2400: Pre-TED

The Pre-TED Form is now required for all transplants, including subsequent transplants on the comprehensive report form track.

All transplant centers participating in the CIBMTR must submit a Pre-TED Form for each allogeneic (related or unrelated) hematopoietic cell transplant (HCT). The Pre-TED is a requirement of the SCTOD for all United States transplant centers when either the stem cell donation or the transplant occurs within the United States. For more information regarding the SCTOD, see General Instructions, Stem Cell Therapeutics Outcomes Database.

Although data regarding recipients receiving autologous HCT are not required to be submitted as part of the C.W. Bill Young Transplant Program, the CIBMTR is highly committed to collecting data on these recipients for research studies. Centers choosing to report autologous data to the CIBMTR must report on all autologous transplants performed at their center. For more information regarding data reporting for autologous HCT, see HCT

The Pre-TED may be submitted to the CIBMTR up to two weeks prior to the start of the recipient's preparative regimen (see Helpful Hint below). The Pre-TED is due the day of the HCT (day 0), and is past due if not received by that date.

Helpful Hint:
In order to avoid having to make changes to the HCT date, complete the data for the Pre-TED (in FormsNet3 or on paper), but do not submit the form until the first dose of the preparative regimen is given.

For recipients receiving a subsequent HCT:
Transplant centers must submit a Pre-TED for all subsequent HCTs; this includes recipients assigned to the TED Forms **and** the Comprehensive Report Forms by the form selection algorithm.

For the majority of subsequent HCTs, the recipient will remain on the original follow-up form track assigned by the form selection algorithm. For more information regarding center type and the form selection algorithm, see Section 1 in the Center Reference Guide. A recipient may need to change tracks if enrolled on a study that requires comprehensive forms.

For recipients of multiple transplants, transplant centers are not granted access to the new Pre-TED Form in

FormsNet3 until the Post-TED (Form 2450) or Post-Infusion Data Form (Form 2100) from the previous transplant has been completed.

Transplant centers can use the FormsNet3 application to determine if a Pre-TED is due by either: 1) accessing the Forms Due Report, or 2) entering the recipient's unique ID (CRID) in the Patient Forms Due field.

Links to Sections of the Form:

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
7/3/19	2400: Pre-TED	Modify	Updated (new text in red and removed text ~~struck out~~ below) the blue note box under question 40 regarding Haploidentical donors: ***Haploidentical Donors*** *A HLA-haploidentical donor is one who shares, by common inheritance, exactly one HLA haplotype with the recipient and is mismatched for a variable number of HLA genes, ranging from ~~zero~~ one to five, on the unshared haplotype. Potential HLA-haploidentical donors include biological parents; biological children; full or half siblings; and even extended family donors such as aunts, uncles, nieces, nephews, cousins, or grandchildren. Indicate **"HLA-mismatched relative"** for question 40 if a haploidentical donor was used for the HCT.*
6/	2400:	Modify	Added additional information (in red below) to the instructional text for question 40

17/19	Pre-TED		to better define the related donor types listed on the form: Indicate the relationship and match between the recipient and the donor. Only consider HLA-A, B, C, and DRB1 when determining the donor's match / mismatched relationship to the recipient. • **Syngeneic:** ◦ *Includes:* Monozygotic (identical) twins. Occurs when a single egg is fertilized to form one zygote, which then divides into two separate embryos. ◦ *Does not include:* Other types of twins or HLA-identical siblings (see below). • **HLA-identical sibling:** ◦ *Includes:* Non-monozygotic (dizygotic, fraternal, non-identical) twins. Occurs when two eggs are fertilized by two different sperm cells at the same time. This category also includes siblings who aren't twins, but have identical HLA types. The patient and donor will be allele-level matched at HLA-A, B, C, and DRB-1. ◦ *Does not include:* Half-siblings (report as "HLA matched other relatives" if their HLA is a match, or "mismatched relative" if it does not match). • **HLA-matched other relative:** ◦ *Includes:* All blood-related relatives, other than siblings, who are HLA matched (e.g., parents, aunts, uncles, children, cousins, half-siblings). The patient and donor will be allele-level matched at HLA-A, B, C, and DRB1. ◦ *Does not include:* Adoptive parents/children or stepparents/ children who are HLA matched. • **HLA-mismatched relative:** ◦ *Includes:* Siblings who are not HLA-identical and all other blood-related relatives who have at least one HLA mismatch (e.g., parents, aunts, uncles, children, cousins, half-siblings). This includes haploidentical donors. The patient and donor will be allele-level mismatched at one or more loci (HLA-A, B, C, or DRB1). ◦ *Does not include:* Adoptive parents/children or stepparents/ children.
2/27/19	2400: Pre-TED	Modify	Modified (removed text is struck out below, updated text is in red) the instructions for question 52 on where to report cellular therapy product data for products that are not intended to achieve hematopoietic engraftment. *If infusions of additional cells (not intended to produce engraftment) were given prior to the HCT being reported (i.e., prior to clinical day 0), the cells must be*

			reported as a product on the Pre-TED Form (Form 2400, question 51) and on a separate Cellular Therapy ~~Infusion~~ Product Form (Form ~~4006~~ 4003). If the additional cells were infused post-HCT, for any reason other than a subsequent HCT, they should be reported as a DCI on the appropriate follow-up form. Reporting the additional cells (given pre-HCT and not intended to produce engraftment) on the Form ~~4006~~ 4003 is the only mechanism the CIBMTR has in place to collect this data and ensure that the quality assurance data is reported to cord blood banks, if applicable.
12/3/18	2400: Pre-TED	Modify	Updated link in the 2400 Pre-TED to reflect current reporting instructions for autologous transplants.
11/20/18	2400: Pre-TED	Add	Added the following text (in red below) for Question 5: Enter the ZIP code in which the recipient resides. Only five digits are required; however, if the ZIP+4 (nine digit) code is available, please report it in this field.
9/20/18	2400: Pre-TED	Add	Added in text that mid-level health care providers (NPs and PAs) can also assign performance scores.
6/1/18	2400: Pre-TED	Modify	Re-formatted the reporting instructions for pre-HCT CMV-antibody results (question 94) and included the following additional consideration (in red below): **Documented history of "reactive" CMV**: In cases where a recipient has a documented history of a "reactive" CMV test and does not have a history of IVIG or blood transfusions from a CMV positive donor, "reactive" should be reported for the CMV status even if the CMV test is repeated during the pre-HCT work-up phase and is "non-reactive".
5/21/18	2400: Pre-TED	Modify	Added (in red below) and removed (struck out below) text from the instructions for reporting comorbidities (questions 98-134). ***Arrhythmia:*** *Any history of any type of arrhythmia that has necessitated the delivery of a specific antiarrhythmic agent. Examples include, but are not limited to, atrial fibrillation or flutter, sick sinus syndrome, or and ventricular arrhythmias ~~requiring treatment~~.* ***Cardiac:*** *Any history of coronary artery disease (one or more vessel coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, and / or ejection fraction ≤ 50% (shortening fraction < 26 for pediatric recipients)% on the most recent test.* ***Cerebrovascular disease:*** *Any history of transient ischemic attack, subarachnoid hemorrhage, and / or ~~cerebrovascular accident~~ cerebral thrombosis embolism, or hemorrhage.* ***Diabetes:*** *Diabetes or steroid-induced hyperglycemia requiring continuous treatment with insulin or oral hypoglycemics in the last 4 weeks. ~~but not diet alone~~* ***Heart valve disease:*** *Moderate or severe valve stenosis or insufficiency (mitral, aortic, tricuspid, or pulmonary) as determined by echocardiogram, prosthetic mitral or aortic valve, and / or symptomatic mitral valve prolapse. ~~Except asymptomatic mitral prolapse.~~* ***Psychiatric disturbance:*** *The presence of any mood, anxiety, or other psychiatric disorder requiring continuous treatment during the last four weeks. Examples include, but are not limited to, depression, anxiety, bipolar disorder, or and schizophrenia requiring psychiatric treatment in the last 4 weeks.* ***Pulmonary (moderate):*** *Corrected diffusion capacity of carbon monoxide (e.g.,*

			DLCOc, DLCOcorr, DLCO) and/or FEV1 66-80% or dyspnea on slight activity at transplant. Use the Dinakara equation below to determine the DLCOc if only an uncorrected value is provided. For recipients assessed by a postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity. *Dinakara Equation: DLCOc = {uncorrected DLCO} / [0.06965 x {hemoglobin g/dL}]* ***Pulmonary (severe):** Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 ≤ 65% or dyspnea at rest or requiring oxygen at transplant. Use the Dinakara equation above to determine the DLCOc if only an uncorrected value is provided. or recipients assessed by a postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity.* ***Renal (moderate/severe):** Serum creatinine > 2 mg/dL or > 176.8 ~~177~~ µmol/L, or on dialysis at transplant, or prior renal transplantation. See note in question 97.*
5/7/18	2400: Pre-TED	Modify	Modified language on how to report Drugs After Transplant, replaced “day 0” with “transplant” to clarify how to report drugs planned for day 0.
5/7/18	2400: Pre-TED	Add	Added note box to capture all comorbidities including those that are considered complications of the primary disease for transplant and provided examples.
1/23/18	2400: Pre-TED	Add	Added text (in red below) to the description of HLA-mismatched relative provided in the instructions for question 40. *Includes: Siblings who are not HLA-identical and all other blood-related relatives who have at least one HLA mismatch (e.g., parents, aunts, uncles, children, cousins, half-siblings). This includes haploidentical donors.*
1/23/18	2400: Pre-TED	Add	Added **Haploidentical Donors** note box to the instructions for question 40.
10/14/17	2400: Pre-TED	Modify	Updated text in Hepatic and Renal Comorbidities note box. Added text is highlighted red and deleted text is struck out. ***Hepatic Comorbidity:** The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between days – 24 ~~& -10 (or between days -40 & -10 if only a single value was reported between days -24 & day -10) before HCT.~~ and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.* ***Renal (Moderate/Severe) Comorbidity:** Serum creatinine > 2 mg/dL or > 177 µmol/L, as detected in at least two lab values on two different days within a period extending between days – 24 ~~& -10 (or between days -40 & -10 if only a single value was reported between days -24 & day -10) before HCT.~~ and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.*
4/4/17	2400: Pre-TED	Modify	Instruction change for questions 91-93: 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 91-93 should be left blank.
3/10/	2400: Pre-TED	Add	Clarification has been added to the instructions for questions 136-155 (in bold below):

17			Use questions 153-155 to report any prior **hematologic** malignancies that were not listed in questions 136-152. **Solid tumors should be reported in questions 144-131, not in questions 153-155.**
1/31/17	2400: Pre-TED	Modify	Version 4 of the 2400: Pre-TED section of the Forms Instruction Manual released. Version 4 corresponds to revision 5 of the Form 2400.

