CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Instructions for Pre-Transplant Essential Data (Pre-TED) Form (Version 2)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Pre-Transplant Essential Data (Pre-TED) Form (Version 2).

Effective December 3, 2007, the Pre- and Post-TED forms replaced the former Pre-Registration (Pre-Reg), Transplant Essential Data (TED), Modified TED (M-TED) and TED Follow-up (TEDFU) registration forms.

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: CIBMTRFormsManualComments@nmdp.org. Comments will be considered for future manual updates and revisions. For questions that require an immediate response, please contact your transplant center's CIBMTR liaison.

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Abbreviations

The following abbreviations are used throughout the Pre- and Post-TED forms. These abbreviations are also listed on page two of the Pre-TED paper form. For a glossary of abbreviations and common terms used throughout the manual, see Appendices A and B.

YYYY = 4-digit year
MM = 2-digit month
DD = 2-digit day
AHOP = Adult, Hematology, Oncology or Pediatric Unit
ALLO = Allogeneic
ANC = Absolute Neutrophil Count
AUTO = Autologous
BM = Bone Marrow
BMT-CTN = Blood & Marrow Transplant Clinical Trials Network
CIBMTR = Center for International Blood & Marrow Transplant Research
CIC = Center Identification Code
CMV = Cytomegalovirus
CR = Complete Remission
DCI = Donor Cellular Infusion
DLI = Donor Lymphocyte Infusion
EBMT = European Group for Blood & Marrow Transplantation
EBV = Epstein Barr Virus
FACT = Foundation for the Accreditation of Cellular Therapy
FGF = Fibroblast Growth Factor (e.g., velafermin)
FISH = Fluorescent In-situ Hybridization
GVHD = Graft versus Host Disease
HSCT = Hematopoietic Stem Cell Transplant
KGF = Keratinocyte Growth Factor (e.g., palifermin, Kepivance)
NMDP = National Marrow Donor Program
NOS = Not Otherwise Specified
NST = Non-myeloablative Stem Cell Transplant
PBSC = Peripheral Blood Stem Cells
PTLD = Posttransplant Lymphoproliferative Disorder
RBC = Red Blood Cell
RCI-BMT = Resource for Clinical Investigations in Blood & Marrow Transplant
RIC = Reduced Intensity Conditioning
SCTOD = Stem Cell Therapeutic Outcomes Database
TBI, TLI, TNI = Total (Body, Lymphoid, Nodal) Irradiation
U = Unclassifiable
UCB = Umbilical Cord Blood
Unit = Adult, Hematology, Oncology, Pediatric (AHOP)
VOD = Veno-occlusive Disease

Pre-Transplant Essential Data (Pre-TED)

All transplant centers participating in the CIBMTR must submit a Pre-TED Form for each recipient receiving a first allogeneic (related or unrelated) HSCT. 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.

Transplant centers are encouraged to submit a Pre-TED for recipients receiving an autologous HSCT. Although data regarding recipients receiving autologous HSCT 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. For more information regarding data reporting for autologous HSCT, see General Instructions, Autologous Hematopoietic Stem Cell Transplant.

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 HSCT (day 0), and is past due if not received by that date.

Helpful Hint:
In order to avoid having to make changes to HSCT date, complete the data for the Pre-TED (in FormsNet2™ or on paper), but do not submit the form until the first dose of the preparative regimen is given.

For recipients receiving a subsequent HSCT:

- *TED only* centers must submit a Pre-TED for all subsequent HSCTs.
- *Comprehensive Report Form* centers must submit a Pre-TED only for recipients assigned to TED forms by the form selection algorithm. For recipients assigned to Comprehensive Report Forms by the form selection algorithm, centers will not submit another Pre-TED, but will instead submit a Recipient Baseline Form (Form 2000).

For all subsequent HSCTs, 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 General Instructions, Center Type and Data Collection Forms.

For recipients of multiple transplants (and who are assigned to the TED forms), transplant centers are not granted access to the current Pre-TED form in FormsNet2™ until the Post-TED from the previous transplant has been completed.

Transplant centers can use the FormsNet2™ application to determine if a Recipient Baseline Form (Form 2000) 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.

Key Fields

Accuracy of the Key Fields is essential for ensuring that:

- Data are being reported for the correct recipient.
- Transplant centers have access to their data.
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other approved agency.

For instructions regarding the completion of the Key Fields, see Appendix K. Key Fields include all fields listed in the *Center Identification* and *Recipient Identification* boxes.

CIBMTR USE ONLY

This box appears only on the paper version of the form and is intended for CIBMTR use only. This box does not appear in the FormsNet2™ application.

Do not write in this box.

Disease Classification

NOTE: Disease Classification

The newest version of the TED forms uses the World Health Organization (**WHO**) disease classifications. Each corresponding Disease Classification Sheet in the disease specific section at the end of the form contains all of the established WHO disease types and subtypes. Therefore, the "other, specify" category should only be used if the recipient's disease is not one of the listed options. For more information regarding disease classification, consult with a transplant physician, contact your center's CIBMTR liaison, or visit the WHO website at: http://www.who.int/classifications/icd/en/.

If the indication for HSCT is due to a combination of diseases or a transformation of one disease to another, multiple Disease Classification Sheets may be required. Tables 1 and 2 list common examples of disease combinations and transformations with the Disease Classification Sheets required.

Table 1. Common Disease Combinations

Disease Combinations	Report primary disease as:	Report disease diagnosis date of:	Required disease classification sheet(s)
FAN or SAA and AML	AML	AML	Anemia/Hemoglobinopathy and AML
FAN or SAA and MDS	MDS	MDS	Anemia/Hemoglobinopathy and MDS
MYE and AMY	MYE	MYE	Plasma Cell Disorders

Table 2. Common Disease Transformations

Disease Transformation	Report primary disease as:	Report disease diagnosis date of:	Required disease classification sheet(s)
MDS or MPS to AML	AML	AML	AML and MDS/MPS
NHL to another NHL	Second NHL diagnosis	First NHL diagnosis	Lymphoma
CLL to NHL (i.e., Richter's Syndrome)	NHL	CLL	Other Leukemias and Lymphoma

AML, acute myelogenous leukemia; AMY, amyloidosis; CLL, chronic lymphocytic leukemia; FAN, Fanconi anemia; MDS, myelodysplastic syndrome; MPS, myeloproliferative syndrome/disease; MYE, myelodysplasia; NHL, Non-Hodgkin's lymphoma; SAA, severe aplastic anemia.

NOTE:
Question numbers correspond to the FormsNet2™ application

Question 1: Indicate the broad disease for which the HSCT is performed (see question 177)
From the list provided, select the primary disease for which the recipient is receiving the HSCT.

Question 2: Date of diagnosis of primary disease for HSCT
The date of diagnosis is important because the interval between diagnosis and HSCT is often a significant indicator for the recipient's prognosis post-HSCT.

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center, and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.

If the exact pathological diagnosis date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

If this is a subsequent HSCT for a new malignancy (or other new indication), report the date of diagnosis of the new malignancy and complete the appropriate Disease Classification Sheet. If the recipient is assigned to the TED forms by the forms selection

algorithm, the diagnosis date and current status of the previous diagnosis will be reported on the Post-TED.

Hematopoietic Stem Cell Transplant (HSCT)

Question 3: Date of this HSCT
Report the intended start date of the HSCT. If the infusion is planned to last several days, enter the **first** day the infusion is scheduled to start.

If the Pre-TED has been submitted prior to day 0, and the planned infusion date has changed, the original planned date of the HSCT will automatically be reported in FormsNet2™ on either the Post-TED or the 100 Days Post-HSCT Data Form (Form 2100). The Pre-TED should be changed using the paper Error Correction Form process. This will change the transplant date for the subsequent form(s).

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

Question 4: Chronological number of this HSCT
An HSCT is defined as an infusion of mobilized peripheral blood stem cells (PBSC), bone marrow, or cord blood. For recipients who have received a previous HSCT (prior to the HSCT for which this series of forms is being completed), the following are examples of how to calculate the chronological number of this HSCT.

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 HSCT, as opposed to three HSCTs and should be counted as *HSCT #1*.

After receiving the infusion, the recipient has relapse of disease. The recipient is scheduled to receive a subsequent HSCT. This HSCT should be reported as *HSCT #2*.

Example 2:
A recipient previously received a HSCT (*HSCT #1*). Then, because of delayed neutrophil recovery, the recipient received additional mobilized cells (i.e., "boost"). Report the boost as *HSCT #2*.

After receiving the boost, the recipient has relapse of disease. The recipient is scheduled to receive a subsequent HSCT. The subsequent HSCT should be reported as *HSCT #3*.

Autologous rescue **should not** be counted as a separate HSCT. Autologous rescue is generally used to treat the recipient's poor graft response rather than disease.

Report the chronological number of this HSCT. If ">1," continue with question 5. If this is the recipient's first HSCT, continue with question 11.

See Appendix O for additional information regarding distinguishing infusion types.

Question 5: If >1, most recent previous HSCT
Reporting the recipient's last HSCT enables the CIBMTR to appropriately account for recipient survival status in the database.

Report the date of the recipient's **last** autologous or allogeneic (related or unrelated) HSCT prior to the one being reported. Although the CIBMTR requests either a Pre-TED and/or Recipient Baseline Form (Form 2000) for each HSCT, there may be circumstances where a prior HSCT was not reported (e.g., prior autologous HSCT).

Question 6: Type
Report the stem cell source of the recipient's **last** HSCT as either autologous or allogeneic.

Questions 7-10: Institution where previous HSCT was performed if different from current
These data are used to identify and link the recipient's existence in the database and, if necessary, to obtain data from the previous transplant center.

Report the name, city, state, and country of the institution where the recipient's **last** HSCT was performed.

NOTE: Questions 11-16
FormsNet2™ application: Check either "yes" or "no" for each option listed.
Paper form submission: Check all that apply.

Questions 11-16: Cell source for this HSCT
More than one cell source or a combination of cellular therapies may be infused in the same HSCT procedure. Select all the cell sources planned for use in the **current** HSCT.

If "other" is chosen, specify the cell source type in question 16.

For more information regarding multiple cell type infusions that occur over a short period of time (e.g., several infusions with different cell sources occurring in less than two weeks), contact your center's CIBMTR liaison.

Question 17: Autologous HSCT?
Indicate if this HSCT is autologous (self-donation). If "yes," continue with question 18. If "no," continue with question 19.

Question 18: Specify number of products
A series of collections should be considered a single product when they are all from the same donor and use the same collection method and technique (and mobilization, if applicable), even if the collections are performed on different days.

Report the number of products used for this autologous HSCT.

Question 19: Multiple donors?
Indicate if multiple donor types, or if multiple cord blood units from different donors are to be used for this HSCT. If "yes," continue with question 20. If "no," continue with question 21.

Question 20: Specify number of donors
Report the number of donors used for this HSCT.

NOTE: Questions 21-28, reporting more than one donor
FormsNet2™ application: Complete questions 21-28 for each donor.
Paper form submission: Copy questions 21-28 and complete for each donor. Check the box on the paper form to indicate additional pages are attached.

Questions 21-22: Allogeneic HSCT donor gender
Indicate the allogeneic donor's biological gender (sex) as "male" or "female."

Question 23: Donor Type
If the product for this HSCT is from an allogeneic donor, indicate the donor type.

- **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.
  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).
  Does not include: Adoptive parents/children or stepparents/children who are HLA matched.

If the donor is a syngeneic, HLA-identical sibling, or HLA-matched other relative, continue with question 29.

- **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).

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

If the donor is an HLA-mismatched relative, continue with question 24.

- **Unrelated donor:**
  Includes: Donor who shares no known ancestry with the recipient, and is usually found through an unrelated donor registry. Include adoptive parents/children or stepparents/children here.

  If the donor is an unrelated donor, continue with question 25.

Question 24: Degree of mismatch
If the donor is an HLA-mismatched relative, indicate the degree of mismatch as either, "1 HLA antigen mismatch" or, "≥ 2 HLA antigen mismatch (full haploidentical)." Haploidentical means that one half of the HLA type matches the recipient. This type of HLA mismatch is common between blood-related parents and children.

Question 25: Registry or UCB Bank
For unrelated donors, specify the registry used to obtain the adult donor or umbilical cord blood unit. The code for NMDP donors is USA1. The code for NMDP cord blood units is U1CB. The Bone Marrow Donors Worldwide (**BMDW**) codes have been adopted to avoid submitting the entire name and address of the donor registry.

A Donor found through DKMS should use the registry code of the registry that facilitated the HSCT.

If the registry code cannot be determined using the BMDW website, continue to question 26.

