome since the date of last report. If "yes," continue with question 507. If "no," continue with question 527.

**Question 507: Date of diagnosis:**

Report the clinical diagnosis date of post-transplant TMA or a similar syndrome, including microangiopathy, TTP, and HUS. For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

**Question 508-512: Specify signs and symptoms:**

For each option listed, indicate whether the recipient had any signs or symptoms due to post-transplant TMA or a similar syndrome during the reporting period.

**Question 513-517: Was TMA evaluated by biopsy?**

Indicate whether TMA was evaluated by a biopsy. If “yes,” report if the results were “positive,” “suggestive,” “negative,” “inconclusive / equivocal,” or “not done” for each option listed. If “other site” is reported, specify the biopsy site in question 516.

Indicate whether documentation was submitted to CIBMTR in question 517. For further instructions on how to attach documents in FormsNet3, refer to the [training guide](#).

**Question 518-524: Was therapy given for TMA?**

Indicate whether the recipient received any therapy intended to treat TMA during the reporting period. Report only agents given to treat a diagnosis of TMA. If “yes,” report all therapy given during the reporting period in questions 519-524. If “no,” continue with question 525.

**Question 525: Did the TMA resolve? (Normalization of renal function, LDH, and resolution or improvement in renal and / or neurologic dysfunction)**

Indicate whether TMA resolved. If “yes,” report the first date the recipient met the following criteria:

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

If TMA did not resolve during the reporting period, skip question 526 and continue with question 527.

## Other Organ Impairment / Disorder

**Question 527: Has the recipient developed any other clinically significant organ impairment or disorder since the date of last report?**

The intent of this question is to identify *serious* conditions or impairments occurring after transplant. For the purposes of this manual, the term “clinically significant” refers to conditions requiring treatment or intervention. Additional guidelines for commonly reported organ impairments and disorders are included



below. Do not report complications that are expected for most transplant recipients and do not require treatment (i.e., minor complications resolving without intervention).

Indicate whether the recipient developed any other clinically significant organ impairment or disorder during the reporting period. If this form is being completed for the 100 day reporting period, include any clinically significant impairments or disorders diagnosed between the *start of the preparative regimen* and the date of contact (question 1). If “yes,” complete questions 528-610. If “no,” continue with question 611.

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

### Questions 528-610: Specify impairment / disorder:

Indicate whether any of the organ impairments or disorders listed were diagnosed during the reporting period. If the recipient developed an impairment during the reporting period, report “yes,” enter the date of diagnosis, and answer any additional questions pertaining to the impairment / disorder. If the diagnosis was determined at an outside center and no documentation of a clinical, pathological, or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported.

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

## Renal

Acute renal failure requiring dialysis: report whether dialysis was ordered or recommended for renal failure. Also report whether the recipient received the treatment. Symptoms of renal failure include dehydration, nausea, blood in the urine, and / or swelling of extremities.

Chronic kidney disease / renal impairment: report whether there was chronic kidney disease or renal impairment (persistent decrease in glomerular filtration to  $<60 \text{ mL/min.1.73m}^2$ ). Also report whether the recipient received treatment.

## Cardiac

Arrhythmia: report whether the recipient developed an arrhythmia, including atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmia. Specify the arrhythmia. If “other arrhythmia” is reported, specify in question 542.

Congestive heart failure (CHF): inability of the heart to supply oxygenated blood to meet the body's needs. Ejection fraction < 40%.

Coronary artery disease: damage or disease in the major blood vessels of the heart. Also called CAD, atherosclerotic heart disease.

Myocardial infarction (MI): an obstruction in the coronary artery resulting in damage / necrosis to the cardiac muscle.

Hypertension (HTN) requiring therapy: report whether treatment was given for high blood pressure.

## **Vascular**

Deep vein thrombosis (DVT) / Pulmonary embolism (PE): development of a blood clot in a deep vein or development of a blood clot in the arteries of the lung.

## **Neurological**

CNS hemorrhage: bleeding within the central nervous system.

Encephalopathy: damage or disease of the brain. Symptoms of encephalopathy include memory loss, personality changes, and declining ability to concentrate and reason.

Neuropathy: nerve damage, usually in hands and feet, which causes pain, weakness, and numbness.

Seizures: sudden, involuntary muscle contractions due to the hyperexcitation of neurons.