Last modified: 2019/07/03

Q1-10: Recipient Data

Question 1: Date of Birth

The date of birth is automatically populated based on the value reported on the CRID Assignment Form (2804). Verify that the date of birth is correct. If an error is noted, correct Form 2804 and verify that the date of birth has been updated on the Pre-TED Form.

Question 2: Sex

The recipient's sex is automatically populated based on the value reported on the CRID Assignment Form (2804). Verify that the recipient's sex is correct. If an error is noted, correct Form 2804 and verify that the recipient's sex has been updated on the Pre-TED Form.

Question 3: Ethnicity

Indicate the recipient's ethnicity. The United States Office of Management and Budget (OMB) has defined ethnicity as culturally or geographically determined. The distinction between Hispanic and non-Hispanic is for the purpose of the United States census and reporting of SCTOD data. According to the OMB, "Hispanic" is an ethnic designation based upon where someone (his or her ancestors) was raised (e.g., "Latin America"). Hispanic people may be of any race. The CIBMTR recognizes regional differences with regard to the interpretation of ethnicity throughout the world.

If the recipient is not a resident of the USA, select "not applicable."

If the recipient declines to provide this information or the recipient's ethnicity is not documented, select "unknown."

For more information regarding ethnicity, see Appendix I.

Reporting More Than One Race
FormsNet3 application: Complete question 4 for each race the recipient identifies with by adding an additional instance in the FormsNet application.
Paper form submission: Copy question 4 and complete for each race the recipient identifies with.

Question 4: Race

Indicate the recipient's race. If this recipient has reported that they are more than one race, you may

indicate each race by adding an additional instance in the FormsNet application. The race groups provided are specific to the United States.

For *non-U.S.* centers, select "not reported" if the rules/regulations of your country prohibit the collection or reporting of race data (or due to lack of documentation). If race is reported, it may be necessary to consult with the recipient to select the race group(s) with which they most closely identify.

If the recipient declines to provide this information, select "not reported."

If the recipient's race is not documented, select "unknown."

For more information regarding race, see Appendix I.

Question 5: ZIP or postal code for place of recipient's residence (USA recipients only)

Enter the ZIP code in which the recipient resides. Only five digits are required; however, if the ZIP+4 (nine digit) code is available, please report it in this field.

Question 6: Is the recipient participating in a clinical trial?

Indicate if the recipient is a registered participant with BMT-CTN, RCI-BMT, USIDNET, COG, and/or another clinical trial sponsor that uses CIBMTR forms to capture outcomes data. If "yes," continue with question 7. If "no," continue with question 11.

- **BMT-CTN:** Blood and Marrow Transplant Clinical Trials Network
- **RCI-BMT:** Resource for Clinical Investigation in Blood and Marrow Transplant
- **USIDNET:** United States Immunodeficiency Network
- **COG:** Children's Oncology Group

Reporting Participation in More Than One Study
FormsNet3 application: Complete questions 7-10 for each study the recipient is participating in by adding an additional instance in the FormsNet application.
Paper form submission: Copy questions 7-10 and complete for each study in which the recipient is participating.
If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.

Questions 7-8: Study Sponsor

Select the study sponsor of the clinical trial the recipient is participating in. If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.

If the study sponsor is reported as “BMT-CTN” or “RCI-BMT,” continue with question 9.

If the study sponsor is reported as “USIDNET” or “COG,” continue with question 10.

If “other sponsor” is reported, specify the study sponsor in question 8 and continue with question 10.

Question 9: Study ID Number

Select the recipient’s Study ID number.

Question 10: Subject ID

Enter the recipient’s USIDNET, COG, or other sponsor Subject ID.

If the recipient is participating in a BMT-CTN study and the EMMES ID is known, enter it here.

If the recipient is participating in an RCI-BMT study, enter the Subject ID given at the time of successful enrollment.

Last modified: 2018/11/20

Q11-28: Hematopoietic Cellular Transplant (HCT)

Question 11: Date of this HCT

Report the intended start date of the HCT. If the infusion is planned to last several days, enter the **first** day the infusion is scheduled to start.

If the Pre-TED was submitted prior to day 0, and the planned infusion date has changed, the original planned date of the HCT will automatically be reported in FormsNet3 on either the Post-TED (Form 2450) or the Post-HCT Data Form (Form 2100). For the recipient's first transplant, the HCT date may be changed on the Form 2804. For a subsequent transplant, the date may be changed on the form (Form 2100 or 2450) where the subsequent transplant was originally reported.

If the recipient is scheduled to receive a combination of cellular therapy and stem cell infusions, contact your center's CIBMTR CRC for reporting requirements.

Question 12: Was this the first HCT for this recipient?

Indicate if this is the recipient's first transplant. First transplant is defined as the first transplant the recipient ever receives, not the first transplant the recipient receives at your facility.

If "yes," and this is an autologous transplant, continue with question 13.

If "yes," and this is an allogeneic transplant, continue with question 29.

If "no," continue with question 15.

Question 13: For autologous HCTs only: Is a subsequent HCT planned as part of the overall treatment protocol (not as a reaction to post-HCT disease assessment)?

If, at the time of the current HCT, a second (tandem transplant) or subsequent HCT is planned according to the protocol, check "yes" even if the recipient does not receive the planned subsequent HCT. The word "planned" **should not** be interpreted as: *if the recipient relapses, then the "plan" is to perform a subsequent HCT.* If "yes," continue with question 14. If "no," continue with question 29.

Question 14: Specify subsequent HCT planned:

Indicate whether the planned subsequent HCT is autologous or allogeneic and continue with question 29.

Question 15: Specify the number of prior HCTs:

Enter the number of prior HCTs for the recipient. An HCT event is defined as an infusion of mobilized peripheral blood stem cells (PBSC), bone marrow, or cord blood. For more information on how to distinguish infusion types [example: HCT versus donor cellular infusion (DCI)], see Appendix D.

For recipients who have received a previous HCT (prior to the HCT for which this form is being completed), the following are examples of how to calculate the number of prior HCTs.

Example 1: A recipient was previously transplanted under a protocol that included an infusion of cells over multiple days: day 0, day +1 and day +2. This series of infusions is considered one HCT event (as opposed to three HCT events) and should be counted as *HCT Event #1*.

After receiving the infusion, the recipient had relapse of disease. The recipient is scheduled to receive a subsequent HCT including a preparative regimen. This HCT is *HCT Event #2.* One prior HCT should be reported.

Example 2: A recipient previously received an **allogeneic** HCT (*HCT Event #1*). Then, due to delayed neutrophil recovery, the recipient received additional cryopreserved **allogeneic** mobilized PBSC from the original donor, without a preparative regimen (i.e., "boost" – *HCT Event #2*).

After receiving the boost, the recipient had relapse of disease. The recipient is scheduled to receive a subsequent allogeneic HCT with preparative regimen (*HCT Event #3*). Two prior HCTs should be reported.

Example 3: A recipient previously received an **autologous** HCT (*HCT Event #1*). Then due to delayed neutrophil recovery, the recipient received additional cryopreserved **autologous** cells without a preparative regimen (i.e., "boost" which is not counted as an HCT event because the intent of the autologous infusion is to treat the graft failure).

The boost is successful, but a few years later the recipient develops a new malignancy. The recipient is scheduled to receive a subsequent autologous HCT with preparative regimen (*HCT Event #2*). One prior HCT should be reported.

! **If the recipient receives an infusion due to poor graft response, count the infusion as a subsequent HCT.** The exception to this is "autologous rescue." Autologous rescue **should not be** counted as a separate HCT, and the data collection forms **will not** start over (i.e., the forms will continue from the previous HCT).

Questions 16-19: What was (were) the prior HCT source(s)?

Select the cellular source for each of the recipient's previous HCTs as either autologous, allogeneic unrelated, allogeneic related, or syngeneic (identical twin).

Question 20: Date of the last HCT (just before current HCT):

Report the date of the recipient's **last** autologous or allogeneic (related or unrelated) HCT. Although the CIBMTR requests a Pre-TED for each HCT, there may be circumstances where a prior HCT was not reported (e.g., prior autologous HCT or HCT performed at another center). Reporting the recipient's last HCT enables the CIBMTR to appropriately account for recipient survival status in the database.

Question 21: Was the last HCT performed at a different institution?

Indicate if the last HCT was performed at another institution. If "yes" continue with question 22. If "no" continue with question 23.

Question 22: Specify the institution that performed the last HCT:

Report the name, city, state, and country of the institution where the recipient's last HCT was performed. These data are used to identify and link the recipient's existence in the database and, if necessary, obtain data from the previous transplant center.

Question 23: What was the HSC source for the last HCT?

Report the stem cell source of the recipient's last HCT as either autologous, allogeneic unrelated or allogeneic related (including syngeneic).

Question 24-28: Reason for current HCT:

Indicate the reason for the current HCT (check only one). If this was a subsequent transplant, verify that this answer is consistent with the reason for the subsequent transplant reported on the previous series of report forms.

No hematopoietic recovery: Additional stem cells are required because the recipient did not recover their granulocytes following previous high-dose therapy and HCT.

Partial hematopoietic recovery: Additional stem cells are required because the recipient's hematopoietic recovery was deemed insufficient or too slow for the recipient to survive following previous high-dose therapy and HCT (ANC was never greater than or equal to 0.5×10^9/L for three consecutive days).

Graft failure/rejection after achieving initial hematopoietic recovery: Additional stem cells are required because the recipient's hematopoietic recovery declined indefinitely after the initial hematopoietic recovery (ANC was greater than or equal to 0.5×10^9/L for three consecutive days, and then declined to below 0.5×10^9/L for three consecutive days). If the reason is graft failure or rejection after initial recovery, also complete question 25.

Persistent primary disease: Additional stem cells are required because the recipient was transplanted with disease present, and never entered a remission following the previous transplant.

Recurrent primary disease: Additional stem cells are required because the disease for which the recipient was transplanted relapsed following the previous transplant. If the reason is recurrent primary disease, also complete question 26. Ensure that the date of recurrent primary disease matches the relapse/progression date reported on the previous transplant's appropriate follow-up form.

Planned second HCT, per protocol: Additional stem cells are given because the protocol planned for a subsequent transplant/infusion. This includes *all planned* subsequent transplants (including triple or quadruple transplants). This transplant is not based upon recovery, disease status, or any other assessment.

New malignancy (including PTLD and EBV lymphoma): Additional stem cells are required because the recipient has developed a new malignancy. This does not include a transformation or progression of the original malignancy for which the recipient was transplanted. If the reason is a new malignancy, also complete question 27, and attach a copy of the pathology report using the "Add Attachment" feature in FormsNet3. Ensure that the date of diagnosis for the new malignancy matches the date of diagnosis for the new malignancy reported on the previous transplant's appropriate follow-up form.

Stable, mixed chimerism: Verify with the transplant physician that the cells given should be reported as a subsequent transplant and that stable, mixed chimerism is the reason for the transplant.