NOTE: Question 25

FormsNet2™ 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.**
http://www.bmdw.org/index.php?id=addresses_members&no_cache=1

Example: Registry name: Against Leukemia Foundation Marrow Donor Registry
Match codes: Poland-ALF MDR [PL3]
Report on Pre-TED: PL3

Question 26: 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. This option should rarely be used.

NOTE: Reporting HLA mismatches on the Pre-TED forms

The Pre-TED currently requires that HLA mismatches are reported for unrelated products at the HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 loci. Validation within the FormsNet3™ data entry system requires that data fields for each locus at the antigenic (2 digits) and allelic (4 digits) be completed. Please review the updated instructions below for guidance in reporting HLA mismatches.

In order to interpret HLA typing results, start at a locus such as HLA-A*. Find the "*" and look at the numbers going to the right. The first two digits are the antigen family. If the digits 1 and 2 match, then move to digits 3 and 4 (and sometimes digit 5). The 3rd, 4th, and occasional 5th digits are at the allelic level.

If the numbers between the donor and the recipient don't match within digits 1 and/or 2, the number of mismatches should be reported in the antigen section. If the numbers between the donor the recipient match within the digits 1 and 2, but not digits 3 and/or 4 (or 5, if applicable), the number of mismatches should be reported in the allele section. However, The HLA typing may contain an "allele string" (e.g., HLA-A*02:01/02/03/04) or an "allele code" (e.g., HLA-A*02:RV), making it impossible to match the product and the donor at the allelic level (4 digits). If there is an allele code after digits 1 and 2, then the match/mismatch should be reported at the antigenic level.

Report mismatches at each loci using the level (antigenic or allelic) where matching is possible. For example, high-resolution DNA typing is available for the recipient, but only intermediate-resolution DNA typing is available for the product and the HLA typing contains an allele code at the A and B loci. In this case, the antigenic level (2 digits) should be completed for the number of mismatches at A and B and the allelic level should be reported as "ND = not done" for those loci.

If matching is possible at the allelic level, the antigenic level should be reported as "ND = not done." Only one result per locus should be reported (antigenic or allelic), and the remaining field should be reported as "ND = not done." Please see the examples below, where each example approximates a different style of HLA report (these examples are not comprehensive and style varies significantly between laboratories):

Example 1.

HLA Results

Relation	Hap	A*	B*	C*	DRB1*	DRB3*	DRB4*	DRB5*	DQB1*
Patient	a	**01:01**	**52:01**	**12:02**	**15:02**	NEG	NEG	POS	**06:BVAH**
	c	**01:01**	**52:01**	**12:02**	**15:02**				**06:BVAH**
Unrelated Donor		**01:BUYK**	**52:FWM**	**12:02**	**15:02**	NEG	NEG	POS	**06:BVAH**

Reporting on the Pre-TED form:

HLA Antigenic (2 digits):		**HLA Allelic (4 digits):**	
HLA-A locus:	0 = matched[1, 6]	HLA-A locus:	ND = not done
HLA-B locus:	0 = matched[1, 6]	HLA-B locus:	ND = not done
HLA-C locus:	ND = not done[2, 6]	HLA-C locus:	0 = matched
HLA-DRB1 locus:	ND = not done[2, 6]	HLA-DRB1 locus:	0 = matched
HLA-DQB1 locus:	0 = matched[1, 6]	HLA-DQB1 locus:	ND = not done
HLA-DPB1 locus:	ND = not done[3, 6]	HLA-DPB1 locus:	ND = not done

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Example 2.

HLA Results (red added for emphasis)

Relation	A	B	Cw	DRB1[4]	DQB1
Patient	***30:01**	***07:02**	***04:01**	***11:02**	***03:19**
	***30:02**	***35:01**	***15:05**	***03:19**	***06:09**
Donor	***30:01**	***07:06**	***04:01**	***15:03**	***03:19**
	***74:01**	***35:01**	***15:05**	***11:02**	***06:02**

Reporting on the Pre-TED form:

HLA Antigenic (2 digits):		**HLA Allelic (4 digits):**	
HLA-A locus:	1 = mismatch	HLA-A locus:	ND = not done[5]
HLA-B locus:	ND = not done[2]	HLA-B locus:	1 = mismatch
HLA-C locus:	ND = not done[2]	HLA-C locus:	0 = matched
HLA-DRB1 locus:	1 = mismatch	HLA-DRB1 locus:	ND = not done[5]
HLA-DQB1 locus:	ND = not done[2]	HLA-DQB1 locus:	1 = mismatch
HLA-DPB1 locus:	ND = not done[3]	HLA-DPB1 locus:	ND = not done

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Example 3.
HLA Results

HLA-	Patient	Donor
A*	01:01/01N, 26:01	01:01/01N, 26:01
B*	08:01, 58:01	08:01, 58:01
Cw*	03:02, 07:01/06/18	03:02, 07:01/06/18
DRB1*	03:01, 03:01/68	03:01, 03:01/68
DQB1*	02:01, 02:01	02:01, 02:01

Reporting on the Pre-TED form:

HLA Antigenic (2 digits):		**HLA Allelic (4 digits):**	
HLA-A locus:	0 = matched[1]	HLA-A locus:	ND = not done
HLA-B locus:	ND = not done[2]	HLA-B locus:	0 = matched
HLA-C locus:	0 = matched[1]	HLA-C locus:	ND = not done
HLA-DRB1 locus:	0 = matched[1]	HLA-DRB1 locus:	ND = not done
HLA-DQB1 locus:	ND = not done[2]	HLA-DQB1 locus:	0 = matched
HLA-DPB1 locus:	ND = not done[3]	HLA-DPB1 locus:	ND = not done

Example 4.
HLA Results

	A	A	B	B	C	C	DRB1	DRB1	DQB1	DQB1
Patient	*24:xx		*07:xx	*44:03	*16:01	*07:02/*0703/*0710	*13:01	*15:01	*06:02	*06:03
Donor	*24:xx	*29:xx	*44:03	*07:xx	*07:xx	*16:01	*13:01	*15:01	*06:02	*06:03

Reporting on the Pre-TED form:

HLA Antigenic (2 digits):		**HLA Allelic (4 digits):**	
HLA-A locus:	1 = mismatch[6]	HLA-A locus:	ND = not done
HLA-B locus:	0 = matched[1]	HLA-B locus:	ND = not done
HLA-C locus:	0 = matched[1]	HLA-C locus:	ND = not done
HLA-DRB1 locus:	ND = not done[2]	HLA-DRB1 locus:	0 = matched
HLA-DQB1 locus:	ND = not done[2]	HLA-DQB1 locus:	0 = matched
HLA-DPB1 locus:	ND = not done[3]	HLA-DPB1 locus:	ND = not done

[1]The loci could not be matched at the allelic level due to the allele string or code in the reported HLA typing. Allele strings or allele codes represent the "lowest resolution" at which matching is possible.

[2]Counting antigenic mismatches is possible with the available HLA data, but counting allelic level mismatches provides more specific information. In cases where counting allelic level mismatches is possible, antigenic level mismatches should be reported as "ND = not done."

[3]DPB1* was not tested for the recipient and/or donor.

[4]The"first" patient DRB1 result matches the "second" donor DRB1 result, while the remaining patient and donor at DRB1 results do not match. This is a single mismatch at the antigenic level for the HLA-DRB1 locus.

[5] The mismatch is present at the antigenic level (2 digits), even though allelic level typing was performed. Since a mismatch is reported at the antigenic level, the allelic level should be reported as "ND = not done."

[6] A blank typing is considered a duplicate of the result that was reported.

Question 27: Complete number of mismatches: Antigenic (2 digits)
For unrelated donors, if HLA testing was serologic or low-resolution DNA typing, or intermediate-resolution DNA Typing, indicate the number of mismatches for each locus (Note: A full match equals "0" mismatches). For assistance with HLA typing and terminology, consult a specialist within your institution, or contact your center's CIBMTR CRC.

Question 28: Complete number of mismatches: Allelic (4 digits)
For unrelated donors, if the HLA testing was allele level typing, indicate the number of mismatches for each locus (Note: A full match equals "0" mismatches). For assistance with HLA typing and terminology, consult a specialist within your institution, or contact your center's CIBMTR CRC.

Question 29: Was there *Ex Vivo Graft Manipulation* other than for red blood cell (RBC) removal or volume reduction?
Ex vivo refers to *outside the body*. Do not report treatments given to the recipient with the intent of affecting the graft.

Cryopreservation or product thaw should not be reported as product manipulation.

If the graft was manipulated ex vivo **other than for RBC removal or volume reduction**, check "yes" and continue with questions 30-37.

If the graft was only manipulated to reduce the volume of the product (to reduce the use of DMSO or cryopreservation) or to remove RBCs (for ABO incompatibility, to prevent hemolysis), check "no" and continue with question 38.

NOTE: Questions 30-37
FormsNet2™ application: Check either "yes" or "no" for each option listed.
Paper form submission: Check all that apply.

Question 30: T-cell depletion
This method of negative selection manipulation is most commonly used for allogeneic HSCT, as it removes some or all of the T-cells to minimize GVHD. The removed T-cells may be infused at a later date (i.e., DLI). Methods of T-cell depletion may include the use of antibodies. For more detail regarding methods of T-cell depletion, see the HSCT Infusion Form (INF Form 2006).

Question 31: Tumor purging
This type of negative selection manipulation removes malignant cells from the collected product. This method is only used for autologous HSCT.

Questions 32-33: Other negative selection
Negative selection refers to removing a specific cell population prior to infusion. If a negative selection method of cell manipulation was used (other than T-cell depletion or tumor purging), check "yes" and specify the method in the space provided.

Question 34: CD34 selection
This manipulation method is also known as "positive selection." This method collects stem cells that have a CD34+ marker on the surface cell, and is commonly done with a CliniMACS/CliniMax or Isolex machine.

Question 35: ex vivo expansion
Using a positive selection manipulation technique, CD34+ cells are selected for ex vivo expansion to increase the quantity of hematopoietic stem cells between collection and infusion. The most common method of ex vivo expansion uses hematopoietic growth factors. Ex vivo expansion is most commonly used with cord blood transplants.

Questions 36-37: Other, specify
If a positive selection method of cell manipulation was used (other than CD34+ selection or ex vivo expansion), check "yes" and specify the method in the space provided.

Questions 38-39: Performance Score pre-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-HSCT 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.

The Karnofsky Scale is designed for recipients aged 16 years and older, and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients less than 16 years old.

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 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.

Questions 40-41: CMV-antibodies (IgG or Total)
Report the cytomegalovirus (CMV) status of the recipient—and for allogeneic HSCTs, the donor—immediately prior to the start of the preparative regimen. For the purposes of this manual, the term "immediately prior" represents the **pre-HSCT 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-HSCT 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.

A large portion of the population has been exposed to CMV. Following acute infection in the tissues, CMV remains dormant. Primary infection or reactivation of CMV can lead to significant infections and substantial complications for transplant recipients. Prior exposure to CMV, and therefore potential for reactivation, is generally tested during the

pre-transplant recipient and donor evaluation. It is estimated that 50%-90% of adults test positive for CMV antibody, but are asymptomatic.

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, the laboratory value must be compared to the reported standards for reactive or non-reactive at the center. Use the "unknown" option only if the test has been completed, but the test results are inconclusive or not known. Selecting the "unknown" option may require a future data query. Use the "not done" option only if CMV status was not evaluated prior to the start of the preparative regimen **or** if the laboratory reports CMV testing by PCR (DNA detection). CMV testing by PCR is used to detect the presence of the CMV virus and does not test for prior exposure.

If the allogeneic donor product was a cord blood unit, "non-reactive" should be reported for the donor CMV status. If the cord blood unit test results are reactive, it's due to transplacental maternal antibodies and do not need to be reported as "reactive."

If multiple donors are used for this HSCT, report *any* positive result as reactive.

Preparative Regimen

Question 42: Was a preparative regimen given?
Recipients are generally transplanted under a specific protocol that defines the radiation and/or chemotherapy 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 may not be given. Examples may include, but are not limited to:

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

If a preparative regimen is prescribed per protocol, check "yes" and continue with questions 43-122. If a preparative regimen is not planned, check "no" and continue with question 123.

For more information regarding the recipient's preparative regimen, consult with a transplant physician or contact your center's CIBMTR liaison.

NOTE: Questions 43-115
FormsNet2™ application: Check either "yes" or "no" for each option listed.
Paper form submission: Check all that apply.

Preparative Regimen: Radiation
The following questions refer to **prescribed** radiation therapy. Do not report the radiation dose that was actually given. If the recipient is assigned to the Comprehensive Report Forms by the forms selection algorithm, then the actual dose given will be reported on the Recipient Baseline Form (Form 2000).