Stroke: loss of brain function due to a disturbance in the blood supply to the brain.

## **Endocrine**

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.

Growth hormone deficiency / short stature: a condition in which the body does not produce enough growth hormone / a reduced overall rate of growth.

Hypothyroidism requiring replacement therapy: decreased activity of the thyroid gland. Diagnosis of hypothyroidism includes high levels of thyroid-stimulating hormone (TSH). Symptoms of hypothyroidism

include fatigue, depression, weakness, weight gain, musculoskeletal pain, decreased taste, hoarseness, and / or puffy face.

Pancreatitis: inflammation of the pancreas.

## **Genitourinary**

Gonadal dysfunction requiring hormone replacement (testosterone or estrogen): Females may experience early symptoms of menopause including amenorrhea. Males may experience decreased spermatogenesis. Low levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and / or testosterone may require hormone replacement therapy.

Hemorrhagic cystitis / hematuria requiring medical intervention (catheterization of bladder, extra transfusions, urology consult): characterized by bleeding and inflammation of the bladder wall. Hemorrhagic cystitis may result from systemic chemotherapy or radiation therapy and / or some viral infections (e.g., BK virus). Report cases with macroscopic (visible to the naked eye) or gross hematuria (WHO Grade III and IV hemorrhagic cystitis). If the etiology is infectious, also report in the Infection section (questions 291-295). Examples of medical intervention include catheterization of bladder, extra transfusions, or a urology consult.

## **Musculoskeletal**

Avascular necrosis: localized tissue death due to inadequate oxygen to the cells. Also known as coagulation necrosis or ischemic necrosis.

Osteonecrosis of the jaw: bones of the jaw weaken and die due to potent antiresorptive medications such as bisphosphonates or RANKL inhibitors, infection, steroid use, and treatment of cancer, including radiation.

Osteoporosis: bones become weak and brittle due to losing bone mass faster than it is created from aging.

Osteoporotic fracture: fractures due to low bone mineral density.

## **Psychiatric**

Depression requiring therapy: mood disorder resulting in persistent feeling of sadness and loss of interest. Common treatments include antidepressant, anxiolytic, and antipsychotic medications. Common names include Amitriptyline, Bupropion (Wellbutrin), Bupirone, and Abilify.

Anxiety requiring therapy: disorder characterized by feelings of worry, anxiety, or fear which are strong enough to interfere with daily activities. Common medications include Duloxetine (Cymbalta), Diazepam (Valium), Buspirone, Pregabalin (Lyrica).

Post-traumatic stress disorder (PTSD) requiring therapy: condition triggered by seeing or experiencing a traumatic event.

## Other

Cataracts: loss of transparency in the lens of the eye.

Hyperlipidemia requiring therapy (high total cholesterol, high LDL cholesterol, and / or high triglyceride levels): high levels of lipids (fat particles) in blood. Common drugs includes Atorvastatin (Lipitor), Simvastatin (Zocor), Ezetimibe (Zetia), and Simvastatin (Vytorin).

Iron overload requiring therapy: condition characterized by having too much iron in the body. Therapy includes phlebotomy and iron chelation. Indicate which therapy is required. If “other therapy” is required, specify if in question 605.

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

Mucositis requiring therapy: inflammation and ulceration of mucous membranes that line the digestive tract, usually due to chemotherapy and radiotherapy. Specify the grade as “0 (none),” “I (mild) – oral soreness, erythema,” “II (moderate) – oral erythema, ulcers, solid diet tolerated,” “III (severe) – oral ulcers, liquid diet only,” or “IV (life-threatening – oral ulcers, oral alimentation impossible.” Do not report mucositis which did not require treatment or intervention during the reporting period.

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

Other impairment or disorder: use this category to report any clinically significant impairment(s) / disorder(s) not listed on the form. Specify the other impairment / disorder in question 610.

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

## **Question 611-613: Has the recipient received a solid organ transplant since the date of last report?**

Indicate whether the recipient received a solid organ transplant since the date of the last report. If “yes,” specify the organ transplanted in question 612. If “other organ” is reported, specify organ in question 613. If

the recipient did not receive a solid organ transplant during the reporting period, report “no” for question 611 and continue with question 616.