Declining chimerism: Additional stem cells are required because the percentage of donor cells present versus recipient cells present is decreasing. This is usually due to an underlying cause such as graft failure, graft rejection, or recurrent disease.

Other: Additional stem cells are required and/or given for a reason other than the options listed. If the HCT is for another reason, select "other" and complete question 28.

Last modified: 2017/06/30

Q29-63: Donor Information

Question 29: Multiple donors

Indicate if cells from multiple different donors (multiple CBUs, combinations of other products from different donors) are to be used for this HCT. If “yes,” continue with question 30. If “no,” continue with question 31.

A supplemental infusion is defined as an infusion of cells given prior to clinical day 0 (of an HCT) for any reason other than to produce engraftment. An infusion of supplemental cells is often given in conjunction with a preparative regimen for HCT. Supplemental infusions should be included when determining if multiple donors were used for this HCT event.

For more information on supplemental infusions, see Appendix D.

Question 30: Specify number of donors

Report the number of donors used for this HCT. Note that this value should never be “1,” since multiple donors were reported in question 29.

Related CBU and Related Product from Same Donor
If the recipient receives a cord blood unit and another product from the same related donor, complete two instances of the Donor Information section (questions 31-62) on the Pre-TED Form 2400.
For example, if a related donor gave a cord blood unit and bone marrow, you would report the cord blood unit information in one instance with the donor type listed as ‘Related cord blood unit’. Create another instance with the donor type reported as ‘Related donor’ to report the bone marrow information. This allows CIBMTR to capture all the necessary donor information needed.
For these cases, complete a Form 2004 for each product. When the donor type is an HLA matched or mismatched relative, only one Form 2005 is required.

Reporting More Than One Donor
FormsNet3 application: Complete questions 31-62 for each donor by adding an additional instance in the FormsNet application.
Paper form submission: Copy questions 31-62 and complete for each donor.

Question 31: Specify donor

Indicate the donor type for this product.

An **autologous** product has cells collected from the recipient for his/her own use.

> If the product was autologous (marrow, PBSC, other product), select “autologous” and continue with question 46.
>
> If the product was an autologous cord blood unit, select “autologous cord blood unit” and continue with question 35.

An **unrelated donor (allogeneic, unrelated)** is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or stepparents/children. Distinguish if the product in an NMDP product or a non-NMDP product. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank, Anthony Nolan, and StemCyte International Cord Blood Center.

> If the product was an NMDP unrelated cord blood unit, select “NMDP unrelated cord blood unit” and continue with question 32.
>
> If the product was from an NMDP unrelated donor (marrow, PBSC, other product), select “NMDP unrelated donor” and continue with question 33.
>
> If the product was from a non-NMDP unrelated donor and was facilitated through another registry, select “non-NMDP unrelated donor” and continue with question 34.
>
> If the product was a non-NMDP cord blood unit, select “non-NMDP cord blood unit” and continue with question 35.

A **related donor (allogeneic or syngeneic, related)** is a blood-related relative. This includes monozygotic (identical twins), non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc.

> If the product was from a related donor (marrow, PBSC, other product), select “related donor” and continue with question 40.
>
> If the product was a related cord blood unit, select “related cord blood unit” and continue with question 35.

Question 32: NMDP cord blood unit ID

Report the NMDP Cord Blood Unit ID. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation. The ID is always numeric and begins with “9” (e.g., 9000-0000-0). If the product ID does not begin with a “9,” the product may not be

an NMDP cord blood unit and the source of the product should be double-checked. Enter the NMDP cord blood unit ID and continue with question 46.

Question 33: NMDP donor ID

Report the NMDP Donor ID (e.g., 0000-0000-0). This ID is unique for each donor and is assigned by NMDP. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation. Enter the NMDP Donor ID (e.g., 0000-0000-0) and continue with question 46.

Question 34: Non-NMDP unrelated donor ID (not applicable for related donors)

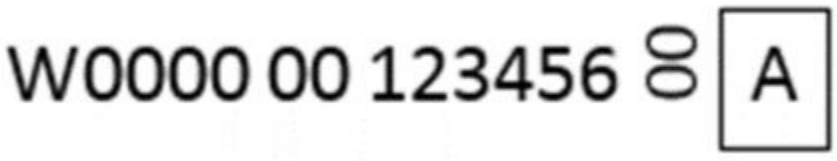
Report the non-NMDP unrelated donor ID. Examples of non-NMDP donor registries include, but are not limited to: Anthony Nolan, Australia Bone Marrow Donor Registry, and REDOME. This ID is often located on the product label, the paperwork accompanying the product, and registry-specific search/product documentation. Enter the non-NMDP unrelated donor ID and continue with question 38.

Question 35: Non-NMDP cord blood unit ID (include related and autologous CBUs)

Report the non-NMDP cord blood unit ID. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank and StemCyte International Cord Blood Center. This ID is often located on the product label, the paperwork accompanying the product, and registry-specific search/product documentation. Enter the non-NMDP cord blood ID. Note that some cord blood banks can ship their units either through the NMDP or directly to the transplant center. Carefully review the accompanying documentation to determine which is appropriate for your unit. You may wish to consult with your center's Transplant Coordinator, as he or she will have insight as to how the product was acquired.

Question 36: Is the CBU ID also the ISBT DIN number?

Report "yes" if the non-NMDP CBU ID is the same as the International Society of Blood Transfusion (ISBT) Donation Identification Number (DIN) and continue with question 38. If the product has an ISBT label on it, the ISBT DIN number is in the upper-left-hand corner and consists of a letter followed by 12 numbers, two sideways numbers, and a letter in a box. Example below:



Please find additional information regarding the ISBT DIN numbers and traceability at http://www.iccbba.org/

uploads/22/82/2282aa443bf8a218788030463681424 4/IN-003-ISBT-128-for-Blood-Components-An-Introduction-v4.pdf. For example, you may see a barcode with an alphanumeric string below it.

If the CBU ID is not the same as the ISBT DIN number, select “no” and continue with question 37.

Question 37: Specify the ISBT DIN number:

Report the ISBT DIN number using the letter, 12 digits, 2 sideways numbers, and the letter in the box.

> **Registry Code(s)**
> **FormsNet3 application**: Select the appropriate registry code from the drop down directory.
> **Paper form submission**: Use the BMDW website to look up the registry’s appropriate match code. **Enter the match code listed in brackets.**

Questions 38: Registry or UCB Bank ID:

Specify the registry used to obtain the adult donor or umbilical cord blood unit. The Bone Marrow Donors Worldwide (BMDW) codes have been adopted to avoid submitting the entire name and address of the donor registry.

The registry code for NMDP donors is USA1 and for NMDP cord units is U1CB.

Some common banks that do not list with BMDW have been added to the FormsNet list, including St Louis Cord Blood Bank (SLCBB) and Viacord (VIAC).

If the donor was found through DKMS, report the registry that facilitated the HCT. Some registries may be listed more than once with BMDW (one way for marrow/PBSC products and differently for cord blood products). Ensure that the appropriate code for the product was selected because distribution of data depends on the code.

If the registry code cannot be determined using the BMDW website, select “other registry” and continue to question 39.

Question 39: Specify other Registry or UCB Bank

If the BMDW website does not list a match code for the adult donor registry or cord blood bank, provide the registry’s official name in the “specify other registry” field.

Please ensure that the registry you are entering under “other” is not already listed in the pull-down list for question 38. For example, NMDP adult donors, NMDP cords, and New York Cord Bank each have their own

entries above in the registry or UCB Bank ID drop down menu.

Question 40: Specify the related donor type:

> **Haploidentical Donors**
> A HLA-haploidentical donor is one who shares, by common inheritance, exactly one HLA haplotype with the recipient and is mismatched for a variable number of HLA genes, ranging from one to five, on the unshared haplotype. Potential HLA-haploidentical donors include biological parents; biological children; full or half siblings; and even extended family donors such as aunts, uncles, nieces, nephews, cousins, or grandchildren. Indicate **"HLA-mismatched relative"** for question 40 if a haploidentical donor was used for the HCT.

Indicate the relationship and match between the recipient and the donor. Only consider HLA-A, B, C, and DRB1 when determining the donor's match / mismatched relationship to the recipient.

Syngeneic:
Includes: Monozygotic (identical) twins. Occurs when a single egg is fertilized to form one zygote, which then divides into two separate embryos.
Does not include: Other types of twins or HLA-identical siblings (see below).

HLA-identical sibling:
Includes: Non-monozygotic (dizygotic, fraternal, non-identical) twins. Occurs when two eggs are fertilized by two different sperm cells at the same time. This category also includes siblings who aren't twins, but have identical HLA types. The patient and donor will be allele-level matched at HLA-A, B, C, and DRB-1.
Does not include: Half-siblings (report as "HLA matched other relatives" if their HLA is a match, or "mismatched relative" if it does not match).

HLA-matched other relative:
Includes: All blood-related relatives, other than siblings, who are HLA matched (e.g., parents, aunts, uncles, children, cousins, half-siblings). The patient and donor will be allele-level matched at HLA-A, B, C, and DRB1.
Does not include: Adoptive parents/children or stepparents/children who are HLA matched.

HLA-mismatched relative:
Includes: Siblings who are not HLA-identical and all other blood-related relatives who have at least one HLA mismatch (e.g., parents, aunts, uncles, children, cousins, half-siblings). This includes haploidentical donors. The patient and donor will be allele-level mismatched at one or more loci (HLA-A, B, C, or DRB1).

Does not include: Adoptive parents/children or stepparents/children

Questions 41-42: Date of birth: (donor/infant)

Report if the donor's/infant's date of birth is "known" or "unknown." If the donor's/infant's date of birth is "known," report the date of birth (YYYY-MM-DD) and continue with question 45. If the donor's/infant's date of birth is "unknown," continue with question 43.

Questions 43-44: Age: (donor/infant)

Report if the donor's/infant's age is "known" or "unknown." If the donor's/infant's age is known, report the donor's/infant's age at the time of product collection in question 44. Report the age in months if the donor is less than 1 year old, otherwise report the age in years. If the donor's/infant's age at collection is unknown, continue with question 45.

Question 45: Sex: (donor/infant)

Indicate the donor's biological sex as "male" or "female." For cord blood units, report the infant's sex.

Questions 46-50: Specify product type:

Indicate "yes" or "no" for each product type listed for the donor specified in question 31.

> Previous CIBMTR forms required you to enter two instances of the donor section when a single donor donated multiple products. **This is no longer required.** Report all products collected from a single donor in the same instance of the donor section.

Examples of "other product" type include, but are not limited to the following:

- Supplemental infusion of NK Cells
- Supplemental infusion of T-regulatory cells
- Supplemental infusion of mesenchymal cells

If "other product" is indicated, report the product type in "specify other product type." If your center has a protocol where using "other products" is common, you should be consistently reporting the same text in the specify field so that the like products can be grouped together.