Question 43: Total Body Irradiation (TBI)
If TBI is prescribed per protocol, check "yes" and continue with question 44. Check "yes" even if certain fields (vital organs) will be blocked or shielded from radiation. If TBI is not prescribed per protocol, check "no" and continue with question 45.

Question 44: TBI – Total Prescribed Dose
Enter the total dose of radiation as prescribed per protocol. If radiation is prescribed as a single dose, the amount of radiation delivered in the single dose constitutes the total dose. If the radiation is prescribed in fractionated doses, multiply the total number of fractions by the dose per fraction to determine the total dose. For example, if the protocol prescribes 200 cGy of radiation given over three days, the total dose is 600 cGy. Enter the total dose of radiation in either grays (Gy) or centigrays (cGy).

Question 45: TLI, TNI, or TAI
If Total Lymphoid Irradiation (**TLI**), Total Nodal Irradiation (**TNI**), or Total Abdominal Irradiation (**TAI**) is prescribed per protocol, check "yes" and continue with question 46. If TLI, TNI, or TAI is not prescribed per protocol, check "no" and continue with question 47.

Question 46: TLI, TNI, or TAI – Total Prescribed Dose
Enter the total dose of radiation as prescribed per protocol. If radiation is prescribed as a single dose, the amount of radiation delivered in the single dose constitutes the total dose. If the radiation is prescribed in fractionated doses, multiply the total number of fractions by the dose per fraction to determine the total dose. For example, if the protocol prescribes 200 cGy of radiation given over three days, the total dose is 600 cGy. Enter the total dose of radiation in either grays (Gy) or centigrays (cGy).

NOTE: Preparative Regimen: Drugs
The following questions refer to **prescribed** drug therapy as 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.).

ATG and Campath given for GVHD prophylaxis planned prior to Day 0 should be reported in the preparative regimen section of the Pre-TED. If ATG and Campath are

planned after Day 0, it should be reported in the GVHD prophylaxis section (questions 145-162).

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 of *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.

Questions 47-115: Drugs

Report the ***total* dose** of each drug as **prescribed** in the preparative regimen section of the HSCT 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.

Report the dose units as either "mg/m^2" or "mg/kg." If the total prescribed dose is reported in a unit other than mg/m^2 or mg/kg, 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 into either mg/m^2 or mg/kg (e.g., Campath, pediatric doses of busulfan), leave the unit field blank and attach a copy of the source document to the Pre-TED using the Log of Appended Documents (Form 2800).

Example: Calculating Drug Doses

Drug doses are calculated either by recipient weight in kilograms (kg) or recipient body surface area (BSA) in m^2. The HSCT protocol will specify "x mg/kg" or "x mg/m2" and the total number of doses to be administered.

For example, if the protocol requires Cyclophosphamide, 60 mg/kg x 2 days (i.e., 2 doses), the "total prescribed dose" should be reported as "120 mg/kg."

Some drugs used as part of the preparative regimen are administered with guidance of serum pharmacokinetic testing to determine the recipient's metabolism of the drug. This allows for "customization" of the drug dosing to the individual to optimize the desired effect and minimize the toxicity.

Busulfan represents a common example of this situation. In some cases, the first dose of the drug is given in the usual fashion as part of the preparative regimen. After the first dose, blood is drawn and sent to a reference lab to determine serum drug levels. Once the lab results are reported, the drug is continued with adjustment of later doses. In other situations, 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.

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 using the first dose of the preparative regimen or if the drug will be given as a "test dose" distinct from the beginning of the preparative regimen. The reporting of the "total prescribed dose" for the Pre-TED depends upon this distinction.

1. The first dose of therapeutic dosing is used for monitoring.
   - **Example:** Patient with MDS is scheduled to receive an allogeneic HSCT from an unrelated donor using Busulfan and Fludarabine preparative regimen. Busulfan is prescribed 0.8 mg/kg every 6 hours over 4 days, total of 16 doses. The protocol states that serum samples will be drawn after the first dose every 30 minutes until the second dose is administered to determine if adjustment to the dosing is needed. The total prescribed dose per protocol should be reported as "13 mg/kg." If the recipient is assigned to the Comprehensive Report Forms by the forms selection algorithm, then the actual dose given will be reported on the Recipient Baseline Form (Form 2000).

2. The test dose is given **≥ 24 hours** prior to the intended therapeutic dosing.
   - **Example:** Patient with AML is scheduled to receive an allogeneic HSCT from sibling using Busulfan and Cyclophosphamide preparative regimen. The patient presents to clinic 9 days before the HSCT, where a dose of Busulfan at 0.5 mg/kg is given intravenously. Blood samples are drawn for the next 6 hours, after which the patient leaves the clinic. The patient's samples are sent to a lab, results are returned the next day and an adjusted dose of Busulfan is calculated to be used for the preparative regimen of 1.0 mg/kg every 6 hours over 4 days, total of 16 doses. The total prescribed dose per protocol should be reported as "16 mg/kg." In this scenario, the "test dose" is not included in the "prescribed total dose."

The "other, specify" category should only be used 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 to the Pre-TED using the Log of Appended Documents (Form 2800).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 HSCT, do not report therapy that was given to treat the recipient's disease (between the previous and current planned HSCTs) in the preparative regimen section.

If there is a change to the chemotherapy preparative regimen (e.g., from Busulfan + Fludarabine to Melphalan + Fludarabine) after form 2400 has been submitted, an error correction must be completed to update the chemotherapy regimen given.

Question 116: Is the intent of the preparative regimen myeloablative (allo only)?
The purpose of a myeloablative HSCT is to destroy malignant cells using high-dose chemotherapy and/or radiation therapy. A myeloablative regimen may also be used for recipients with a non-malignant disease requiring a stem cell transplant for marrow reconstitution (i.e., immunodeficiencies) or to produce a complete donor chimerism.

In contrast, a non-myeloablative (**NST**) or reduced-intensity (**RIC**) preparative regimen generally uses lower doses of chemotherapy and/or radiation therapy to prevent graft rejection and to suppress the recipient's hematopoietic immune system without eliminating it completely. A NST relies on the immune cells of the donor to destroy the disease (called graft versus tumor, or GVT), and typically produces a mixed chimerism. NST is a common treatment option for recipients who are older or who have other health problems, as the lower chemotherapy and/or radiation doses are better tolerated.

Currently, there are no published definitions of the difference between NST and RIC preparative regimens. However, in general, a RIC includes any regimen not meeting the criteria for either myeloablative or NST regimens.

Examples of myeloablative preparative regimens:
- busulfan (16 mg/kg) and cyclophosphamide (120 mg/kg)
- cyclophosphamide (120 mg/kg) and TBI (12 Gy)

Examples of non-myeloablative preparative regimens:
- 2 Gy TBI
- fludarabine (180 mg/m2) and cyclophosphamide (120 mg/kg)
- TLI (8 Gy) and ATG (8 mg/kg)

Centers must attribute the intent of the regimen based on the standards at their center. Generally speaking, the attribution should be based on the protocol or on the opinion of the physician overseeing the care of the recipient at your center.

If the intent of the preparative regimen is myeloablative (resulting in marrow ablation or pancytopenia by destroying blood-producing cells in the bone marrow), check "yes" and continue with question 123.

If the preparative regimen is intended to be NST or RIC, check "no" and continue with question 117.

NOTE: Questions 117-122
FormsNet2™ application: Check either "yes" or "no" for each option listed.
Paper form submission: Check all that apply.

Questions 117-122: Reason for NST/RIC
Indicate the reason or reasons a non-myeloablative or reduced-intensity preparative regimen was prescribed.

Co-Morbid Conditions

NOTE: Questions 123-144
The following co-morbid condition questions are optional for non-U.S. centers.

Question 123: Is there a history of mechanical ventilation?
A history of mechanical ventilation may impact the recipient's pulmonary function post-HSCT. 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 a 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 the following:

- 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 HSCT event (excluding mechanical ventilation during surgery) check "yes." If the recipient does not have a history of mechanical ventilation, check "no."

Question 124: 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 positive node **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 HSCT, check "yes." If the recipient has not had a history of a proven invasive fungal infection, check "no." For both primary and subsequent HSCT, report any documented invasive fungal infections in the recipient's medical history.

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 pneumocytosis.

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

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

NOTE: Questions 125-144
Prior to answering question 125, review the list of co-existing disease(s) and/or organ impairments listed under questions 126-144.

Question 125: Were there *clinically significant* co-existing disease or organ impairment at the time of patient assessment prior to preparative regimen?
Report "yes" to question 125 if the recipient has a documented history and/or current diagnosis of any of the following:

Documented Medical History	Question Number
Arrhythmia	126
Cardiac[a]	127
Cerebrovascular disease	128
Heart valve disease[b]	130
Inflammatory bowel disease	134
Peptic ulcer	136
Rheumatologic	141
Solid tumor, prior [c]	142
Current diagnosis at the time of pre-HSCT evaluation	**Question Number**
Diabetes	129
Hepatic, mild	131
Hepatic, moderate/severe	132
Infection	133
Obesity	135
Psychiatric disturbance	137
Pulmonary, moderate	138

Pulmonary, severe	139
Renal, moderate/severe[d]	140
Other (specify)	143 (144)

[a] Ejection fraction (EF) ≤ 50% should be reported only if present at the time of the pre-HSCT evaluation
[b] Excluding mitral valve prolapse
[c] Excluding nonmelanoma skin cancer
[d] Including Renal transplantation at any time in the patient's history

The intent of this question is to identify serious pre-existing conditions that may have an effect on the outcome of the HSCT. For the purposes of this manual, the term "clinically significant" refers to conditions that are being treated at the time of pre-HSCT evaluation, or that have affected the recipient's medical history and may cause complications post-HSCT. 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 HSCT should not be reported.

Additionally, for the purposes of this manual, the term "at the time of patient assessment" is defined as the pre-HSCT evaluation period, prior to the start of the preparative regimen. If the HSCT is ***allogeneic***, and the recipient does not have a documented history of clinically significant disease(s) or organ impairment(s), check "no" and continue with question 145.

If the HSCT is ***autologous***, and the recipient does not have a documented history of clinically significant disease(s) or organ impairments, check "no" and continue with question 163.

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

Questions 126-144: Co-existing diseases or organ impairments
For each listed co-existing disease or organ impairment, check "yes," "no," or "not done."

Pulmonary (moderate or severe) coexisting disease/impairments should be measured using the *corrected* DLCO (e.g., DLCOc, DLCOcorr, DLCO(Hb)) values.

The "other, specify" category should be used to report co-morbid conditions that are of similar clinical concern as the other listed options. For example, if a recipient has a current or prior history of malignancy other than the disease for which the HSCT is being performed, report this malignancy in the "other, specify" field. This would include diseases such as a prior leukemia or lymphoma. Any history of a malignant solid tumor should be reported as "solid tumor, prior." For assistance with reporting co-morbid conditions, consult with a transplant physician.

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

GVHD Prophylaxis (allogeneic only)

Questions 145: Was GVHD prophylaxis planned/given?
Following an allogeneic HSCT, specific immunosuppressive therapy may be administered to prevent GVHD or to immunosuppress the host marrow, thereby promoting engraftment of the donor stem cells. Most transplant centers have specific GVHD prophylaxis protocols and graft rejection protocols. Any **planned** agent a recipient is scheduled to receive as a result of these protocols should be included in this section.

If GVHD prophylaxis is planned per protocol, check "yes" and continue with question 146. If GVHD prophylaxis is not planned per protocol, check "no" and continue with question 163.

NOTE: Questions 146-162
FormsNet2™ application: Check either "yes" or "no" for each option listed.
Paper form submission: Check all that apply.

Questions 146-162: GVHD prophylaxis drugs
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.

Do not report T-cell depletion of the graft source or drugs administered after the onset of GVHD.

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 HSCT, fax or e-mail an explanation to your center's CIBMTR liaison and request it be scanned as part of the form documentation.

Post-HSCT Disease Therapy Planned as of Day 0

Question 163: Is this HSCT part of a planned multiple (sequential) graft/HSCT protocol?
If, at the time of the current HSCT, a second (tandem transplant) or subsequent HSCT is planned according to the protocol, check "yes" even if the recipient does not receive

the planned second HSCT. The word "planned" **should not** be interpreted as: *if the recipient relapses, then the "plan" is to perform a subsequent HSCT*. If this HSCT is not part of a planned multiple graft/HSCT protocol, check "no."

Questions 164: Is additional post-HSCT therapy planned?
If additional post-HSCT 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-HSCT therapy is not planned per protocol, check "no" and continue with question 175.