*Solid organ transplant questions cannot be answered on the day 100 or 6 month forms. These questions will be answered for all subsequent reporting periods.*

**Question 614: Date of transplant:**

If the recipient received a solid organ transplant during the reporting period, report the date of the solid organ transplant.

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

**Question 615: Specify solid organ donor type:**

Specify if the solid organ donor was a “living related donor,” “living unrelated donor,” or a “cadaveric donor.

# Q616-639: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder

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## [Post-Transplant Lymphoproliferative Disorder Instructions section](#)

**Question 616: Did a new malignancy, myelodysplastic, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the HCT or cellular therapy was performed? (Include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders)**

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

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

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

- Skin cancers (basal, squamous, melanoma)
- New leukemia
- New myelodysplasia
- Solid tumors
- 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)

### **Recurrent Skin Cancers**

For most malignancies, do not report recurrence, progression or transformation of the recipient's primary disease (disease for which the transplant was performed) or relapse of a prior malignancy in the "New Malignancy" section. However, in the case of a basal cell or squamous cell skin cancer, report each discreet episode.

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 discreet lesion. These discreet episodes should be reported in the "Other skin malignancy" questions on the Post-HCT Data Forms (revision 4, questions 616-622).

If a new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was diagnosed during the reporting period, report "yes" and completed questions 617-639. If no new malignancies or disorders were diagnosed during the reporting period, report "no" and continue with question 640.

Copy and complete questions 617-639 to report each new malignancy diagnosed since the date of last report. The submission of a pathology report or other supportive documentation for each reported new malignancy is strongly recommended.

#### **Questions 617-619: Specify the new malignancy:**

Indicate which new malignancy / disorder was diagnosed during the reporting period and indicate the date of diagnosis in question 619. Report the pathologic diagnosis date. If the original assessment confirming diagnosis is not available, report the date of diagnosis indicated in the progress notes.

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

#### **Question 620-621: Was the new malignancy donor / cell product derived?**

Indicate whether the new malignancy originated from the donor / cell product. If "yes," indicate whether documentation was submitted to CIBMTR (e.g., cell origin evaluation (VNTR, cytogenetics, FISH)) in question 621.

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

#### **Question 622: Was documentation submitted to the CIBMTR? (e.g., pathology report, autopsy report)**

Indicate whether documentation of the new malignancy, lymphoproliferative disorder, or myeloproliferative disorder was submitted to CIBMTR (e.g., pathology report, autopsy report).

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

## Post-Transplant Lymphoproliferative Disorder



Questions 623-639 can only be answered if Post-transplant lymphoproliferative disorder is selected in question 617. For all other new malignancies / disorders, skip to question 640.

### Question 623: Was there EBV reactivation in the blood?

If reactivation in the blood was confirmed during the reporting period, report “yes” and continue with question 624. If reactivation did not occur during the reporting period report “no” and continue with question 629.

Indicate “unknown” if no EBV testing was performed during the reporting period.

### Question 625-628: How was EBV reactivation diagnosed?

Indicate the method of detection for EBV reactivation.

If reactivation was diagnosed by “qualitative PCR of blood,” continue with question 629.

If the diagnosis was made by “quantitative PCR of blood,” report the number of copies detected in question 626. Also, indicate whether repeat testing was performed during the reporting period in question 627. If repeat testing was performed, report the results of the most recent test performed during the reporting period in question 628.

If the diagnosis was made by “Other method,” specify the method of detection in question 625 and then continue with question 630.

### Question 627: Quantitative EBV viral load of blood (at diagnosis of EBV)

If EBV reactivation was diagnosed by quantitative PCR of blood, report the EBV viral blood load at diagnosis.

### Question 629: Was there lymphomatous involvement? (e.g., a mass)

Indicate whether a mass or other lymphomatous involvement was detected during the reporting period. If there was lymphomatous involvement was confirmed during the reporting period, report “yes” and complete questions 630-637. If lymphomatous involvement was not confirmed during the reporting period, report “no” and continue with question 638.



**Question 630-637: Specify sites of PTLD involvement:**

For each site listed, indicate whether there was post-transplant lymphoproliferative disorder (PTLD) involvement. Sites may be identified by radiographic or pathologic methods. If there was PTLD involvement at a site not listed, report “other site” and specify in question 637.