Question 51: Specify number of products infused from this donor:

Report the number of products infused from the donor specified in question 31.

Single Product: CIBMTR defines a *single product* (i.e., cellular product) as **cells collected from a single donor using the same mobilization cycle and collection method regardless of the number of collection days.**

Example 1 (multiple bags): A G-CSF-stimulated donor had two PBSC collections on subsequent days. The products collected over the two days were divided into four bags. Although the product is contained in multiple bags, this collection is considered a single product, as there was no change in mobilization technique or collection method.

Multiple Products: For the purposes of this manual, the CIBMTR defines *multiple products* as **cells collected using more than one mobilization technique and/or collection method.**

Example 2 (multiple collection methods): A G-CSF-stimulated donor had a PBSC collection and the product was cryopreserved. One month later the donor had a marrow collection; both products were infused at the time of transplant. Each collection is considered a separate product because different collection methods were used.

Example 3 (change in mobilization): A G-CSF-stimulated donor had a PBSC collection, but the cell count was poor. GM-CSF was administered and the donor was re-collected. Each collection is considered a separate product due to the change in mobilization.

Example 4 (re-mobilization): A G-CSF-stimulated donor had a PBSC collection, but the cell count was poor. The donor was re-mobilized with G-CSF and a second PBSC collection was performed. Each collection is considered a separate product due to the re-mobilization of the donor.

Example 5 (two different product types): A cord blood unit is infused at the same time as marrow. Each collection is considered a separate product.

Question 52: Specify the number of these products intended to achieve hematopoietic engraftment:

If infusions of additional cells (not intended to produce engraftment) were given prior to the HCT being reported (i.e., prior to clinical day 0), the cells must be reported as a product on the Pre-TED Form (Form 2400, question 51) and on a separate Cellular Therapy Product Form (Form 4003). If the additional cells were infused post-HCT, for any reason other than a subsequent HCT, they should be reported as a DCI on the appropriate follow-up form. Reporting the additional cells (given pre-HCT and not intended to produce engraftment) on the Form 4003 is the only mechanism the CIBMTR has in place to collect this data and ensure that the quality assurance data is reported to cord blood banks, if applicable.

Report the number of products administered to achieve hematopoietic engraftment.

> ! The following mobilization questions are for autologous HCT recipients only. If other than autologous, continue with question 61.

Question 53: Did the recipient have more than one mobilization event to acquire cells for HCT?

Stem cells do not typically circulate in the bloodstream. Therefore, in order to increase the quantity of cells for collection, an agent is frequently given to the autologous recipient. The purpose of the agent is to move the stem cells from the bone marrow into the peripheral blood. This practice is often referred to as *mobilization* or *priming*. Occasionally, a bone marrow product may be primed using a growth factor.

For the purposes of this manual, the CIBMTR defines a *mobilization event* as the planned administration of growth factors or systemic therapy designed to enhance stem cell collection. If the donor requires an additional mobilization at a later date to collect an additional product, this should be considered an additional mobilization event. Additionally, if the mobilization methods change (e.g., plerixafor is required starting on Day 3 of collection) this would be considered an additional mobilization event.

Example 1: An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. Since the collection and mobilization methods remained the same over the duration of the collection, this is considered one mobilization event.

Example 2: An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection, but the cell count was poor. GM-CSF was administered and the autologous recipient was re-collected. This is considered two mobilization events due to the change in mobilization.

Example 3: An autologous recipient was mobilized with G-CSF and underwent a one-day PBSC collection, but the cell count was poor. The recipient then received plerixafor to enhance the mobilization. This is considered two mobilization events due to the change in mobilization.

Question 54: Specify the total number of mobilization events performed for this HCT (regardless of number of collections or which collections were used for this HCT):

Report the total number of mobilization events performed for this HCT. Include all mobilization events, even if a product from the mobilization event for this HCT was not used during the transplant.

Questions 55-60: Specify all agents used in the mobilization reported above:

Report if any of the following products were used in the mobilization event(s) reported in questions 53-54. Select “yes” or “no” for each question.

G-CSF: granulocyte colony-stimulating factor, filgrastim, Neupogen®

GM-CSF: granulocyte macrophage colony-stimulating factor, sargramostim, Leukine®
Peglygated G-CSF: pegfilgrastim, Neulasta®
Plerixafor: Mozobil®
Other CXCR4 inhibitor: examples include POL6326 and AMD3465. Report experimental and other CXCR4 inhibitors used to mobilize the donor here.
Combined with chemotherapy: Systemic therapies used to enhance the stem cell product may include cyclophosphamide or ICE chemotherapy (Ifosfamide, carboplatin, and etoposide) with or without rituximab.

Question 61: Was this donor used for any prior HCTs?

Indicate if the donor reported in question 31 was used for prior HCTs for this recipient. If this is the recipient's first HCT select "no." If this is an autologous infusion, select "no."

Question 62: Donor CMV-antibodies (IgG or Total) (Allogeneic HCTs only)

CMV is a common virus that infects 50-80% of adults worldwide, and is transmitted from person to person through bodily fluids. The virus that causes CMV is part of the herpes virus family and, like other herpes viruses, CMV may be dormant for a period of time before the virus is activated in the host. CMV infections are usually harmless in a healthy immune system and typically cause only mild symptoms, if any. However, if a person's immune system is seriously weakened (as in an immunosuppressed stem cell recipient) the virus can have serious consequences such as pneumonia, liver failure, and even death.

Most laboratory reports indicate a positive result as *reactive*, and a negative result as *non-reactive*. Occasionally, laboratory reports show a specific antibody titer. In this case, compare the laboratory result to the reported standards to determine if the result was reactive or non-reactive.

If the laboratory reports a CMV IgM antibody only, not total IgG/IgM or CMV IgG antibody; report the result as "not done."

If the laboratory reports the results as "inconclusive" or "equivocal," select "not done."

If the laboratory reports CMV testing by PCR (DNA detection), report the result as "not done." CMV testing by PCR is used to detect the presence of the CMV virus and does not test for prior exposure.

Indicate the test result documented on the laboratory report as either "reactive," "non-reactive," "not done," or "not applicable (cord blood unit)."

Question 63: Was plerixafor (Mozobil) given at any time prior to the preparative regimen? (Related HCTs only)

Stem cells do not typically circulate in the bloodstream. Therefore, in order to increase the quantity of cells for collection, an agent is frequently given to the allogeneic donor or autologous recipient. The purpose of the agent is to move the stem cells from the bone marrow into the peripheral blood. This practice is often referred to as *mobilization* or *priming*. Indicate if the donor received plerixafor at any time prior to the start of stem cell collection.

Last modified: 2019/07/03

Q64-71: Consent

To be compliant with Federal Regulations for human research subject protection, centers must obtain IRB-approved informed consent from recipients and donors (if applicable, for the related donor sample repository) to allow data submitted to the CIBMTR to be used for observational research. Informed consent must also be obtained from recipients and donors prior to submitting blood samples to the Research Sample Repository. The NMDP/CIMBTR has written protocols and informed consent documents for the Observational Database and Research Sample Repository. All centers must have local IRB approval for the Observational Database protocol. All centers that are NMDP member centers must also have local IRB approval for the Research Sample Repository protocol. With the exception of some selected sites (participating in the related sample repository), centers performing only related donor transplants and/or autologous transplants will not be submitting research samples and do not need to obtain local IRB approval for the repository protocol. The NMDP IRB has approved these protocols and consent forms, and the documents are provided to participating sites to include with their local IRB submissions.

International Centers must obtain consent of each patient participating in the Observational Database in a manner consistent with the laws and regulations of that country.

Under federal legislation, U.S. centers are required to submit outcomes data on all allogeneic transplants, related and unrelated. Data submitted without informed consent from the recipient should be reported on the TED Forms and will only be used for federally required research such as the center-specific outcomes analysis.

Question 64: Has the recipient signed an IRB-approved consent form for submitting research data to the NMDP/CIBMTR?

When a recipient consents to participate in the Observational Database, their data are contained in the CIBMTR's Observational Database and used for research. The database includes recipient baseline and outcome data for related and unrelated allogeneic transplants from any cell source, and for autologous transplants. Data are also collected on unrelated donors and their donation experiences.

The primary purpose of the Observational Database is to have a comprehensive source of data that can be used to study hematopoietic cellular transplantation. Studies using these data include:

- How well recipients recover from their transplants.
- How recovery after transplantation can be improved.
- What the long-term outcomes are after transplantation.
- How access to transplantation for different groups of recipients can be improved.

- How well donors recover from collection procedures.
- The application and success of transplantation in the management of marrow-toxic injuries.

Indicate if the recipient has signed an IRB-approved consent form to participate in the Observational Database. If “yes (patient consented),” continue with question 64. If “no (patient declined)” or “not applicable (patient not approached),” continue with question 68.

When to use the “Not Approached” option for the Research Database Consent
CIBMTR expects all transplant centers to approach all patients for the Research Database consent. The “not approached” option should only be used in the rare event when the physician feels it would be in the best interest of the patient not to be consented.

Recipients who transfer to another facility for a subsequent HCT
Any time a recipient transfers to another transplant center, an IRB approved research database consent would need to be obtained at the new center before data could be reported to the CIBMTR.

See the table below for additional information regarding how to report consent status for those with planned tandem or previous transplants.

Transplant Types	Instructions
Tandem Autologous Transplants	Most transplant centers would consider tandem autologous transplants as part of the same treatment plan and would consent the patient prior to the 1st HCT only. If that’s the case, the center should report “yes” to the consent question for the 2nd HCT and provide the date when the consent was first obtained.
Tandem Autologous-Allogeneic Transplants	Most transplant centers would consider tandem autologous-allogeneic transplants as part of the same treatment plan and would consent the patient prior to the 1st HCT only. If the center has one IRB approved consent covering both the autologous and allogeneic transplants, then the center should report “yes” to the consent question for the 2nd HCT and provide the date when the consent was first obtained. In the case where a center has separate research database consents for autologous and allogeneic HCTs, the center should obtain both consents from the patient prior to the 1st HCT. The center should then report “yes” to the consent question for the 2nd HCT & provide the date when the consent was first obtained.
Autologous HCT followed by subsequent autologous HCTs (not a	In this scenario, CIBMTR does not require an additional consent form to be signed. The only consent required would be the one obtained at the time of the first autologous HCT. The center should report “yes” to the consent question for the subsequent HCT and provide the date when the consent was first obtained. However, a center’s IRB may require a second database consent form to be signed in this situation, and centers should refer to the higher standard set by their IRB.

tandem autologous HCT)	
Allogeneic HCT followed by subsequent allogeneic HCTs (not a tandem allogeneic HCT)	In this scenario, CIBMTR does not require an additional consent form to be signed. The only consent needed would be the one obtained at the time of the first allogeneic HCT. The center should report “yes” to the consent question for the subsequent HCT and provide the date when the consent was first obtained. However, centers must follow their own institutional policy as well, which may require the patient be re-consented to the Research Database for a subsequent HCT.
Autologous HCT followed by subsequent allogeneic HCTs (not a tandem autologous HCT)	If the center has one IRB approved consent form covering both autologous and allogeneic transplants, then the center should report “yes” to the consent question for the 2nd HCT and provide the date when the consent was first obtained. In the case where a center has separate research database consent forms for autologous and allogeneic HCTs, the patient would need to be re-approached prior to the subsequent allogeneic transplant and asked to sign the appropriate consent form. If the patient was not asked to sign a 2nd consent form, then “not approached” must to be reported on the Pre-TED.