NOTE: Questions 165-174
FormsNet2™ application: Check either "yes" or "no" for each option listed.
Paper form submission: Check all that apply.

Questions 165-174: Additional post-HSCT planned therapy (optional for non-US centers)
Indicate if the options listed on the form are intended to be part of the post-HSCT planned therapy according to the protocol or standard of care. Report other planned therapies in the "other, specify" category.

Other Toxicity Modifying Regimen

Questions 175-176 are optional for non-US centers.

Question 175: 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.

Question 176: Was FGF (velafermin) started or is there a plan to use it?
Check "yes" if FGF was started or planned. Check "no" if FGF was not started or planned.

Check "masked trial" if the recipient is part of an FGF 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 given to the recipient is known.

Pre-TED Disease Classification Sheet

NOTE: Disease Classification Sheet

The newest version of the TED forms uses the World Health Organization (**WHO**) disease classifications. Each Disease Classification Sheet contains all of the established WHO disease types and subtypes. The "other, specify" category should **only** be used if the recipient's disease is not one of the listed options. For more information regarding disease classification, consult a transplant physician, contact your center's CIBMTR liaison, or visit the WHO website at: http://www.who.int/classifications/icd/en/.

Several of the Disease Classification Sheets ask for ***"Status at Transplantation."*** Although there are many interpretations of disease response criteria**, when reporting data to the CIBMTR, use the guidelines in this manual to determine disease status**. A majority of the disease response criteria are established by an international working group. Citations of resources used to define disease responses are included where applicable.

If the recipient's status is unclear, consult with the transplant physician for further information or contact your center's CIBMTR liaison.

NOTE: Malignant vs. Non-malignant

Malignant diseases involve cells dividing without control that can spread to other parts of the body through blood and lymph systems. These diseases are usually characterized by unlimited, aggressive growth, invasion of surrounding tissues, and metastasis.

Non-malignant diseases involve cell overgrowth, but lack the malignant properties of cancer.

Question 177: Indicate the primary disease for which the HSCT was performed

Using the appropriate Disease Classification Sheet, select the detailed disease classification within the broad disease group for which this HSCT was performed.

If the indication for HSCT is due to a combination of diseases or a transformation of one disease to another, multiple Disease Classification Sheets may be required. For examples of common disease combinations and transformations, see Tables 1 and 2.

Helpful Hint:
The CIBMTR database disease codes are represented in parentheses after the disease subtype on the Disease Classification Sheet and can be helpful in mapping diagnosis [e.g., Myeloid Sarcoma (295)], and determining if the disease is malignant or non-malignant. Disease codes (10-299) indicate a malignant disease, with the exception of Paroxysmal Nocturnal Hemoglobinuria (PNH) (56). A disease code of (300) or above indicates a non-malignant disease, with the exception of disease code (900), which could indicate either a malignant or non-malignant disease.

Leukemias

Acute Myelogenous Leukemia (AML) or Acute Nonlymphocytic Leukemia (ANLL)

Question 178: Select most specific WHO classification for AML
Indicate the disease classification at diagnosis; the older FAB classifications are shown in brackets, e.g., {M0}.

Question 179: Did AML transform from MDS or MPS?
AML often evolves from MDS or MPS. This transformation is typically distinguished by the percentage of blasts in the bone marrow.

AML that transforms from MDS or MPS has a lower survival prognosis because of the association with unfavorable cytogenetic abnormalities.

AML can also evolve from Juvenile Myelomonocytic Leukemia (JMML). JMML is a rare form of chronic leukemia that affects young children, usually before the age of five. JMML results from DNA mutations in cells called monocytes. Normal monocytes attack invading microorganisms and assist lymphocytes in carrying out immune functions. Abnormal monocytes, or JMML cells, accumulate in the bone marrow and interfere with the production of normal white blood cells, red blood cells, and platelets.

If AML transformed from MDS or MPS (including JMML), check “yes” and complete **both the AML and MDS/MPS** Disease Classification Sheets (questions 222-234). If AML did not transform from MDS or MPS, check “no.”
If MDS is suspected, but not confirmed by documented laboratory or pathologic findings, or if there is documentation of MDS **concurrent** with AML, check “no.”

Question 180: Was AML therapy related?
Agents such as radiation or systemic therapy used to treat other diseases (e.g., Hodgkin’s lymphoma, Non-Hodgkin’s lymphoma, or breast cancer) can damage the marrow and lead to a secondary malignancy, such as AML. If the diagnosis of AML is therapy-related, check “yes” and continue with question 181. If the diagnosis of AML is

not therapy related, check “no” and continue with question 184. If it is not known whether the AML diagnosis is therapy related, check “unknown” and continue with question 230.

Do not answer this question “yes” if the recipient developed AML after an environmental exposure (e.g., exposure to benzene).

NOTE: Questions 181-183
FormsNet2™ application: Check either “yes” or “no” for each option listed.
Paper form submission: Check all that apply.

Questions 181-183: AML, therapy related
Indicate the therapy associated with the diagnosis of AML.

Question 184: Was imatinib mesylate given for pre-transplant therapy any time prior to start of preparative regimen?
Imatinib mesylate is also known as Gleevec, Glivec, STI-571, or CGP57148B. Indicate “yes,” “no,” or “unknown.”

Question 185: Status at Transplantation
Indicate the disease status of AML immediately prior to the start of the preparative regimen.

Disease Status	Definition
Never Treated	The recipient was diagnosed with acute myelogenous leukemia and never treated. For example, MDS was initially diagnosed and treated, the MDS then transformed into AML, and a decision was made to proceed immediately to transplant instead of treating the AML with therapy.
Primary Induction Failure (PIF)	The recipient was treated for acute leukemia, **but never achieved complete remission (CR)** with any therapy.
Complete Remission (CR)* *If yes, also complete questions 186-188*	A treatment response where **all** of the following criteria are met for at least four weeks:** • < 5% blasts in the bone marrow • Normal maturation of all cellular components in the bone marrow (myeloid, erythroid, and megakaryocytic lineages) • No blasts with Auer rods (AML only) • No extramedullary disease (e.g., central nervous system or

	soft tissue involvement) • ANC of > 1,000/µL • Platelets ≥ 100,000/µL • Transfusion independent **Exception: There may not be a four-week interval between the completion of treatment for disease and the disease assessment immediately prior to the HSCT. If this is the case, CR should still be reported as the status at transplantation as it represents the "best assessment" prior to HSCT. The pre-HSCT disease status ***should not be changed*** based on early relapse or disease assessment ***post-HSCT*****.** Report recipient as being in CR at the time of transplant no matter how many courses of therapy it may have taken to achieve that CR. Recipients who meet all the criteria of CR, but who have persistent cytogenetic and/or molecular abnormalities, should be reported as being in CR. The cytogenetic and/or molecular abnormalities should be reported in the appropriate section (see questions 186-187). Do not include recipients with extramedullary disease. They should be considered to have persistent disease, or to be in relapse. **NOTE: Recipients with MDS that transformed to AML** If the recipient has residual MDS following treatment for AML, report the AML disease status as either PIF or relapse (i.e., the recipient cannot be in an AML CR if there is evidence of MDS at the time of assessment).
Relapse *If yes, also complete question 189.*	Recurrence of disease after CR. Relapse is defined as: • > 5% blasts in the marrow • Extramedullary disease • Reappearance of cytogenetic abnormalities and/or molecular markers associated with the diagnosis at levels that, as determined by a physician, represent relapse.

**Sources of disease response definitions:*
1) www.uptodate.com
2) http://www.cancer.gov/
3) www.jco.ascopubs.org Cheson 21(24):4642-4649.

FOR HEMATOLOGIC CR
Hematologic CR includes all the criteria listed for CR above. Indicate in questions 186-187 if the response also qualified as a cytogenetic or molecular remission.

Question 186: Cytogenetic remission
Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormalities that reflect the recipient's disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

Cytogenetic remission is a treatment response where **both** of the following criteria are met:

- The karyotype reverts to normal, and
- There are no clonal chromosomal abnormalities detected in the blood and/or marrow.

If cytogenetic abnormalities associated with the recipient's disease were identified previously, but the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If cytogenetic abnormalities associated with the recipient's disease were identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No cytogenetic assessments were performed.
- Cytogenetic abnormalities associated with the recipient's disease were identified previously and no cytogenetic assessment was performed prior to the start of the preparative regimen.
- Cytogenetic abnormalities associated with the recipient's disease were not identified on previous testing and no cytogenetic abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

Question 187: Molecular remission
Molecular assessment involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection, and can indicate known genetic abnormalities. RFLP testing (with PCR amplification) is an example of a molecular testing method.

Molecular remission is a treatment response in which no minimal residual disease in the blood and/or marrow can be detected by molecular methods (e.g., PCR).

If molecular abnormalities associated with the recipient's disease were identified previously, but the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If molecular abnormalities associated with the recipient's disease were identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No molecular assessments were performed.
- Molecular abnormalities associated with the recipient's disease were identified previously and no molecular assessment was performed prior to the start of the preparative regimen.
- Molecular abnormalities associated with the recipient's disease were not identified on previous testing and no molecular abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

Question 188: Number
Indicate the number of this hematologic CR.

FOR RELAPSE

Question 189: Number
Indicate the number of this relapse using the following guidelines:

1st relapse: one prior complete remission

2nd relapse: two prior complete remissions

3rd or higher: three or more complete remissions followed by relapse

Do not include a partial response (PR) when calculating the number of relapses. Recipients who achieve a PR to treatment should be reported as either PIF (if never in CR previously) or relapse. PR in AML is generally of short duration and unlikely to predict clinical benefit.

Acute Lymphoblastic Leukemia (ALL)

Question 190: Specify (disease classification)
Indicate the disease classification at diagnosis; the older FAB classifications are shown in brackets, e.g., {L2}.

Due to the aggressive nature of Precursor T- and Precursor B-cell lymphoblastic lymphoma (or lymphoma/leukemia), the primary disease reported for recipients with these malignancies should be acute lymphoblastic leukemia (Precursor T-cell ALL or Precursor B-cell ALL).

The current WHO disease classification for ALL is divided between precursor B-cell and precursor T-cell. If cytogenetic abnormalities present at diagnosis are among the other options listed on the Pre-TED form, check the sub-type rather than precursor B-cell ALL option.

Question 191: Was imatinib mesylate given for pre-transplant therapy any time prior to start of prep regimen?
Imatinib mesylate is also known as Gleevec, Glivec, STI-571, or CGP57148B. Indicate "yes," "no," or "unknown."

Questions 192-196: Status at Transplantation
Indicate the disease status of ALL immediately prior to the start of the preparative regimen.

Disease Status	Definition
Never Treated	The recipient was diagnosed with acute lymphoblastic leukemia and never treated.
Primary Induction Failure (PIF)	The recipient was treated for acute lymphoblastic leukemia, **but never achieved CR** with any therapy. PIF is not limited to the number of treatments used unsuccessfully. This status only applies to recipients who have **never** been in CR.
Complete Remission (CR)* *If yes, also complete questions 193-195*	A treatment response where **all** of the following criteria are met for at least four weeks:** • < 5% blasts in the bone marrow • Normal maturation of all cellular components in the bone marrow (myeloid, erythroid, and megakaryocytic lineages) • No extramedullary disease (e.g., central nervous system or soft tissue involvement) • ANC of > 1,000/µL • Platelets ≥ 100,000/µL • Transfusion independent **In some cases, there may not be a four-week interval between the completion of treatment for disease and the disease assessment immediately prior to the HSCT. If this is the case, CR should still be reported as the status at transplantation. Although this is an exception to the general condition that CR is "durable" beyond four weeks, the status of CR represents the "best assessment" prior to HSCT. **The pre-HSCT disease status should not be changed based on early relapse or disease**

	assessment post-HSCT. Report that the recipient is in CR at the time of transplant no matter how many courses of therapy it may have taken to achieve that CR. Include recipients with persistent cytogenetic and/or molecular abnormalities who otherwise meet all the criteria of CR. The cytogenetic and/or molecular abnormalities should be reported in the appropriate section (see questions 193-194). Do not include recipients with extramedullary disease. They should be considered to have persistent disease, or to be in relapse.
Relapse *If yes, also complete question 196*	Recurrence of disease after CR. Relapse is defined as: • > 5% blasts in the marrow • Extramedullary disease • Reappearance of cytogenetic abnormalities and/or molecular markers associated with diagnosis at levels that, as determined by a physician, represent relapse.

**Sources of disease response definitions:*
1) www.uptodate.com
2) http://www.cancer.gov/
3) www.jco.ascopubs.org Cheson 21(24):4642-4649.