**Question 638-639: Was PTLD confirmed by biopsy?**

Indicate whether PTLD was confirmed by a biopsy. If PTLD was confirmed by a biopsy, report “yes” and indicate whether documentation was submitted to CIBMTR (e.g., pathology report) in question 639. If a biopsy did not confirm the diagnosis of PTLD, report “no” and continue with question 640.

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

## Q640-660: Functional Status

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**Questions 640-644 will only be answered on the day 100 Form. Centers will not be able to complete these questions for any subsequent reporting periods.**

### **Question 640: Was the intent to complete HCT procedure (conditioning, infusion, and period of recovery from neutropenia) as an outpatient?**

Report “yes” if the plan was to complete all conditioning, infusions, and recovery in the outpatient setting. If the plan was to admit the patient for any part of the transplant, report “no” and continue with question 642.

Report “yes” even if the recipient required an unplanned admission. This admission will be captured in question 641.

### **Question 641: Did the recipient require an unplanned admission?**

Report whether the recipient required an unplanned admission during the reporting period. This includes unplanned admissions for the purpose of completing an HCT as well as admissions to address any post-HCT complications. If an unplanned admission was required, report “yes” and continue with question 642. If the recipient did not require an unplanned admission, report “no” and continue with question 644.

### **Question 642-643: Was the recipient discharged prior to the date of contact?**

If the recipient was discharged from the hospital during the reporting period, report “yes” for question 642 and report the discharge date in question 643. If the recipient was admitted to the hospital multiple times during the reporting period, report first discharge date. If the recipient was not discharged from the hospital during the reporting period, report “no.”

If the recipient died without ever being discharged from the hospital, report “no.”

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

### **Question 644: Total number of inpatient days (day 0 to day 100) in first 100 days post-HST**

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

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

If the recipient receives a subsequent 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 645-647: Recipient height: (most recent)**

*Questions 645-647 will only be enabled / answered for pediatric patients ( $\leq 16$  years old) when the form visit ID is 6 months or greater. These questions will be disabled / not answered for all recipients on the day 100 follow-up form.*

Indicate whether the recipient's height is known. If "known," report the recipient's most recent height and specify the units in question 646. Also, report the date the recipient's height was last measured in question 647. If the recipient's height was not measured during the reporting period, report "unknown" and continue with question 648.

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

#### **Question 648-650: Recipient weight: (most recent)**

Indicate whether the recipient's weight is known. If "known," report the recipient's most recent weight and specify the units in question 649. Also, report the date the recipient's weight was last measured in question 650. If the recipient's weight was not measured during the reporting period, report "unknown" and continue with question 651.

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

#### **Question 651-653: Functional status**

The CIBMTR uses the Karnofsky / Lansky scale to determine the functional status of the recipient on the date of contact. The Karnofsky Scale is designed for recipients aged 16 years and older, and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. If the recipient is less than one year old, leave questions 651-653 blank.

Select the appropriate performance scale, Karnofsky or Lansky, based on the recipient's age. Using this scale, select the score (10-100) that best represents the recipient's activity status immediately prior to the date of last actual contact. Acceptable performance scores include those recorded within 14 days prior to

100 Day and Six Month contact dates. For the annual reporting periods, performance scores may be reported if dictated within one month of the contact date. The only valid scores are 10-100; zero is not a valid response for this scale, nor are values not ending in zero, such as “85.” The Karnofsky / Lansky scale can be found in [Appendix L](#).

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. Determination of performance status is ideally performed by a healthcare provider. Centers are encouraged to put tools in place to facilitate this collection. If a Karnofsky / Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician’s clinic note), data professionals are encouraged to discuss a determination with the 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.



### **Pregnancy Questions**

Questions 654 and 655 will only be answered for recipients between the ages of 10 and 60.

#### **Question 654: Was the recipient pregnant at any time in this reporting period? (Female only)**

Indicate whether the recipient was pregnant at any time during the reporting period. Skip this question for male recipients. If “yes,” complete questions 656-657. If “no,” continue with question 658.

**Question 655: Was the recipient's female partner pregnant at any time in this reporting period (Male only)**

Indicate whether the recipient's female partner was pregnant at any time during the reporting period. Skip this question for female recipients. If "yes," complete questions 656-657. If "no," continue with question 658.