Question 65: Date form was signed:

Report the date the research database consent form was signed by the recipient. Do not report the date that the witness or health care professional signed the consent form.

Question 66: Did the recipient give permission to be directly contacted for future research?

Indicate if the recipient has given permission to be directly contact by the NMDP/CIBMTR for future research as documented on the research database consent form. If “yes (patient provided permission),” continue with question 67. If “no (patient declined)” or “not approached,” continue with question 68.

Below is an example of this permission found in the NMDP/CIBMTR Research Database for Hematopoietic Cell Transplantation and Cellular Therapy Consent Form.

> *VIII. PERMISSION TO CONTACT FOR FUTURE CIBMTR RESEARCH STUDIES*
> Do you agree to give the CIBMTR permission to contact you in the future to tell you about research studies for which you are eligible? These studies are different from the studies that use your medical data. These studies would involve you directly, for example, asking you to complete a survey. You may decide if you want to participate in a specific study when you are contacted. By checking the “AGREE” box below, you are only agreeing that the CIBMTR can contact you to tell you about the study.
> Due to the need to follow up with you after your transplant, please tell your transplant center if your contact information changes. If the contact information on file is no longer valid, it might be necessary to

> use an internet-based search service to find you. By agreeing to be contacted for future studies, you authorize the CIBMTR to use such a service to search public and non-public information only for the purpose of trying to locate you.
>
> ☐ **I AGREE** to allow CIBMTR to contact me about future studies.
>
> ☐ **I DO NOT** want CIBMTR to contact me about future studies.

If the recipient declined to take part in the CIBMTR Research Database (as indicated in question 64) but gave permission to be contacted for future CIBMTR studies, ensure that there is documentation before selecting “yes.”

Question 67: Date form was signed:

Report the date the research database consent form was signed by the recipient. Do not report the date that the witness or health care professional signed the consent form.

Question 68: Has the recipient signed an IRB-approved consent form for submitting research blood samples to the NMDP/CIBMTR?

The Research Sample Repository contains blood samples from unrelated recipients and/or their adult volunteer donors or cord blood units. Related allogeneic recipients and/or donors will participate at selected transplant centers.

The primary objective of the Research Repository is to make blood samples available for research studies related to histocompatibility and hematopoietic cellular transplantation.

Studies in which these data may be used include:

- Improving the understanding of tissue matching for hematopoietic cellular donors and recipients.
- Determining and evaluating the factors that affect transplant outcomes.
- Studying the distribution of HLA tissue types in different populations (e.g., study tissue typing differences between different racial and ethnic populations to help develop methods to improve tissue matching between donors and recipients, including testing of rare HLA types).

Indicate if the recipient signed an IRB-approved consent form to donate research blood samples to the NMDP/CIBMTR. If “yes (patient consented),” continue with question 69. If “no (patient declined),” “not approached,” or “not applicable (center not participating),” continue with question 70.

Blood samples are not submitted for subsequent transplants, however, this question is asked for

subsequent transplants. If the recipient previously consented to submit research blood samples to NMDP/CIBMTR, select “yes (patient consented).”

Question 69: Date form was signed:

Report the date the research sample consent form was signed by the recipient. Do not report the date that the witness or health care professional signed the consent form.

Question 70: Has the donor signed an IRB-approved consent form for submitting research blood samples to the NMDP/CIBMTR? (Related donors only)

Indicate if the donor signed an IRB-approved consent form to donate research blood samples to the CIBMTR. If “yes (donor consented),” continue with question 71. If “no (donor declined),” “not approached,” or “not applicable (center not participating),” continue with question 72.

Question 71: Date form was signed:

Report the date the research sample consent form was signed by the donor. Do not report the date that the witness or health care professional signed the consent form.

Last modified: 2017/01/31

Q72-90: Product Processing/Manipulation

Question 72: Was the product manipulated prior to infusion?

If any part of the product was manipulated in any way prior to infusion at the transplant center, select "yes." **Do not report cryopreservation (including plasma removal as part of cryopreservation) as a method of manipulation; cryopreservation of the product(s) is reported on the 2006 form, if applicable.**

If the product was shipped to your facility, do not report manipulation of the product performed at the collection center.

If the product was not manipulated, select "no" and continue with question 91.

Question 73: Specify portion manipulated:

Indicate the portion of the product that was manipulated. If the entire product was manipulated, select "entire product" and continue with question 74. If a portion of the product was removed and manipulated, select "portion of product" and continue with question 75.

If different portions of the product were manipulated in different ways, select "portion of product" to indicate that the manipulation were not performed on the entire product.

Questions 74-90: Specify all methods used to manipulate the product:

Indicate the method(s) of stem cell manipulation. Answer each question as "yes" or "no" and do not leave any questions blank.

> **Steps in Manipulation**
> If the manipulation consists of several steps, individual steps do not need to be reported as separate manipulations. For example, washing that is part of CD34+ expansion does not need to be reported as a separate manipulation. Similarly, T-cell depletion that is part of expansion does not need to be reported.
> In the cases above, if T-cell depletion and/or washing are done as stand-alone manipulations, they should be reported.

Washed: Washing is performed to remove cryoprotectant (such as DMSO) from the product.

Diluted: Dilution is performed to reduce the cell concentration.[1]

Buffy coat enriched: Buffy coat enrichment is performed to reduce/remove mature erythrocytes and plasma.[1]

B-cell reduced: B cell reduction is performed to reduce/remove the quantity of B cells in the product.[1]

CD8 reduced: CD8 reduction is performed to reduce/remove the population of CD8 cells in the product.[1] The removal of CD8 cells may mitigate the risk of GVHD.

Plasma reduced (removal): Plasma reduction is performed to remove plasma via sedimentation or centrifugation.[1]

Plasma reduction may be done in order to minimize the risks associated with ABO mismatched products or to prevent volume overload. Previous versions of the Form 2006 made a distinction between plasma removal and volume reduction; for the purpose of this form, both volume reduction and plasma removal should be reported here.

Plasma reduction/removal that is part of the cryopreservation process should not be reported as manipulation.

RBC reduced: RBC reduction is performed to reduce/remove mature erythrocytes from the product.[1]

Cultured (ex-vivo expansion): Ex-vivo expansion is a method of culturing cells to “activate, expand, or promote development of a specified cell population in the presence of specific additive(s).”[1]

Genetic manipulation (gene transfer/transduction): Gene manipulation refers to any method used to modify the genes in the product cells. Gene transduction refers to the transfer of genes from one cell to another. Genetic manipulation is still in the early investigative phase of research.

PUVA treated: Product treated with psoralen and ultraviolet light (PUVA).[1]

CD34 enriched (CD34+ selection): CD34+ selection is a manipulation method also known as “positive selection.” This method identifies and selects stem cells that have a CD34+ marker on the cell surface.

CD133 enriched: CD133 enrichment identifies and selects stem cells that have a CD133 marker on the cell surface.

Monocyte enriched: Monocyte enrichment identifies and selects monocytes.

Mononuclear cells enriched: Mononuclear cell enrichment identifies and selects mononuclear cells.

T-cell depletion: T-cell depletion removes some or all of the T-cells in an effort to minimize GVHD. Methods of T-cell depletion include antibody affinity column, antibody-coated plates, antibody-coated plates and soybean lectin, antibody + toxin, immunomagnetic beads, and CD34 affinity column plus sheep red blood cell resetting.

If a method of manipulation was performed on the product, but is not listed above, select “yes” for question 89 and specify using question 90. Do not report cryopreservation (or processing used in the cryopreservation process) as manipulation.

[1] ISTB 128. *Standard Terminology for Medical Products of Human Origin.* ICCBBA ST-002. Version. 7.1. January 2017. Accessed at: https://iccbba.org/uploads/00/8a/008acf140f7f5f7560d60bde2187a3f7/Standard-Terminology-for-Medical-Products-of-Human-Origin-v7.1.pdf Accessibility verified on March 5, 2015

Last modified: 2017/01/31

Q91-94: Clinical Status of Recipient Prior to the Preparative Regimen (Conditioning)

Question 91: What scale was used to determine the recipient's functional status?

The CIBMTR uses the Karnofsky/Lansky scale to determine the functional status of the recipient immediately prior to the start of the preparative regimen. 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 91-93 blank.

Questions 92-93: Performance score prior to the preparative regimen:

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. The CIBMTR uses the Karnofsky/Lansky scale to determine the functional status of the recipient immediately prior to the start of the preparative regimen. For the purposes of this manual, the term "immediately prior" represents the **pre-HCT work-up phase**, or **approximately one month** prior to the start of the preparative regimen. In cases where the pre-transplant work-up occurs in months prior to transplant (i.e., the pre-transplant workup occurs more than one month prior to transplant), a documented performance score may be submitted ***if*** the recipient does not have a score closer to the start of the preparative regimen, the recipient receives no additional treatment after the date of assessment, and the recipient's status does not clearly decline.

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 start of the preparative regimen. For an example of the Karnofsky/Lansky scale, see Appendix L.

If a Karnofsky/Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician's clinic note), data management professionals **should not** assign a performance score based on analysis of available documents. Rather, a physician or mid-level health care provider (NPs and PAs) should provide documentation of the performance score.

The CIBMTR recognizes that some transplant centers prefer to collect 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 11 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. For centers that collect only an ECOG performance score, CIBMTR

will make the following accommodations when auditing the source data:

- Centers collecting 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. This practice should be clear and reproducible.

For more information regarding converting an EGOG score to a Karnofsky/Lansky score, see Appendix L.

Question 94: Recipient CMV-antibodies (IgG or Total):

Report the cytomegalovirus (CMV) status of the recipient immediately prior to the start of the preparative regimen. For the purposes of this manual, the term “immediately prior” represents the **pre-HCT work-up phase**, or **approximately one month** prior to the start of the preparative regimen. An exception to this definition would apply to a recipient with a documented history of a “reactive” CMV test result. In this case, the CMV test may not be repeated during the pre-HCT work-up phase. Therefore a timeframe of greater than one month prior to the start of the preparative regimen is acceptable. In cases where the pre-transplant work-up occurs in months prior to transplant (i.e., the pre-transplant workup occurs more than one month prior to transplant), a CMV assessment may be submitted if the recipient does not have an assessment closer to the start of the preparative regimen.