FOR HEMATOLOGIC CR

Questions 193-195: For hematologic CR

Hematologic CR includes all the criteria listed for CR above. For recipients who achieve a hematologic CR, indicate in questions 193-195 if the response also qualified as a cytogenetic or molecular remission.

Question 193: Cytogenetic remission

Cytogenetic assessment involves testing blood or bone marrow for the presence of known cytogenetic abnormalities that reflect the recipient's disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

Cytogenetic remission is a treatment response where **both** of the following criteria are met:

- The karyotype reverts to normal, and
- There are no clonal chromosomal abnormalities detected in the blood and/or marrow.

If cytogenetic abnormalities associated with the recipient's disease were identified previously and the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If cytogenetic abnormalities associated with the recipient's disease were identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No cytogenetic assessments were performed.
- Cytogenetic abnormalities associated with the recipient's disease were identified previously, but no cytogenetic assessment was performed prior to the start of the preparative regimen.
- Cytogenetic abnormalities associated with the recipient's disease were not identified on previous testing and no cytogenetic abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

Question 194: Molecular remission

Molecular assessment involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection, and can indicate known genetic abnormalities. RFLP testing (with PCR amplification) is an example of a molecular testing method.

Molecular remission is a treatment response in which no minimal residual disease in the blood and/or marrow can be detected by molecular methods (e.g., PCR).

If molecular abnormalities associated with the recipient's disease were identified previously and the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If molecular abnormalities associated with the recipient's disease were identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No molecular assessments were performed.
- Molecular abnormalities associated with the recipient's disease were identified previously and no molecular assessment was performed prior to the start of the preparative regimen.
- Molecular abnormalities associated with the recipient's disease were not identified on previous testing and no molecular abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

Question 195: Number
Indicate the number of this hematologic CR.

FOR RELAPSE

Question 196: Number
Indicate the number of this relapse using the following guidelines:

1st relapse: one prior complete remission

2nd relapse: two prior complete remissions

3rd or higher: three or more complete remissions followed by relapse

Do not include a partial response (PR) when calculating the number of relapses. Recipients who achieve a PR to treatment should be reported as either PIF (if never in CR previously) or relapse.

Other Acute Leukemia

Questions 197-198: Specify (disease classification)
Indicate the disease classification at diagnosis. The "other, specify" category should only be used if the recipient's disease is not one of the listed options.

- Acute undifferentiated leukemia is a type of AML characterized by immature predominating cells that cannot be classified.
- Biphenotypic, bilineage, or hybrid leukemias have characteristics representative of both myeloid and lymphoid lineages.
- Mast cell leukemia is characterized by an increased number of tissue mast cells in the peripheral blood.

Question 199: Was imatinib mesylate given for pre-transplant therapy any time prior to start of prep regimen?
Imatinib mesylate is also known as Gleevec, Glivec, STI-571, or CGP57148B. Indicate "yes," "no," or "unknown."

Questions 200-204: Status at Transplantation
Indicate the disease status immediately prior to the start of the preparative regimen.

Disease Status	Definition*
Never Treated	The recipient was diagnosed with acute leukemia and never treated.
Primary Induction Failure (PIF)	The recipient was treated for acute leukemia, **but never achieved CR** with any therapy. PIF is not limited to the

	number of treatments used unsuccessfully. This status only applies to recipients who have **never** been in CR.
Complete Remission (CR) *If yes, also complete questions 201-203*	A treatment response where **all** of the following criteria are met for at least four weeks:** • < 5% blasts in the bone marrow • Normal maturation of all cellular components in the bone marrow (myeloid, erythroid, and megakaryocytic lineages) • No extramedullary disease (e.g., central nervous system or soft tissue involvement) • ANC of > 1,000/µL • Platelets ≥ 100,000/µL • Transfusion independent **In some cases, there may not be a four-week interval between the completion of treatment for disease and the disease assessment immediately prior to the HSCT. If this is the case, CR should still be reported as the status at transplantation. Although this is an exception to the general condition that CR is "durable" beyond four weeks, the status of CR represents the "best assessment" prior to HSCT. **The pre-HSCT disease status should not be changed based on early relapse or disease assessment post-HSCT.** Report that the recipient is in CR at the time of transplant no matter how many courses of therapy it may have taken to achieve that CR. Include recipients with persistent cytogenetic and/or molecular abnormalities who otherwise meet all the criteria of CR. The cytogenetic and/or molecular abnormalities should be reported in the appropriate section (see questions 201-202). Do not include recipients with extramedullary disease. They should be considered to have persistent disease, or to be in relapse.

Relapse *If yes, also complete question 204*	Recurrence of disease after CR. Relapse is defined as: • > 5% blasts in the marrow • Extramedullary disease • Reappearance of cytogenetic abnormalities and/or molecular markers associated with the diagnosis at levels that, as determined by a physician, represent relapse.

**Sources of disease response definitions:*
1) www.uptodate.com
2) http://www.cancer.gov/
3) www.jco.ascopubs.org Cheson 21(24):4642-4649.

FOR HEMATOLOGIC CR

Questions 201-203: For hematologic CR

Hematologic CR includes all the criteria listed for CR above. For recipients who achieve a hematologic CR, indicate in questions 193-195 if the response also qualified as a cytogenetic or molecular remission.

Question 201: Cytogenetic remission

Cytogenetic assessment involves testing blood or bone marrow for the presence of known cytogenetic abnormalities that reflect the recipient's disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

Cytogenetic remission is a treatment response where **both** of the following criteria are met:

- The karyotype reverts to normal, and
- There are no clonal chromosomal abnormalities detected in the blood and/or marrow.

If cytogenetic abnormalities associated with the recipient's disease were identified previously and the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If cytogenetic abnormalities associated with the recipient's disease were identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No cytogenetic assessments were performed.

- Cytogenetic abnormalities associated with the recipient's disease were identified previously and no cytogenetic assessment was performed prior to the start of the preparative regimen.
- Cytogenetic abnormalities associated with the recipient's disease were not identified on previous testing and no cytogenetic abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

Question 202: Molecular remission
Molecular assessment involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection, and can indicate known genetic abnormalities. RFLP testing (with PCR amplification) is an example of a molecular testing method.

Molecular remission is a treatment response in which no minimal residual disease in the blood and/or marrow can be detected by molecular methods (e.g., PCR).

If molecular abnormalities associated with the recipient's disease were identified previously and the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If molecular abnormalities associated with the recipient's disease were identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No molecular assessments were performed.
- Molecular abnormalities associated with the recipient's disease were identified previously and no molecular assessment was performed prior to the start of the preparative regimen.
- Molecular abnormalities associated with the recipient's disease were not identified on previous testing and no molecular abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

Question 203: Number
Indicate the number of this hematologic CR.

FOR RELAPSE

Question 204: Number
Indicate the number of this relapse using the following guidelines:

1st relapse: one prior complete remission

2nd relapse: two prior complete remissions

3rd or higher: three or more complete remissions followed by relapse

Do not include a partial response (PR) when calculating the number of relapses. Recipients who achieve a PR to treatment should be reported as either PIF (if never in CR previously) or relapse.

Chronic Myelogenous Leukemia (CML)

Question 205: Philadelphia chromosome+, Ph+, t(9;22)(q34;q11), or variant OR bcr/abl+
Indicate the disease classification at diagnosis. The WHO disease classification requirements state that a diagnosis of CML must include the following: Philadelphia chromosome, complex variation and/or variant form, or bcr/abl gene rearrangement (see table 3 below). Evidence of these chromosomal abnormalities may be found at any time between diagnosis and the start of the preparative regimen.

Report the combination that best describes the chromosomal abnormalities. If none of the listed abnormalities are identified, but CML is suspected, report under "Other Leukemias" and give "Atypical chronic myeloid leukemia" as the detailed disease classification (questions 235-237).

Table 3. CML Classification Requirements

Term	Definition
Philadelphia chromosome t(9;22)(q34;q11)	An exchange of genetic material between region q34 of chromosome 9 and region q11 of chromosome 22.
Complex variation	Translocation of three or more chromosomes, one of which must be chromosome 22 [e.g., t(3; 9; 22)].
Variant form	Any translocation involving 22q11, or 22.q11.2 in which CML is the suspected diagnosis [e.g., t(13; 22)(p3;q11)].

Question 206: Did recipient receive treatment prior to this HSCT?
If the recipient received therapy to treat CML prior to this HSCT, check "yes" and continue with question 207. If the recipient did **not** receive therapy to treat CML, check "no" and continue with question 215.

NOTE: Questions 207-214
FormsNet2™ application: Check either "yes" or "no" for each option listed.
Paper form submission: Check all that apply.

Questions 207-214: CML treatment
Indicate the therapy the recipient received to treat CML prior to this HSCT. If the recipient's treatment consisted of a combination of chemotherapeutic agents, check the "combination chemotherapy" box **and** each drug included in the combination from the list provided. The "other, specify" category should only be used if the drug is not one of the listed options. For example, if the recipient received a combination of interferon and cytarabine, check all of the following: "combination chemotherapy," "interferon," and "other, specify: cytarabine."

Questions 215-220: Status at Transplantation
Indicate the disease status of CML immediately prior to the start of the preparative regimen.

Disease Response: Phase	**Definition**
Hematologic Complete Remission (CR) *If yes, also complete questions 216-218 and 221*	A treatment response where **all** of the following criteria are met: • White blood count is < 10 x 10^9/L, without immature granulocytes and with < 5% basophils. • Platelet count < 450 x 10^9/L. • Non-palpable spleen.
Chronic Phase *If yes, also complete questions 219-221*	Characterized by relatively few blasts (<10%) present in the blood and bone marrow. Symptoms are often not present. The chronic phase may last several months to years depending on the recipient and the treatment received.
Accelerated Phase* *If yes, also complete question 221*	**One or more** of the following must be present: • 10%-19% blasts in blood or marrow • ≥ 20% basophils in peripheral blood • Clonal marrow cytogenetic abnormalities in addition to the single Philadelphia chromosome (clonal evolution) • Increasing spleen size, unresponsive to therapy • Increasing WBC, unresponsive to therapy • Thrombocytopenia (platelets < 100,000), unrelated to therapy • Thrombocytosis (platelets > 1,000,000), unresponsive to therapy

Blast Crisis *If yes, also complete question 221*	Characterized by ≥ 20% blasts (formerly ≥ 30%) in the peripheral blood or bone marrow. Having extramedullary blastic infiltrates (i.e., myeloid sarcoma, granulocytic sarcoma, or chloroma) also qualifies as blast phase. The red cell, platelet, and neutrophil counts may decrease, and episodes of infection and bleeding may result. Symptoms such as fatigue, shortness of breath, abdominal pain, bone pain, and spleen enlargement may occur. Blast crisis is similar to acute leukemia in its signs and its effects on the recipient, and can involve lymphoid or myeloid lineages (so-called lymphoid blast crisis or myeloid blast crisis).

FOR HEMATOLOGIC CR

NOTE:
Question 216 is not required for EBMT centers.

Question 216: CML disease status before treatment that achieved this CR
From the options listed below, indicate the disease status of CML immediately prior to the treatment that achieved this complete remission.

- **Chronic Phase:** Characterized by relatively few blasts (<10%) present in the blood and bone marrow. Symptoms are often not present. The chronic phase may last several months to years depending on the individual recipient and the treatment received.**Accelerated Phase: One or more** of the following must be present (WHO definition):
  - 10%-19% blasts in blood or marrow
  - ≥ 20% basophils in peripheral blood
  - Clonal cytogenetic abnormalities in addition to the single Philadelphia chromosome (clonal evolution)
  - Increasing spleen size, unresponsive to therapy
  - Increasing WBC, unresponsive to therapy
  - Thrombocytopenia (platelets < 100,000) unrelated to therapy
  - Thrombocytosis (platelets > 1,000,000) unresponsive to therapy
- **Blast Phase:** Characterized by ≥ 20% blasts (formerly ≥ 30%) in the peripheral blood or bone marrow. Having extramedullary blastic infiltrates (i.e., myeloid sarcoma, granulocytic sarcoma, or chloroma) also qualifies as blast phase. The red cell, platelet, and neutrophil counts may decrease, and episodes of infection and bleeding may result. Symptoms such as fatigue, shortness of breath, abdominal pain, bone pain, and spleen enlargement may occur. Blast crisis is similar to acute leukemia in its signs and its effects on the recipient, and can

involve lymphoid or myeloid lineages (so-called lymphoid blast crisis or myeloid blast crisis).

Questions 217-218: Indicate if the response also qualified as a cytogenetic or molecular remission.