**Question 656: Was the recipient or recipient's partner still pregnant at the date of last contact?**

Indicate whether the recipient or recipient's partner was still pregnant on the date of last contact? If the recipient or recipient's partner was still pregnant on the date of last contact, report "yes" and continue with question 658. If the recipient or recipient's partner was not pregnant at the date of last contact, report "no" and indicate the outcome in question 657.

**Question 657: Specify the outcome of pregnancy:**

Specify the outcome of the pregnancy using the options provided on the form.

**Question 658-660: Has the recipient smoked tobacco cigarettes since the date of last report?**

The intent of this question is to determine the recipient's history of smoking cigarettes only. Do not report the use of cigars, pipe tobacco, chewing tobacco, or other drugs. Indicate whether the recipient has smoked tobacco cigarettes since the date of the last report. If "yes," complete questions 659-660. If the recipient has not smoked tobacco cigarettes since the date of the last report, or their smoking history is not known, report "no" or "unknown" respectively and continue with question 661.

## Q661-668: Subsequent HCT

### \* Subsequent Transplant

Complete this section if the recipient received a subsequent HCT (question 3, answered “yes”).

In addition to this section, a new Pre-TED Form (Form 2400) and Recipient Baseline Data Form (Form 2000) must be completed for the subsequent HCT. The exception to this is an autologous HCT (question 666) performed for graft failure / insufficient hematopoietic recovery (question 664). 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 D](#).

#### Question 661: Date of subsequent HCT

Report the date when the recipient received the subsequent HCT.

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

#### Question 662: Was the subsequent HCT performed at a different institution?

Indicate whether the subsequent HCT was performed at another institution. If the subsequent HCT was performed at a different institution, report “yes” and continue with question 663. If the subsequent HCT was not performed at a different institution, report “no” and continue with question 664.

#### Question 663: 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 664-665: What was the indication for subsequent HCT?

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

- **Graft failure / insufficient hematopoietic recovery:** Additional hematopoietic stem cells are required because the hematopoietic recovery indefinitely declined after the initial hematopoietic recovery (ANC was greater than or equal to  $0.5 \times 10^9/L$  for three consecutive days, and then declined

to below  $0.5 \times 10^9/L$  for at least three consecutive days). This option also includes primary graft failure (no ANC recovery following HCT).

- **Persistent primary disease:** Additional hematopoietic stem cells are required because of the persistent presence of disease pre and post-transplant (i.e., complete remission was never achieved following the previous transplant).
- **Recurrent primary disease:** Additional hematopoietic stem cells are required because of relapsed primary disease (i.e., complete remission was achieved pre or post-transplant, but the disease relapsed following the previous transplant).
- **Planned second HCT, per protocol:** Additional hematopoietic stem cells are given as defined by the protocol for a subsequent transplant / infusion. This transplant is not based upon recovery, disease status, or any other assessment.
- **New malignancy (including PTLD and EBV lymphoma):** Additional hematopoietic stem cells are required because the recipient has developed a new malignancy. This does not include a transformation or progression of the original malignancy for which the recipient was transplanted (refer to question 617 for more information). If “new malignancy” is selected, also complete questions 617-640.
- **Insufficient chimerism:** In the case of a stable, mixed donor chimerism, the infusion of additional cells (usually lymphocytes and not mobilized hematopoietic stem cells) is typically classified as a DCI. Verify with the transplant physician that the cells given should be reported as a subsequent transplant and that stable, mixed chimerism is the reason for the transplant. In the case of declining chimerism—when the percentage of donor cells is sequentially decreasing on several studies, indicating possible impending graft failure—additional stem cells are required. Usually the donor chimerism has fallen below 30-50%.
- **Other:** If additional hematopoietic stem cells are given for a reason other than the options listed, select “other” and complete question 665.

### Question 666-668: Source of HSCs

Report the hematopoietic stem cell source of the recipient’s subsequent HCT.

If “allogeneic, related” is selected, indicate whether the same donor was used in question 667 and submit the form.

If “allogeneic, unrelated” is selected, indicate whether the same donor was used in question 667 and specify the product / donor type in question 668. Submit the form after completing questions 666-668.

If “autologous” is selected, skip questions 667-668 and submit the form.

If more than one product is infused, copy and complete questions 664-668 for each product.