CMV is a common virus that infects 50-80% of adults worldwide, and is transmitted from person to person through bodily fluids. The virus that causes CMV is part of the herpes virus family and, like other herpes viruses, CMV may be dormant for a period of time before the virus is activated in the host. CMV infections are usually harmless in a healthy immune system and typically cause only mild symptoms, if any. However, if a person’s immune system is seriously weakened (as in an immunosuppressed stem cell recipient) the virus can have serious consequences such as pneumonia, liver failure, and even death.

Most laboratory reports indicate a positive result as *reactive*, and a negative result as *non-reactive*. Occasionally, laboratory reports show a specific antibody titer. In this case, compare the laboratory result to the reported standards to determine if the result was reactive or non-reactive.

If the laboratory reports a CMV IgM antibody only, not total IgG/IgM or CMV IgG antibody, report the result as “not done”.

If the laboratory reports the results as “inconclusive” or “equivocal,” select “not done.”

Indicate the test result documented on the laboratory report as either “reactive,” “non-reactive,” or “not done.”

Additional Considerations:

- **Recipients < 6 months**: If the recipient is less than 6 months old, report any positive CMV antibody results as “not done” due to the presence of maternal antibodies. However, in infants greater than 6 months old, positive CMV PCR results indicate a CMV infection and the results may be reported as “reactive.”
- **Exposure to IVIG**: Exposure to IVIG may result in a false positive CMV antibody result. If the recipient has been exposed to IVIG leading up to HCT (within 3-6 months), indicate the CMV antibody results using the following guidelines:
    - If the recipient had a non-reactive CMV antibody result prior to IVIG therapy and then routine CMV PCR results showed no copies of CMV, the CMV antibody may be reported as “non-reactive,” even if the CMV antibody became reactive during IVIG treatment.
    - If CMV PCR results quantified copies of CMV DNA (i.e., was positive) during IVIG treatment, the results may be reported as “reactive.”
    - If the recipient did not have a CMV antibody test prior to the initiation of IVIG, but had a positive antibody test during the IVIG therapy, report “not done.”
    - “Not done” should be reported if no CMV antibody tests were done prior to the initiation of IVIG therapy, even if CMV PCR testing was negative during IVIG treatment (because CMV PCR only detects active infection, not prior exposure).
- **Documented history of “reactive” CMV**: In cases where a recipient has a documented history of a “reactive” CMV test and does not have a history of IVIG or blood transfusions from a CMV positive donor, “reactive” should be reported for the CMV status even if the CMV test is repeated during the pre-HCT work-up phase and is “non-reactive”.
- **CMV testing by PCR**: If the laboratory reports CMV testing by PCR (DNA detection) but no CMV antibody testing is done during the pre-transplant work-up or within one month prior to transplant, report the result as “not done.” CMV testing by PCR is used to detect the presence of the CMV virus and does not test for prior exposure.

Last modified: 2018/09/20

Q95-155: Comorbid Conditions

Question 95: Is there a history of mechanical ventilation?

A history of mechanical ventilation may impact the recipient's pulmonary function post-HCT. Mechanical ventilation is any assisted ventilation on behalf of the recipient. Mechanical ventilation can occur as both an endotracheal tube and ventilator, or as a BIPAP machine with a tight fitting mask in continuous use. The one exception to BIPAP is CPAP used for sleep apnea, which generally involves overnight use only for patients with documented sleep apnea. Therefore, **do not** report a CPAP used for sleep apnea, as it does not have the same implications as other forms of mechanical ventilation.

Indications for mechanical ventilation include, but are not limited to:

- Apnea with respiratory arrest (excludes sleep apnea)
- Acute lung injury
- Vital capacity < 15 mL/kg
- Chronic obstructive pulmonary disease (COPD)
- Clinical deterioration
- Respiratory muscle fatigue
- Obtundation or coma
- Hypotension
- Tachypnea or bradypnea

If the recipient was placed on mechanical ventilation at any time prior to this HCT event (excluding mechanical ventilation during surgery) check "yes." If the recipient does not have a history of mechanical ventilation, check "no."

Question 96: Is there a history of proven invasive fungal infection?

Fungal infections play a major role in the clinical outcome of transplant recipients. For the purposes of this manual, the term "proven" is defined as a pathologic specimen or culture that yields a positive result. For example, a chest x-ray that reveals a nodule **is not** considered a "proven" diagnosis of aspergillus. A biopsy of a specimen with a positive culture for aspergillus **is** a proven diagnosis.

If the recipient has a history of **proven** invasive fungal infection at any time prior to this HCT, check "yes." If the recipient has not had a history of a proven invasive fungal infection, check "no." For a subsequent HCT, report any documented significant fungal infections in the recipient's medical history, starting with the preparative regimen of the previous HCT to the time prior to the preparative regimen for the current HCT.

Examples of proven invasive fungal infections include, but are not limited to: invasive aspergillosis, zygomycosis and other molds, invasive candidiasis, cryptococcosis, endemic mycosis, other yeasts, and pneumocystosis.

Non-invasive fungal infections such as thrush and nail fungus should not be reported.

For assistance with reporting fungal infections, consult a transplant physician.

Questions 97-134
Prior to answering question 97, review the list of co-existing disease(s) and/or organ impairments listed under questions 98-134.

Question 97: Were there *clinically significant* co-existing disease or organ impairment at the time of patient assessment prior to preparative regimen?

Hepatic and Renal Comorbidities[1]
In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities
Hepatic Comorbidity: The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.
Renal (Moderate/Severe) Comorbidity: Serum creatinine > 2 mg/dL or > 177 µmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

[1] Sorror, M. L. (2013). How I assess comorbidities before hematopoietic cell transplantation. *Blood*, 121(15), 2854-2863.

Report “yes” to question 97 if the recipient has a documented history and/or current diagnosis of any of the following:

Documented Medical History	Question Number
Arrythmia	98
Cardiac[2]	99

Cerebrovascular disease	100
Heart valve disease[3]	102
Inflammatory bowel disease	106
Peptic ulcer	108

Current Diagnosis at the Time of Pre-HCT Evaluation	Question Number
Rheumatologic	113
Solid tumor, prior[4]	114
Diabetes	101
Hepatic, mild[5]	103
Hepatic, moderate/severe	104
Infection	105
Obesity	107
Psychiatric disturbance	109
Pulmonary, moderate	110
Pulmonary, severe	111
Renal, moderate/severe[6]	112
Other (specify)	133 and 134

[2] Ejection fraction (EF) ≤ 50% should be reported only if present on most recent test

[3] Excluding asymptomatic mitral valve prolapse

[4] Excluding non-melanoma skin cancer, leukemia, lymphoma, or multiple myeloma

[5] Including any history of hepatitis B or hepatitis C infection

[6] Including renal transplantation at any time in the patient's history

Report all comorbidities including those that are considered complications of the primary disease for transplant. See examples below.

Examples of complications of the primary disease for transplant that should be reported as comorbidities.

- A patient with sickle cell had a stroke prior to HCT, the comorbidity to report would be “cerebrovascular disease”.
- A toddler with Hurler Syndrome has cardiomyopathy, cardiac valvular disease and an ejection fraction of 45%, the comorbidities to report would be “cardiac” & “heart valve disease”.

The intent of this question is to identify serious pre-existing conditions that may have an effect on the outcome of the HCT. For the purposes of this manual, the term “clinically significant” refers to conditions that are being treated at the time of pre-HCT evaluation, or are in the recipient’s medical history and could cause complications post-HCT. Conditions listed in the recipient’s medical history that have been resolved (e.g., appendectomy), and/or that would not pose a concern during or after the HCT should not be reported.

Additionally, for the purposes of this manual, the term “at the time of patient assessment” is defined as the pre-HCT evaluation period prior to the start of the preparative regimen. If the recipient does not have a documented history of clinically significant disease(s) or organ impairment(s), check “no” and continue with question 135.

For information regarding reporting clinically significant co-existing disease or organ impairment, see Appendix J.

Questions 98-134: Co-existing diseases or organ impairments

For each listed co-existing disease or organ impairment, check “yes,” “no,” or “unknown.” The definitions for each of the categories below are taken from Sorror, M. L. (2013). How I assess comorbidities before hematopoietic cell transplantation. Blood, 121(15), 2854-2863.

Arrhythmia: Any history of any type of arrhythmia that has necessitated the delivery of a specific antiarrhythmic agent. Examples include, but are not limited to, atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmias.

Cardiac: Any history of coronary artery disease (one or more vessel coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, and / or ejection fraction ≤ 50% (shortening fraction < 26% for pediatric recipients) on the most recent test.

Cerebrovascular disease: Any history of transient ischemic attack, subarachnoid hemorrhage, and / or cerebral thrombosis embolism, or hemorrhage.

Diabetes: Diabetes or steroid-induced hyperglycemia requiring continuous treatment with insulin or oral hypoglycemics in the last 4 weeks.

Heart valve disease: Moderate or severe valve stenosis or insufficiency (mitral, aortic, tricuspid, or pulmonary) as determined by echocardiogram, prosthetic mitral or aortic valve, and / or symptomatic mitral valve prolapse.

Hepatic (mild): Chronic hepatitis, bilirubin > upper limit of normal to 1.5x upper limit of normal, or AST/ALT > upper limit of normal to 2.5x upper limit of normal, or any history of hepatitis B or hepatitis C infection. *See note in question 97.*

Hepatic (moderate/severe): Liver cirrhosis, bilirubin > 1.5x upper limit of normal, or AST/ALT > 2.5x upper limit of normal. *See note in question 97.*

Infection: Documented infection, fever of unknown origin, or pulmonary nodules requiring continuation of antimicrobial treatment after day 0.

Inflammatory bowel disease: Any history of Crohn's disease or ulcerative colitis requiring treatment.

Obesity: Patients with a body mass index > 35.00 kg/m^2 or BMI-for-age ≥ 95% (pediatric recipients only) during pre-transplant work-up period.

Peptic ulcer: Any history of peptic ulcer confirmed by endoscopy and requiring treatment.

Psychiatric disturbance: The presence of any mood, anxiety, or other psychiatric disorder requiring continuous treatment during the last four weeks. Examples include, but are not limited to, depression, anxiety, bipolar disorder, and schizophrenia requiring psychiatric consult or treatment in the last 4 weeks.

Pulmonary (moderate): Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 66-80% or dyspnea on slight activity at transplant. Use the Dinakara equation below to determine the DLCOc if only an uncorrected value is provided. For recipients assessed by a postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity.

Dinakara Equation: DLCOc = {uncorrected DLCO} / [0.06965 x {hemoglobin g/dL}]

Pulmonary (severe): Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO) and/or FEV1 ≤ 65% or dyspnea at rest or requiring oxygen at transplant. Use the Dinakara equation above to determine the DLCOc if only an uncorrected value is provided. or recipients assessed by a postbronchodilator test, only the prebronchodilator FEV1 values are considered for evaluation of pulmonary comorbidity.