Question 217: Cytogenetic remission
Cytogenetic response is determined by either conventional or FISH cytogenetics for the Philadelphia chromosome [t(9;22)].

Cytogenetic responses are divided into several categories:

- Complete: Ph+ 0%
- Partial: Ph+ 1%-35%
- Minor: Ph+ 36%-65%
- Minimal: Ph+ 66%-95%
- None: Ph+ >95%

If the recipient had a “complete” cytogenetic response at the last evaluation prior to the start of the preparative regimen, indicate “complete.”

If the recipient had a “partial,” “minor,” “minimal,” or “none” cytogenetic response at the last evaluation prior to the start of the preparative regimen, indicate “no.”

Indicate “unknown” if one of the following applies:

- No cytogenetic assessments were performed.
- The Philadelphia chromosome associated with the recipient’s disease was identified previously and no cytogenetic assessment was performed prior to the start of the preparative regimen.
- The Philadelphia chromosome associated with the recipient’s disease was not identified on previous testing and no cytogenetic abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

Question 218: Molecular remission
PCR testing reveals no molecular evidence of the BCR-ABL fusion gene in the blood (e.g., BCR-ABL transcript is non-detectable and non-quantifiable in an assay that has at least 4-5 log range of detection).

Molecular remission is a treatment response in which no minimal residual disease in the blood and/or marrow can be detected by molecular methods (e.g., PCR).

If the BCR-ABL fusion gene associated with the recipient's disease was identified previously and the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If the BCR-ABL fusion gene associated with the recipient's disease was identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No molecular assessments for the BCR-ABL fusion gene were performed.
- The BCR-ABL fusion gene associated with the recipient's disease was identified previously, but no molecular assessment was performed prior to the start of the preparative regimen
- The BCR-ABL fusion gene associated with the recipient's disease was not identified on previous testing and the BCR-ABL fusion gene was not identified at the last evaluation prior to the start of the preparative regimen.

FOR CHRONIC PHASE

Questions 219-220: Indicate if the response also qualified as a cytogenetic or molecular remission.

Question 219: Cytogenetic remission
Cytogenetic response is determined by either conventional or FISH cytogenetics for the Ph chromosome (t(9;22)).

Cytogenetic responses are divided into several categories:

- Complete: Ph+ 0%
- Partial: Ph+ 1%-35%
- Minor: Ph+ 36%-65%
- Minimal: Ph+ 66%-95%
- None: Ph+ >95%

If the recipient had a "complete" cytogenetic response at the last evaluation prior to the start of the preparative regimen, indicate "complete."

If the recipient had a "partial," "minor," "minimal," or "none" cytogenetic response at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No cytogenetic assessments were performed.

- The Philadelphia chromosome associated with the recipient's disease was identified previously and no cytogenetic assessment was performed prior to the start of the preparative regimen.
- The Philadelphia chromosome associated with the recipient's disease was not identified on previous testing and no cytogenetic abnormalities were identified at the last evaluation prior to the start of the preparative regimen.

Question 220: Molecular remission
PCR testing reveals no molecular evidence of the BCR-ABL fusion gene in the blood (e.g., BCR-ABL transcript is non-detectable and non-quantifiable in an assay that has at least 4-5 log range of detection).

If the BCR-ABL fusion gene associated with the recipient's disease was identified previously and the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If the BCR-ABL fusion gene associated with the recipient's disease was identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- No molecular assessments for the BCR-ABL fusion gene were performed.
- The BCR-ABL fusion gene associated with the recipient's disease was identified previously, but no molecular assessment was performed prior to the start of the preparative regimen
- The BCR-ABL fusion gene associated with the recipient's disease was not identified on previous testing and the BCR-ABL fusion gene was not identified at the last evaluation prior to the start of the preparative regimen.

Question 221: Status at Transplantation – Number
Indicate the number of the disease phase reported in question 215.

Myelodysplastic (MDS) or Myeloproliferative Diseases (MPS)

NOTE: MDS
If the recipient is being transplanted for AML that has transformed from MDS, the primary disease for HSCT must be reported as AML. Disease Classification Sheets must be completed for both AML and MDS.

MDS and MPS contain a range of disorders that may transform from one subtype to another during the course of the disease. Therefore, indicate the recipient's disease classification both at diagnosis and immediately prior to the start of the preparative regimen.

Question 222: Classification, specify at diagnosis
Indicate the recipient's disease classification at diagnosis.

Question 223: Status at transplantation
Indicate the recipient's disease classification immediately prior to the start of the preparative regimen.

If MDS or MPS transformed to AML, continue to question 224 **and** complete both the MDS and the AML Disease Classification Sheets.

Question 224: If AML, date of MDS diagnosis
If MDS or MPS transformed into AML between the initial diagnosis and the start of the preparative regimen, enter the MDS or MPS diagnosis date. (Report the AML diagnosis date in question 2.) Report the date of the first pathological diagnosis (e.g., bone marrow biopsy) of MDS/MPS. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.

NOTE:
Question 225 should only be answered if the recipient is being transplanted for a chronic myeloproliferative disease (**MPS**).

Question 225: Was Janus kinase 2 (JAK2) gene mutation positive?
The JAK2 pathway is responsible for activation of proteins that are involved in the development and function of the immune system, and that also play a role in maintaining immune tolerance and tumor surveillance. JAK2 disruption has been associated with a variety of myeloproliferative disorders due to resulting immunosuppression and enhanced tumor survival. If the JAK2 testing was positive at any time prior to the start of the preparative regimen, report "yes." If the JAK2 testing was negative, report "no." If JAK2 testing was not performed, report "not done."

Questions 226: Was MDS/MPS therapy related?
Agents such as radiation or systemic therapy used to treat other diseases (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, and breast cancer) can damage the marrow and lead to a secondary malignancy, such as MDS/MPS. If the diagnosis of MDS/MPS is therapy-related, check "yes" and continue with question 227. If the diagnosis of MDS/MPS is not therapy-related, check "no" and continue with question 230. If it is not known whether the MDS/MPS diagnosis is therapy-related, check "unknown" and continue with question 230.

Questions 227-229: MDS, therapy related
Indicate the therapy associated with the diagnosis of MDS/MPS.

MDS/MPS/Chronic Myelomonocytic Leukemia (CMML)

Questions 230-233: Status at Transplantation
Indicate the disease status of MDS/MPS/CMML immediately prior to the start of the preparative regimen.

NOTE:
MDS/MPS/CMML to AML transformation
If the recipient is being transplanted for AML that has transformed from MDS/MPS/CMML, the status at transplantation (questions 230-233) should be left blank. Override these errors in the FormsNet2™ application and complete the Disease Classification Sheet for AML.

Disease Status	Definition
Supportive care or treatment without chemotherapy	Examples of this status include but are not limited to: • Observation with periodic blood count tests (also known as "watch and wait") • Blood transfusions and iron chelation therapy • Administration of erythropoietin (EPO) and other blood cell growth factors • Therapy with antithymocyte globulin (ATG) • Immune modulation agents including thalidomide and lenalidomide
Treated with chemotherapy* *If yes, also complete questions 231-232*	Examples of this status include but are not limited to: • Low intensity chemotherapy including cytarabine, azacitidine (Vidaza®), and decitabine (Dacogen®) • High intensity chemotherapy that may include aggressive antileukemic therapy such as a combination of cytarabine and idarubicin
Relapsed after CR* *If yes, also complete questions 233*	A treatment response where **one or more** of the following criteria are met: • Return to pre-treatment bone marrow blast percentage • Decrease of ≥ 50% from maximum response

	levels in granulocytes or platelets • Transfusion dependence or hemoglobin level ≥ 1.5g/dL lower than prior to therapy

**Source of disease response definition: CIBMTR Pre-HSCT MDS/MPS Disease Form 2014*

FOR RECIPIENTS TREATED WITH CHEMOTHERAPY

Question 231: Status at Transplantation, specify
From the options listed below, indicate the recipient's disease status immediately prior to the start of the preparative regimen.

Disease Status	Definition
Complete Remission (CR) *If yes, also complete question 232.*	A treatment response where **all** of the following criteria are met and maintained for ≥ 4 weeks*: • Bone marrow evaluation: – < 5% myeloblasts with normal maturation of all cell lines • Peripheral blood evaluation: – hemoglobin ≥ 11 g/dL untransfused and without erythropoietin support – ANC ≥ 1000/mm^3 without myeloid growth factor support – platelets ≥ 100 x 10^9/L without thrombopoietic support – 0% blasts *If the timeframe between achieving CR and the start date of the HSCT (i.e., day 0) is less than four weeks, and the recipient is documented to be in CR, report the status at transplantation as CR. *Important: if within four weeks following transplant the recipient's status is determined to* ***not be CR***, an Error Correction Form must be submitted changing the pre-HSCT status.

Improvement, but no CR	A treatment response where **one or more** of the following criteria are met and maintained for ≥ 8 weeks without ongoing cytotoxic therapy: • Hematologic Improvement (HI)-E – Hemoglobin increase of ≥ 1.5 g/dL untransfused – For RBC transfusions performed for Hgb ≤ 9.0, reduction in RBC units transfused in 8 weeks by ≥ 4 units compared to the pre-treatment transfusion number in the previous 8 weeks
Improvement, but no CR (cont.)	• HI-P – For pre-treatment platelet count of > 20 x 10^9/L/L, platelet absolute increase of ≥ 30 x 10^9/L/L – For pre-treatment platelet count of < 20 x 10^9/L/L, platelet absolute increase of ≥ 20 x 10^9/L /L and ≥ 100% from pre-treatment level • HI-N – Neutrophil count increase of ≥ 100% from pre-treatment level and an absolute increase of ≥ 500/mm^3
NR – no response	A treatment response that does not meet the criteria for the "improvement, but not CR" category, and that has no evidence of disease progression.
Progressive/Worse	A treatment response where **one or more** of the following criteria are met in the absence of another explanation (e.g., infection, bleeding, ongoing chemotherapy, etc.): • ≥ 50% reduction from maximum response levels in granulocytes or platelets • Reduction in hemoglobin by ≥ 1.5 g/dL • Transfusion dependence

FOR CR

Question 232: Number
Indicate the number of this CR.

FOR RELAPSED FROM CR

Question 233: Number
Indicate the number of this relapse using the following guidelines:

1st relapse: one prior complete remission

2nd relapse: two prior complete remissions

3rd or higher: three or more complete remissions followed by relapse

Do not include PRs when calculating the number of relapses.

Juvenile Myelomonocytic Leukemia (JMML)

NOTE:
JMML to AML transformation
If the recipient is being transplanted for AML that has transformed from JMML, the status at transplantation (question 234) should be left blank. Override this error in the FormsNet2™ application and complete the Disease Classification Sheet for AML.

Question 234: Status at Transplantation
Indicate the recipient's disease status of JMML immediately prior to the start of the preparative regimen.

Disease Status	Definition
Continued Complete Response (CCR)*	Recipient achieved CR and has remained in CR. Continued absence of all known disease after achieving CR following a previous line of therapy.
Complete Response (CR)*	Characterized by normalization of WBC and organomegaly.
Partial Response (PR)*	≥ 50% reduction in WBC and/or organomegaly.
Minimal Response (MR)*	Requires **one or more** of the following: • 25%-50% reduction in WBC and organomegaly • Partial response in WBC but no change in

	organomegaly • Partial response in organomegaly but no change in WBC
Stable Disease (SD)*	≤ 25% reduction in WBC and/or organomegaly.
Progressive Disease (PD)*	Characterized by an increase in WBC and/or organomegaly.
Not Assessed*	No assessment of the recipient's disease has been done. This option should rarely be used.

**Source of disease response definition: CIBMTR Pre-HSCT JMML/JCML Disease Form 2015*

Other Leukemias

Questions 235-236: Classification
Indicate the disease classification at diagnosis. The "other, specify" category should only be used if the recipient's disease is not one of the listed options.

Question 237: Status at Transplantation
Each disease classification has different criteria for disease status. Use the disease-specific criteria listed in the tables below to determine the recipient's disease status immediately prior to the start of the preparative regimen.

- **Atypical CML** is a chronic myeloproliferative disorder that is similar to chronic myelogenous leukemia (**CML**). The criteria for atypical CML include, but are not limited to, lack of Philadelphia chromosome and bcr/abl or PDGFR-beta rearrangements; 10%-20% immature granulocytes; significant granulocytic dysplasia; < 2% basophils, and < 10% monocytes.

Disease Status	Definition
Never Treated	The recipient was diagnosed with atypical CML and never treated.

Complete Remission (CR)	**All** of the following criteria are met and maintained for ≥ 4 weeks: • Marrow with normal maturation of all cellular components • ≤ 5% blasts in the marrow • No signs or symptoms of the disease If the timeframe between achieving CR and the start date of the HSCT (i.e., day 0) is less than four weeks, and the recipient is believed to be in CR, report the status at transplantation as CR. *Important: if within four weeks following transplant the recipient's status is determined to **not be CR***, an Error Correction Form must be submitted to change the pre-HSCT status. Report that the recipient is in CR at the time of transplant no matter how many courses of therapy it may have taken to achieve that CR.
Complete Remission (CR) (cont.)	Include recipients with persistent cytogenetic abnormalities who otherwise meet all the criteria of CR. Do not include recipients with extramedullary disease. They should be considered to have persistent disease, or to be in relapse.
Nodular Partial Remission (nPR)	Not applicable for atypical CML.
Partial Remission (PR)	Not applicable for atypical CML.
No Response/Stable Disease (NR/SD)	The recipient was treated for atypical CML **but never achieved CR** with any therapy. PIF is not limited to the number of treatments used unsuccessfully. This status only applies to recipients who have **never** been in CR.
Progression	Not applicable for atypical CML.
Relapse (untreated)	Recurrence of disease after CR. Relapse is defined as:

	• > 5% blasts in the marrow • Extramedullary disease • Reappearance of cytogenetic abnormalities and/or molecular markers associated with the diagnosis at levels that, as determined by a physician, represent relapse.

- **CLL** is known as either chronic lymphocyctic leukemia or chronic lymphoblastic leukemia, and is characterized by an increased number of lymphoblasts in the blood and bone marrow.

Disease Status	Definition
Never Treated	The recipient was diagnosed with CLL and never treated.
Complete Remission (CR)*	Requires **all** the following: • No radiographic evidence of lymphadenopathy • No organomegaly • Neutrophils > 1.5 x 10^9/L • Platelets > 100 x 10^9/L • Hemoglobin >11g/dL • Lymphocytes < 4 x 10^9/L/L • Bone marrow < 30% lymphocytes • Absence of constitutional symptoms (e.g., fatigue, fevers, night sweats)
Nodular Partial Remission (nPR)*	Complete response with persistent lymphoid nodules in bone marrow.
Partial Remission (PR)*	Requires **all** of the following: • ≥ 50% decrease in peripheral blood lymphocyte count from pretreatment value • ≥ 50% reduction in lymphadenopathy if present pretreatment • ≥ 50% reduction in liver and spleen size if

	enlarged pretreatment **AND one or more** of the following: • Neutrophils ≥ $1.5x10^9$/L or 50% above baseline • Platelets > $100x10^9$/L or 50% improvement over baseline • Hemoglobin > 11.0 g/dL or 50% improvement over baseline
No Response/Stable Disease (NR/SD)*	No change. Not complete response, partial response, or progressive disease.
Progression*	Requires **one or more** of the following: • ≥ 50% increase in the sum of the products of ≥ 2 lymph nodes (≥ 1 node must be ≥ 2 cm) or new nodes • ≥ 50% increase in liver or spleen size, or new hepatomegaly or splenomegaly • ≥ 50% increase in absolute lymphocyte count to ≥ 5 x 10^9/L • Transformation to a more aggressive histology
Relapse (untreated)	The re-appearance of disease after complete recovery. Relapse should be determined by one or more diagnostic tests.

**Source of disease response definition: CIBMTR Pre-HSCT CLL Disease Form 2013*

- **Hairy cell leukemia** is characterized by the presence of abnormal B-lymphocytes in the bone marrow, peripheral blood, and spleen.

Disease Status	Definition
Never Treated	The recipient was diagnosed with hairy cell leukemia and never treated.
Complete Remission (CR)*	Disappearance of all evidence of disease. Requires **all** of the following: • Neutrophils ≥ 1.5 x 10^9

	• Hemoglobin ≥ 12.0 g/dL • Platelets ≥ 100 x 10^9/L • Absence of hairy cells on peripheral blood smear • No palpable lymphadenopathy or hepatosplenomegaly
Nodular Partial Remission (nPR)	Not applicable for hairy cell leukemia.
Partial Remission (PR)*	Requires **all** of the following: • ≥ 50% reduction in the absolute hairy cell count in the peripheral blood and the bone marrow • ≥ 50% improvement of all cytopenias • ≥ 50% reduction in abnormal lymphadenopathy or hepatosplenomegaly
No Response/Stable Disease (NR/SD)	Not applicable for hairy cell leukemia.
Progression	Not applicable for hairy cell leukemia.
Relapse (untreated)*	**Relapse after CR:** • Reappearance of hairy cells in the peripheral blood smear and/or bone marrow (regardless of the degree of infiltration) • Development of peripheral blood cytopenias • Splenomegaly **Relapse after PR:** • ≥ 50% increase of residual hairy cells in the marrow • Development of cytopenias • Splenomegaly insufficient to qualify as PR Or

	• Reappearance of hairy cells in the bone marrow of those patients classified as partial responders based on residual splenomegaly only

**Source of disease response definition:*
http://bloodjournal.hematologylibrary.org/cgi/content/full/92/6/1918

- **PLL,** or prolymphocytic leukemia, is a type of CLL and is characterized by an increased presence of immature prolymphocytes in the bone marrow and peripheral blood.

Disease Status	Definition
Never Treated	The recipient was diagnosed with PLL and never treated.
Complete Remission (CR)*	Requires **all** the following: • No radiographic evidence of lymphadenopathy • No organomegaly • Neutrophils > 1.5 x 10^9/L • Platelets > 100 x 10^9/L • Hemoglobin > 11g/dL • Lymphocytes < 4 x 10^9/L/L • Bone marrow < 30% lymphocytes • Absence of constitutional symptoms (e.g., fatigue, fevers, night sweats)
Nodular Partial Remission (nPR)*	Complete response with persistent lymphoid nodules in bone marrow.
Partial Remission (PR)*	Requires **all** of the following: • ≥50% decrease in peripheral blood lymphocyte count from pretreatment value • ≥50% reduction in lymphadenopathy if present pretreatment • ≥50% reduction in liver and spleen size if enlarged pretreatment **AND one or more** of the following:

	• Neutrophils ≥ $1.5x10^9$/L or 50% above baseline • Platelets > $100x10^9$/L or 50% improvement over baseline • Hemoglobin > 11.0 g/dL or 50% improvement over baseline
No Response/Stable Disease (NR/SD)*	No change. Not complete response, partial response, or progressive disease.
Progression*	Requires **one or more** of the following: • ≥ 50% increase in the sum of the products of ≥ 2 lymph nodes (≥ 1 node must be ≥ 2 cm) or new nodes • ≥ 50% increase in liver or spleen size, or new hepatomegaly or splenomegaly • ≥ 50% increase in absolute lymphocyte count to ≥ 5 x 10^9/L • Transformation to a more aggressive histology
Relapse (untreated)	The re-appearance of disease after complete recovery. Relapse should be determined by one or more diagnostic tests.

**Source of disease response definition: CIBMTR Pre-HSCT CLL Disease Form 2013*

- **Other:** This category should be used only if the recipient's disease does not fit one of the other leukemia options listed. To determine the disease status, use the criteria for the leukemia that most closely resembles the disease for which this form is being completed. For questions, contact your transplant center's CIBMTR liaison.

Lymphomas

NOTE: Waldenstrom Macroglobulinemia

On previous versions of the CIBMTR forms, Waldenstrom Macroglobulinemia was classified as a Plasma Cell Disorder. Per the WHO disease classifications, Waldenstrom Macroglobulinemia is now classified in the Non-Hodgkin's Lymphoma section.

NOTE: Precursor T- and Precursor B-cell Lymphoblastic Lymphoma/Leukemia

Due to the aggressive nature of precursor T- and precursor B-cell lymphoblastic lymphoma (or lymphoma/leukemia), the primary disease reported for recipients with these malignancies should be acute lymphoblastic leukemia (precursor T-cell ALL or precursor B-cell ALL).

Hodgkin's Lymphoma (**HL**) and Non-Hodgkin's Lymphoma (**NHL**) are WHO disease classification subtypes of Lymphoma. HL and NHL often transform into other disease subtypes. NHL can transform into other NHL subtypes, or into HL subtypes, but HL will rarely transform into NHL. Additionally, HL and NHL can occur at the same time.

In order to complete the correct Disease Classification Sheet for a recipient who has a history of both HL and NHL, **it is important to determine which disease is active prior to the start of the preparative regimen**.

The following two scenarios are examples of the data reporting practice for recipients with a combination of HL and NHL.

> **Scenario 1:** A recipient is being transplanted for active NHL, but has a history of HL that is in remission at the start of the preparative regimen. Report the active NHL on the Disease Classification Sheet for Lymphomas, and report HL as a prior malignancy in the "other, specify" field in the co-morbid condition section (questions 139-140).
>
> **Scenario 2:** A recipient is being transplanted for both active NHL and active HL. Complete the Disease Classification Sheet for "Other" Disease (code 900). Do not complete the Disease Classification Sheet for Lymphomas.

Hodgkin's Lymphoma

Question 238: Specify disease type
Indicate the disease classification at diagnosis.

Questions 239-243: Status at Transplantation
Indicate the recipient's disease status immediately prior to the start of the preparative regimen.

Disease Status	Definition
Never Treated	The recipient was diagnosed with HL and never treated.
Primary Refractory (less than PR to initial therapy)/PIF res	The response of the lymphoma to treatment is less than in a partial response (PR). This status would also include recipients who achieved a prior PR (but never CR) but are not in either PR or relapse immediately prior to transplant.

Partial Response (PR)* *If yes, also complete question 240*	Reductions of ≥ 50% in greatest diameter of all sites of known disease and no new sites.
Complete Remission (CR) Confirmed* *If yes, also complete question 241*	Complete disappearance of all known disease for ≥ 4 weeks.
CR Unconfirmed (CRU)* *If yes, also complete question 241*	Complete disappearance of all known disease for ≥ 4 weeks with the exception of persistent scan abnormalities of unknown significance.
Relapse (Rel) *If yes, also complete questions 242-243*	Recurrence of disease after CR. This may involve an increase in size of known disease or new sites of disease.

**Source of disease response definition: CIBMTR Pre-HSCT Lymphoma Disease Form 2018*

FOR PR

Question 240: Specify
Partial response may be represented as PR1, PR2, etc. There are differing interpretations of what the number after "PR" represents. To avoid confusion, distinguish the type of PR with the following: "**without** prior CR" and "**with** prior CR," as that is what is important in CIBMTR analysis. Note: "with prior CR" is analogous to relapse-sensitive (Rel sen). Report PR that included a prior CR in the relapse-sensitive category and indicate which relapse (number) the recipient is in.

FOR CR/CRu

Question 241: Number
Indicate the number of this CR.

For the purposes of this manual, the term "confirmed" is defined as a laboratory and/or pathological radiographic determination. The term "unconfirmed" is defined as scan abnormalities of unknown significance that are not biopsied or otherwise evaluated.

FOR RELAPSE

Question 242: Number
Indicate the number of this relapse using the following guidelines:

1st relapse: one prior complete remission

2nd relapse: two prior complete remissions

3rd or higher: three or more complete remissions followed by relapse.

Do not include PRs when calculating the number of relapses.

Question 243: Sensitivity to Chemotherapy:*
Sensitivity is measured based on the **last chemotherapy given within the six months prior to HSCT**. Indicate the recipient's sensitivity to chemotherapy using the following guidelines:

Sensitive: ≥ 50% reduction in the bi-dimensional diameter of all disease sites with no new sites of disease (PIF sen, PR1, CR, CRU, REL sen)

Resistant: < 50% reduction in the diameter of all disease sites or development of new disease sites (PIF sen, REL res)

Untreated: no chemotherapy was given within the 6 months prior to the preparative regimen (disease untreated, REL unt)

Unknown: (PIF unk, REL unk)

Non-Hodgkin's Lymphoma

Question 244: Specify disease type
Indicate the disease classification at diagnosis.

If Follicular NHL is reported, for paper form submission, indicate the grade at diagnosis. In the FormsNet2™ application, select the appropriate grade at diagnosis.

If Non-Hodgkin's Lymphoma transforms from one subtype to another, report the most current subtype. Report the initial diagnosis date of the first subtype in Question 2.

Question 245: Diffuse large B-cell lymphoma – If known, indicate subtype
If the recipient has a diagnosis of diffuse large B-cell lymphoma, indicate the subtype. If the subtype is unknown, write "unknown" on the paper form, or override the question with the "unknown" override option in FormsNet2™.