Renal (moderate/severe): Serum creatinine > 2 mg/dL or > 176.8 µmol/L, or on dialysis at transplant, or prior renal transplantation. *See note in question 97.*

Rheumatologic: Any history of systemic lupus erythematosus, rheumatoid arthritis, polymyositis, mixed connective tissue disease, or polymyalgia rheumatica requiring treatment (do NOT include degenerative joint disease, osteoarthritis)

Solid tumor (prior): Treated at any time point in the patient's past history, excluding non-melanoma skin cancer, leukemia, lymphoma, or multiple myeloma. For each listed prior solid tumor, check "yes" or "no." If "yes," enter the year of diagnosis of the corresponding solid tumor.

Other co-morbid condition: The "other, specify" category should be used to report co-morbid conditions that are of similar clinical concern as the other listed options. Chromosomal abnormalities, impairments and/or disorders associated with the primary disease should not be reported in this section, (e.g., Ph+ for CML/ALL recipients).

The physician performing the recipient's pre-HCT evaluation may use the HCT Co-Morbidity Index (HCT-CI) to document co-morbid conditions (see Appendix J).

Question 135: Was there a history of malignancy (hematologic or non-melanoma skin cancer) other than the primary disease for which this HCT is being performed?

The intent of this question is to identify other malignancies that may have an effect on the outcome of the HCT. A history of any benign tumor(s) should **not** be reported in this section. Malignancies reported in the previous solid tumor options should not be reported again here.

If the recipient is transplanted for a disease that has transformed from one disease to another, the original malignancy should **not** be reported in this section. Details regarding disease transformation will be captured on the Pre-TED Disease Classifiation form (Form 2402). For more information regarding disease combinations and transformations, refer to the Common Disease Combinations and Common Disease Transformations tables in the Primary Disease for HCT section of the Pre-TED Disease Classification Form (Form 2402).

Indicate if there was a history of malignancy other than the disease for which this HCT is being performed.

Question 136-155: Specify which malignancy(ies) occurred:

For each listed prior malignancy, check "yes" or "no." If "yes," enter the year of diagnosis of the corresponding malignancy.

Use questions 153-155 to report any prior hematologic malignancies that were not listed in questions

136-152. Solid tumors should be reported in questions 144-131, not in questions 153-155.

Last modified: 2019/12/13

Q156-316: Pre-HCT Preparative Regimen (Conditioning)

Question 156: Height at initiation of pre-HCT preparative regimen:

Report the recipient's height just prior to the start of the preparative regimen. The intent of this question is to determine the height used when calculating preparative regimen drug doses. This height is usually documented on the transplant orders (for radiation and/or systemic therapy) or admitting orders. Report height to the nearest whole centimeter or inch (round up if 0.5 or greater).

Even if the recipient does not receive a preparative regimen, the height is still required.

Question 157: Actual weight at initiation of pre-HCT preparative regimen:

Report the recipient's actual body weight just prior to the start of the preparative regimen. The intent of this question is to report the actual weight at the time the preparative regimen starts (which may be different than the weight used to determine preparative regimen doses). This weight is usually documented on the transplant orders (for radiation and/or systemic therapy) or admitting orders. Report weight to the nearest whole kilogram or pound (round up if 0.5 or greater). Do not report adjusted body weight, lean body weight, or ideal body weight.

Even if the recipient does not receive a preparative regimen, the weight is still required.

Question 158: Was a pre-HCT preparative regimen prescribed?

Recipients are generally transplanted under a specific protocol that defines the radiation and/or systemic therapy the recipient is intended to receive as a preparative regimen. This protocol, which may be either a research protocol or standard of care protocol, should be referred to when completing this section.

However, there are instances when a preparative regimen is not given. Examples may include, but are not limited to:

- Primary diagnosis of an immune deficiency.
- Subsequent allogeneic HCT due to loss of, or poor, neutrophil engraftment.

If a preparative regimen is prescribed per protocol, check "yes" and continue with question 159. If a preparative regimen is not prescribed, check "no" and continue with question 317.

For more information regarding the recipient's preparative regimen, consult a transplant physician or contact

your center's CIBMTR CRC.

Question 159: Classify the recipient's prescribed preparative regimen:

Myeloablative pre-transplant conditioning destroys bone marrow cells using high-dose radiation and/or systemic therapy. It is used to eliminate the recipient's immune system and to leave space in the bone marrow niche for the donated cells. A myeloablative regimen is sometimes used for recipients with non-malignant diseases who require HCT for marrow reconstitution (i.e., immunodeficiencies) or to produce a complete donor chimerism.

Non-myeloablative stem cell transplant (**NMA** or **NST**) and reduced-intensity conditioning (**RIC**) preparative regimens generally use lower doses of radiation and/or systemic therapy to prevent graft rejection and to suppress the recipient's hematopoietic immune system, but not eliminate it completely. Non-myeloablative protocols rely on the immune cells of the donor to destroy the disease (called graft versus tumor or GVT effect), and typically produces mixed chimerism. NST is a common treatment option for recipients who are older or who have other health problems, as the lower radiation and/or systemic therapy doses are easier for the recipient to tolerate.

In general, RIC includes any regimen that does not meet the criteria for either myeloablative or non-myeloablative regimens.

Based on the CIBMTR operational guidelines below, report if the regimen was myeloablative, reduced intensity, or non-myeloablative. The determination of whether the intent of the regimen was reduced intensity or non-myeloablative should be based either on the protocol at your center or the opinion of the physician overseeing the care of the recipient at your center. However, if there's a protocol utilized at your center that doesn't fall within CIBMTR operational guidelines for regimen intensity, you may report the regimen intensity based on the protocol intent.

Examples of Myeloablative, Reduced Intensity, and Non-Myeloablative Regimens

Myeloablative Regimens	Reduced Intensity and Non-Myeloablative Regimens
• TBI > 500 cGy (single) or > 800 cGy (fractionated) • Cyclophosphamide + TBI (> 500 cGy (single) or > 800 cGy (fractionated)) • Cyclophosphamide + Etoposide + TBI (> 500 cGy (single) or > 800 cGy (fractionated)) • Busulfan > 7.2 mg/kg IV or >9.0mg/kg orally • Busulfan >300 mg/m2 IV or >375 mg/m^2 orally • Busulfan (> 7.2 mg/kg IV or >9.0mg/kg orally) + Cyclophosphamide	• TBI ≤ 500 cGy (single) or ≤ 800 cGy (fractionated) • ATG + Cyclophosphamide • BEAM (Carmustine [BCNU], Etoposide, Cytarabine [Ara-C], Melphalan) • Busulfan ≤ 7.2 mg/kg IV or ≤ 9.0mg/kg orally • Busulfan ≤ 300 mg/m^2 IV or ≤ 375 mg/m^2 orally • Melphalan ≤ 150 mg/m^2 • Fludarabine + Cytarabine

• Busulfan (>7.2 mg/kg IV or >9.0 mg/kg orally) + Melphalan >150 mg/m^2 • Melphalan >150 mg/m^2 • Thiotepa ≥ 10 mg/kg • Treosulfan > 30,000 mg/m^2 or > 30 g/m^2	• Fludarabine + Cyclophosphamide • Fludarabine + TBI ≤ 500 cGy (single) or ≤ 800 cGy (fractionated) • Thiotepa < 10 mg/kg • Treosulfan ≤ 30,000 mg/m^2 or ≤ 30 g/m^2 • Etoposide + Cyclophosphamide

! These values represent the total prescribed doses. For example, if a recipient is scheduled to receive Melphalan 100 mg/m^2 for two days (200 mg/m^2), the regimen would be myeloablative because the total prescribed dose is > 150 mg/m^2.

Indicate whether the intent of the preparative regimen was “myeloablative” (to produce marrow ablation or pancytopenia), “non-myeloablative,” or “reduced intensity.”

Question 160: Date pre-HCT preparative regimen began (irradiation or drugs):

Enter the date the preparative regimen began. Use the earliest date from questions 161-167 (radiation) or 168-315 (chemotherapy). All dates reported in the preparative regimen section must be equal to or after the date reported for this question.

Question 161: Was irradiation planned as part of the pre-HCT preparative regimen?

If irradiation is planned as part of the preparative regimen, check “yes” and continue with question 162. If irradiation is not planned, check “no” and continue with question 169. Irradiation performed as previous treatment should not be reported in this section. Report irradiation performed as previous treatment on the appropriate Disease Specific Form.

Question 162: What was the prescribed radiation field?

Indicate if the planned irradiation was to “total body,” “total body by tomotherapy,” “total lymphoid or nodal regions,” or “thoracoabdominal region.”

Question 163: Total prescribed dose:

Enter the total dose of radiation prescribed. If radiation was prescribed as a single dose, the amount of radiation delivered in the single dose constitutes the total dose. If the radiation was prescribed in fractionated doses, multiply the dose per fraction by the total number of fractions to determine the total dose. Enter the total dose of radiation in either grays (Gy) or centigrays (cGy).

Example:

Radiation Order: TBI, 200 cGy/day for three days (3 doses)
Total dose: 200 cGy x 3 doses = 600 cGy
Report "Total Dose" as: 600 cGy

Question 164: Date started:

Enter the date the single dose or first fraction of radiation was administered.

Question 165: Was the radiation fractionated?

Radiation is either delivered as a single dose or in several treatments (fractions). Radiation is fractionated to increase the loss of diseased cells, as they do not recover as quickly as disease-free cells.

If the radiation was fractionated, check "yes" and continue with question 166. If the radiation was not fractionated, check "no" and continue with question 169.

Question 166: Prescribed dose per fraction:

Enter the prescribed dose per fraction in either grays (Gy) or centigrays (cGy).

The dose per fraction multiplied by the total number of fractions (question 168) must be equal to the total dose reported in question 163.

Question 167: Number of days:

Enter the total number of days radiation therapy was prescribed, including any days of rest between days when therapy was administered. The number of days radiation was administered can be greater than the number of fractions.

Example:
Radiation Order: TBI, 200 cGy/day every other day (Mon-Wed-Fri) x 3 doses
Total dose: 200 cGy x 3 doses = 600 cGy
Report "Number of days" as: 5

Question 168: Total number of fractions:

Enter the total number of fractions (treatments) of radiation that were administered. The recipient may receive more than one fraction per day (hyperfractionation).

The total number of fractions multiplied by the dose per fraction (question 166) must be equal to the total dose reported in question 163.

Questions 169-316: Drugs

Preparative Regimen – Drugs
The following questions report the **prescribed** drug therapy that was part of the preparative regimen. Do not report the dose that was actually given. If the recipient has comprehensive report forms due, the actual dose given will be reported on the Recipient Baseline Form (Form 2000). **Do not include drugs that are intended to offset the side effects of the chemotherapy** (e.g., corticosteroids for nausea, MESNA for hemorrhagic cystitis, etc.).

Drugs After Transplant
Occasionally, protocols list drugs that may be given before and after transplant. If the drugs are planned to be given before and after transplant, only the doses given before transplant should be quantified in the preparative regimen section. The doses given after transplant should be reported in the **Post-HCT Disease Therapy Planned as of Day 0** or **GVHD Prophylaxis** section. For example, if bortezomib or rituximab is planned to be given on Days -2, +1, +4, and +7, report the Day -2 dose in the preparative regimen section, and the post-transplant doses as planned post-HCT therapy.

ATG or alemtuzumab (Campath) given for GVHD prophylaxis planned prior to Day 0 should be reported in the preparative regimen section of the Pre-TED. If ATG, alemtuzumab or cyclophosphamide is planned after Day 0, it should be reported in the GVHD prophylaxis section (questions 317-343).

In this section, include any intrathecal drugs the recipient received for prophylaxis or treatment of CNS disease within 14 days prior to the start date of the preparative regimen.

The form lists each drug by the generic name. The form also lists some drugs by broad categories, with specific drugs listed individually. For example, *anthracycline* is listed as the broad drug category, followed by the specific drugs *daunorubicin*, *doxorubicin*, and *idarubicin*. The following website provides the trade names under which generic drugs are manufactured: http://www.rxlist.com/script/main/hp.asp.

Report the ***total* dose** of each drug as **prescribed** in the preparative regimen section of the HCT protocol. **Do not report the prescribed *daily* dose**. Drug doses must be reported in whole numbers. If the total dose includes a decimal, round to the nearest whole number. For paper submission, do not modify the number of boxes or include decimal values. The pharmacy record or Medication Administration Record (MAR) should be used for determining the date the drug was started.

Report the dose units as either “mg/m^2,” “mg/kg,” “target total AUC (µmol x min/L),” “mCi,” or “MBq.” If the total prescribed dose is reported in a unit other than those listed, convert the dose to the appropriate unit. See the example below or consult with a transplant pharmacist for the appropriate conversion. If drug doses

cannot be converted to the unit listed (e.g., Campath), leave the unit field blank, override the error (using "unable to answer"), and attach a copy of the source document to the Pre-TED using the attachment feature in FormsNet3.

Example: Calculating Total Drug Doses
Drug doses are calculated either by recipient weight in kilograms (kg) or recipient body surface area (BSA) in m^2. The HCT protocol will specify "x mg/kg" or "x mg/m^2" and the total number of doses to be administered.
For example, if the protocol requires cyclophosphamide at 60 mg/kg x 2 days (i.e., 2 doses), the "total prescribed dose" should be reported as "120 mg/kg."

Pharmacokinetic testing can be used to determine whether the drug concentration in the bloodstream is appropriate to the dose given. This reflects the speed of absorption and elimination of the drug. These tests are usually performed using the first dose of systemic therapy, or a test dose, where multiple samples are drawn at specific time points following the first dose. The samples are sent to a laboratory that performs the testing to determine the drug concentration. If carboplatin was prescribed, indicate if pharmacokinetic testing was performed to determine the preparative regimen dosing. If it is not known whether or not this testing was performed, consult a transplant physician.

A common example of this situation occurs in the use of busulfan. In some cases, a "test dose" of the drug is given before the actual preparative regimen is started, and this dose is used for acquiring drug levels that are used to adjust the dose that will be used in the preparative regimen. In other situations, the first dose of the drug is given in the usual fashion as part of the preparative regimen. After this first dose, serum drug levels are drawn and sent to a reference lab. The drug is continued at the starting dose until the lab results are reported and adjustment is made to later doses.

When a drug is used for the preparative regimen where pharmacokinetics will be tested, it is important to distinguish whether the testing will be done with a "test dose" before beginning the preparative regimen or using the first dose of the preparative regimen. The reporting of the dosing for the CIBMTR forms depends upon this distinction. This helps distinguish whether the dose is part of the therapeutic regimen, or not.

1. A test dose was given **> 24 hours** prior to the intended therapeutic dosing.
    - **Example:** A patient with AML underwent allogeneic HCT from a sibling; busulfan and cyclophosphamide were used as the preparative regimen. The patient presented to clinic 9 days before the HCT, where a dose of busulfan at 0.5 mg/kg was given intravenously. Blood samples were drawn for the next 6 hours, after which the patient left the clinic. His samples were sent to a lab, results were returned the next day, and an adjusted dose of busulfan was calculated. He returned to the hospital 6 days before HCT, and began to receive busulfan at the adjusted dose intravenously for 4 days, followed by cyclophosphamide, and proceeded to receive his cells.

Since he received 0.5 mg/kg as a “test dose,” this would not be reported in his total preparative regimen dose.

If a test dose was given, where the dose was distinct from the therapeutic dosing preparative regimen (often 1-2 or more days prior to the initiation of regular dosing), the following should be reported:

- On the Pre-TED (2400) form, the total prescribed dose per protocol would NOT include the test dose.
- On the Baseline (2000) form, the start date of the chemotherapy agent should be reported as the date the first therapeutic dose was administered. The actual dose received would NOT include the test dose.

2. The first dose of therapeutic dosing is used for monitoring.
    - **Example:** A patient with MDS received an allogeneic HCT from an unrelated donor; busulfan and fludarabine were used as the preparative regimen. She was admitted to the hospital 7 days before her HCT, and received a dose of busulfan at 0.8 mg/kg IV at 6:00 AM. Serum samples were drawn every 30 minutes until the next dose of Busulfan at 0.8 mg/kg IV was given at 12:00 noon. Her blood was sent to a reference lab, and she continued to receive busulfan every 6 hours. On day -6, the lab called with her drug levels, and it was determined that the current dose was correct. No adjustment was made, and she completed all 16 doses of busulfan. Since the dose of busulfan (0.8 mg/kg) that was used for drug testing was ALSO her first dose of the preparative regimen, it should be included in the amount of drug that was given for preparative regimen. The total prescribed dose per protocol should be reported as “13 mg/kg.” (0.8 mg/kg x 16 doses = 12.8 mg/kg rounded to 13 mg/kg).

      If the first dose of the preparative regimen was used to determine pharmacokinetics, the following should be reported:

      - On the Pre-TED (2400) form, the total prescribed dose per protocol would include the dose used for monitoring.
      - On the Baseline (2000) form, the start date of the chemotherapy agent should be reported as the date the first dose was administered. The actual dose received would include the dose used for monitoring.

Test doses must be reported consistently at your center. Since most centers follow a consistent approach to pharmacokinetic testing, it should be straightforward for the center to adopt a consistent approach to the reporting of test doses.

The “other, specify” category should be used only if the drug is not one of the listed options. If more than one “other” drug is prescribed, list the name of the drugs in the space provided **and** attach a copy of the source document using the attachment feature in FormsNet3. Do not report additional sites of radiation (e.g., cranial boost) in the “other” drug category. If the recipient is assigned to the Comprehensive Report Forms by the form selection algorithm, the additional sites of radiation will be reported on the Recipient

Baseline Form (Form 2000). If the recipient is assigned to TED Forms by the form selection algorithm, the additional sites of radiation will not be reported.

If the Pre-TED is being completed for a subsequent HCT, do not report therapy that was given to treat the recipient's disease (between the previous and current planned HCTs) in the preparative regimen section.

If there is a change to the chemotherapy preparative regimen (e.g., from busulfan + fludarabine to melphalan + fludarabine) after the Form 2400 has been submitted, an error correction must be completed in FormsNet to update the chemotherapy regimen given.

Last modified: 2018/05/07

Q317-343: GVHD Prophylaxis

! The following GVHD prophylaxis questions are to be completed for allogeneic HCTs only. Autologous and syngeneic HCTs continue with question 344.

✻ If it was planned that ATG or Campath were to be given for GVHD prophylaxis prior to Day 0, this should be reported in the preparative regimen section of the Pre-TED (questions 169-316). If it was planned that ATG, Campath, or cyclophosphamide were to be given after Day 0, this should be reported in the GVHD prophylaxis section (questions 317-343).

Question 317: Was GVHD prophylaxis planned/given?

After allogeneic HCT, specific immunosuppressive therapy may be administered to prevent GVHD or to immunosuppress the host marrow, thereby promoting engraftment of the donor stem cells. Most transplant centers have specific GVHD prophylaxis protocols and graft rejection protocols. **Planned** agents a recipient received as a result of these protocols should be included in this section.

If GVHD prophylaxis was planned per protocol, check “yes” and continue with question 318. If GVHD prophylaxis was not planned per protocol, check “no” and continue with question 344.

Questions 318-343: Specify:

The prophylactic drug options listed on the form are intended to be administered in a **systemic or oral form**. If the recipient received one of the listed drugs in a topical form, report the drug in the “other, specify” category.

If doses ALG, ALS, ATG, or ATS are planned to be given after infusion, report the total planned post-infusion dose (in mg / kg) in question 319. Do not include any doses administered prior to infusion.

The Pre-TED Form lists the generic chemotherapy drug names. The following website provides the trade names under which generic drugs are manufactured: http://www.rxlist.com/script/main/hp.asp

If GVHD prophylaxis is used for a syngeneic (monozygotic or identical twin) or autologous HCT, attach a copy of the source document using the attachment feature in FormsNet3.

Last modified: 2017/01/31

Q344: Other Toxicity Modifying Regimen

The following other toxicity modifying regimen question is optional for non-U.S. centers.

Question 344: Was KGF (palifermin, Kepivance) started or is there a plan to use it?

Check “yes” if KGF was started or planned. Check “no” if KGF was not started or planned.

Check “masked trial” if the recipient is part of a KGF study where the agent the recipient received is not known (e.g., placebo, drug, or other agent). Use the error correction process to update the data field once the trial is over and the agent the recipient was given is known.

Last modified: 2017/01/31

Q345-357: Post-HCT Disease Therapy Planned as of Day 0

Question 345: Is this HCT part of a planned multiple (sequential) graft/HCT protocol?

If the current HCT is part of a planned multiple graft/HCT protocol, check “yes.” The HCT for which the form is being completed could be for any of the transplants within the planned multiple graft/HCT protocol. The word “planned” **should not** be interpreted as: *if the recipient relapses, then the “plan” is to perform a subsequent HCT*. If this HCT is not part of a planned multiple graft/HCT protocol, check “no.”

Question 346: Is additional post-HCT therapy planned?

If additional post-HCT therapy is planned according to the protocol or standard of care, check “yes” even if the recipient does not receive the planned therapy. The word “planned” **should not** be interpreted as: *if the recipient relapses, then the “plan” is to treat with additional therapy*. If additional post-HCT therapy is not planned per protocol, check “no” and submit the form.

✻ The following post-HCT planned therapy questions are optional for non-U.S. centers.

Questions 347-357: Additional post-HCT planned therapy

Indicate if the options listed on the form are intended to be part of the post-HCT planned therapy according to the protocol or standard of care. Report other planned therapies in the “other, specify” category.

Last modified: 2017/01/31