Question 246: Other B-cell lymphoma, specify
This category should be used only if the recipient's disease does not fit one of the other B-cell options listed (e.g., B-cell lymphoma, unclassifiable with a feature between large B-cell lymphoma and Burkitt's lymphoma).

Question 247: Other T/NK cell lymphoma, specify
This category should be used only if the recipient's disease does not fit one of the other T/NK cell options listed.

Questions 248-252: Status at Transplantation
Indicate the recipient's disease status immediately prior to the start of the preparative regimen.

Disease Status	Definition
Never Treated	The recipient was diagnosed with NHL and never treated.
Primary Refractory (less than PR to initial therapy)/PIF res	The response of the lymphoma to treatment is less than in a partial response (PR). This status would also include recipients who achieved a prior PR (but never CR) but are not in either PR or relapse immediately prior to transplant.
Partial Response (PR)* *If yes, also complete question 249*	Reductions of ≥ 50% in greatest diameter of all sites of known disease and no new sites.
Complete Remission (CR) Confirmed* *If yes, also complete question 250*	Complete disappearance of all known disease for greater than or equal to four weeks.
CR Unconfirmed (CRU)* *If yes, also complete question 250*	Complete disappearance of all known disease for ≥ 4 weeks with the exception of persistent scan abnormalities of unknown significance.*
Relapse (Rel) *If yes, also complete questions 251-252*	Recurrence of disease after CR. This may involve an increase in size of known disease or new sites of disease.

**Source of disease response definitions: CIBMTR Pre-HSCT Lymphoma Disease Form 2018*

FOR PR

Question 249: Specify
Partial response may be represented as PR1, PR2, etc. There are differing interpretations of what the number after "PR" represents. To avoid confusion, distinguish the type of PR with the following: "**without** prior CR" and "**with** prior CR," as that is what is important in CIBMTR analysis. Note: "with prior CR" is analogous to relapse-sensitive (Rel sen). Report PR that included a prior CR in the relapse-sensitive category and indicate which relapse (number) the recipient is in.

FOR CR/CRu

Question 250: Number
Indicate the number of this CR.

For the purposes of this manual, the term "confirmed" is defined as a laboratory and/or pathological radiographic determination. The term "unconfirmed" is defined as scan abnormalities of unknown significance that are not biopsied or otherwise evaluated.

FOR RELAPSE

Question 251: Number
Indicate the number of this relapse using the following guidelines:

1st relapse: one prior complete remission

2nd relapse: two prior complete remissions

3rd or higher: three or more complete remissions followed by relapse.

Do not include PRs when calculating the number of relapses.

Question 252: Sensitivity to Chemotherapy:*
Sensitivity is measured based on the **last chemotherapy given within the six months prior to HSCT**. Indicate the recipient's sensitivity to chemotherapy using the following guidelines:

Sensitive: ≥ 50% reduction in the bi-dimensional diameter of all disease sites with no new sites of disease (PIF sen, PR1, CR, CRU, REL sen)

Resistant: < 50% reduction in the diameter of all disease sites or development of new disease sites (PIF sen, REL res)

Untreated: no chemotherapy was given within the 6 months prior to the preparative regimen (disease untreated, REL unt)

Unknown: (PIF unk, REL unk)

Plasma Cell Disorders

Plasma cells produce and release immunoglobulins (or antibodies) to attack and destroy disease-causing bacteria and viruses. Immunoglobulins typically contain two large *heavy chains* and two small *light chains*. There are five types of immunoglobulin heavy chains: IgG, IgA, IgD, IgE, and IgM; and there are two types of light chains: lambda and kappa.

Abnormal plasma cells can produce tumors in the bone marrow. A single plasma cell tumor is referred to as a *plasmacytoma.* Tumors that spread throughout the bone marrow are referred to as *myeloma* or *multiple myeloma.*

Symptoms of plasma cell disorders (PCD) include, but are not limited to: bone pain and fractures, anemia, decreased immunity to infection, kidney dysfunction, muscle weakness, malaise and fatigue, and mental confusion.

For more information regarding multiple myeloma, see the Multiple Myeloma 2016 Manual.

Question 253: Classification
Indicate the disease classification at diagnosis.

For recipients diagnosed with more than one PCD, either sequentially or concurrently, see table 4 below.

Table 4. Plasma Cell Disorders: Disease Combinations

Disease Combination	Required disease classification sheet:	Report the disease diagnosis date of (Question 2):
Plasmacytoma transformed to Myeloma	Myeloma	Myeloma
Myeloma and Plasma Cell Leukemia	Plasma Cell Leukemia	Plasma Cell Leukemia
Myeloma and Amyloidosis	Myeloma	Myeloma

If the recipient's disease classification is one of the following, continue with question 254.

1. Multiple myeloma - IgG
2. Multiple myeloma - IgA
3. Multiple myeloma - IgD
4. Multiple myeloma - IgE
5. Multiple myeloma - IgM (not Waldenstrom macroglobulinemia)
6. Multiple myeloma - light chain only

If the recipient's disease classification is the following, neither kappa nor lambda light chains will be present; therefore, continue with question 255 (Durie-Salmon) or question 257 (I.S.S.).

7. Multiple myeloma - non-secretory

If the recipient's disease classification is one of the following, continue with question 261.

8. Plasma cell leukemia
9. Solitary plasmacytoma (no evidence of myeloma)
10. Primary amyloidosis

If the recipient's disease classification is the following, continue with question 260.

11. Other Plasma Cell Disorder

Question 254: Light Chain
Indicate the presence of light chains as either kappa or lambda.

NOTE: Questions 255-259, Stage at Diagnosis
Report the recipient's stage at diagnosis using either the Durie-Salmon staging system (questions 255-256) **or** the International Staging System (I.S.S.) (questions 257-259).

Questions 255-256: Stage at Diagnosis: Durie-Salmon
Indicate stage and sub-classification. If the Durie-Salmon stage and sub-classification is not documented in the medical record, see Table 5 below to determine the appropriate stage and sub-classification.

Table 5. Durie-Salmon Staging System for Multiple Myeloma

Stage	Criteria
I	All of the following: • Hemoglobin >10 g/dL

	• Serum calcium normal (≤12 mg/dL) • On radiograph, normal bone structure or solitary bone plasmacytoma only • Low M-component production rate (IgG < 5 g/dL, IgA <3 g/dL), Urinary light chain M-component on electrophoresis (<4 g/24 hr)
II	Fitting neither stage I nor stage III
III	One or more of the following: • Hemoglobin < 8.5 g/dL • Serum calcium >12 mg/dL • Advanced lytic bone lesions (scale 3) • High M-component product rate (IgG >7 g/dL, IgA >5 g/dL), Urinary light chain M-component on electrophoresis (> 12 g/24 hr)
Sub-classification **(either A or B)**	A: Relatively normal renal function (serum creatinine <2.0 mg/dL) B: Abnormal renal function (serum creatinine ≥2.0 mg/dL)

Adapted from Durie BG, Salmon SE: A clinical staging system for multiple myeloma: Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. Cancer 1975;36:842-854.

Questions 257-259: Stage at Diagnosis: I.S.S.
Report the recipient's lab values from diagnosis **and/or** the stage of myeloma.

Question 260: Other Plasma Cell Disorder, specify
On occasion, a recipient could have two heavy-chain types; this is known as biclonal myeloma (e.g., IgA Kappa and IgG Kappa). Other examples of "other plasma cell disorders" include: Light Chain Deposition Disease (LCDD), light chain only myeloma with associate LCDD, and osteosclerotic myeloma (POEMS). In this instance, report "other plasma cell disorder" and specify the appropriate type.

In situations of tandem autologous HSCT, oligoclonal reconstitution from a previous HSCT should not be reported as a new subtype. Oligoclonal reconstitution is the appearance of a new M-protein not present at diagnosis. For questions regarding oligoclonal reconstitution, contact your transplant center's CIBMTR liaison.

Questions 261-262: Status at Transplant
Indicate the recipient's disease status immediately prior to the start of the preparative regimen.

For information regarding reporting multiple myeloma disease status at transplant, see Appendix V.

Table 6. Disease Status Definitions

Disease Status	Definition
Never Treated	No treatment given in the six months prior to HSCT.
Stringent Complete Remission (sCR) *If yes, also complete question 262*	Follow criteria for CR as defined below, **plus all of the following**: • Normal free light chain ratio, • Absence of clonal cells in the bone marrow by immunohistochemistry or immunofluorescence (confirmation with repeat bone marrow biopsy not needed). (Presence and/or absence of clonal cells is based upon the κ/λ ratio. An abnormal κ/λ ratio by immunohistochemistry and/or immunofluorescence requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting the presence of an abnormal clone is κ/λ of > 4:1 or < 1:2.) sCR requires two consecutive assessments (of the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of progressive or new bone lesions. Radiographic studies are not required to satisfy sCR requirements.

Disease Status	Definition
Complete Remission (CR) *If yes, also complete question 262*	A treatment response where **all** of the following criteria are met: • Negative immunofixation on serum and urine samples • Disappearance of any soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) **NOTE: CR Requirements** For recipients with light chain only myeloma, **all** of the following criteria must be met: • Normal serum free light chain ratio • Negative immunofixation on urine samples • Disappearance of any soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) For recipients with non-secretory myeloma, **all** of the following criteria must be met: • Disappearance of all soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) CR requires two consecutive assessments (of the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of progressive or new bone lesions. Radiographic studies are not required to satisfy CR requirements.
Very Good Partial Response (VGPR) *If yes, also complete question 262*	**One or more** of the following must be present: • Serum and urine M-protein detectable by immunofixation but not on electrophoresis • ≥ 90% reduction in serum M-protein and urine M-protein level < 100 mg/24 hours. VGPR requires two consecutive assessments (of the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of progressive or new bone lesions. Radiographic studies are not required to satisfy VGPR requirements.

Disease Status	Definition
Partial Response (PR) *If yes, also complete question 262*	**Both** of the following must be present: • ≥ 50% reduction in serum M-protein • Reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg/24 hours. If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria): • serum M-protein ≥ 1 g/dL, • urine M-protein ≥ 200 mg/24 hours; then a ≥ 50% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level > 10 mg/dL and the serum free light chain is abnormal). If serum and urine M-protein *and* serum-free light assay are not measurable, a ≥ 50% reduction in bone marrow plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was ≥ 30%. In addition to the above listed criteria, a ≥ 50% reduction in the size of soft tissue plasmacytomas is also required, if present at baseline. PR requires two consecutive assessments (of the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of progressive or new bone lesions. Radiographic studies are not required to satisfy PR requirements.
Stable Disease (SD)	Does not meet the criteria for CR, VGPR, PR, or PD. SD requires two consecutive assessments (of the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of progressive or new bone lesions. Radiographic studies are not required to satisfy SD requirements.

Disease Status	Definition
Progressive Disease (PD) *If yes, also complete question 262*	Requires **one or more** of the following: Increase of ≥ 25% from the lowest response value achieved in: • Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); **and/or** • Urine M-component with an absolute increase ≥ 200 mg/24 hours; **and/or** • For recipients without measurable serum and urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL; **and/or** • Bone marrow plasma cell percentage with absolute percentage ≥ 10%; **and/or** • Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas; **and/or** • Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol) that can be attributed solely to the plasma cell proliferative disorder. PD requires two consecutive assessments (of the same method) made at any time before classification as disease progression, and/or the institution of any new therapy.
Relapse from CR (untreated) *If yes, also complete question 262*	Requires **one or more** of the following: • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or • Development of ≥ 5% plasma cells in the bone marrow (relapse from CR has a 5% cutoff vs. 10% for other categories); and/or • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). Relapse requires two consecutive assessments (of the same method) made at any time before classification as relapse, and/or the institution of any new therapy.

Source of disease response definitions: CIBMTR Pre-HSCT Multiple Myeloma/Plasma Cell Leukemia Disease Form 2016

Question 262: Number

Indicate the number of this CR, sCR, VGPR, PR, Progression or Relapse.

Breast Cancer

Question 263: Classification
Indicate the disease classification at diagnosis as either "inflammatory" or "non-inflammatory."

Inflammatory breast cancer is characterized by a red and swollen appearance. The skin of the breast may also feel warm to the touch and show a pitted appearance known as *peau d'orange* (i.e., orange peel).

NOTE: Question 264
If the recipient is considered stage IV, select stage III for question 264, and select "metastatic" for question 265.

Question 264: Stage at Diagnosis
Indicate the recipient's disease stage (stage I-IV) at diagnosis. Cancer stage is based on the size of the tumor, whether the cancer is invasive or non-invasive, whether lymph nodes are involved, and whether the cancer has spread beyond the breast.

The most common system used to describe the stages of breast cancer is the American Joint Committee on Cancer (AJCC) TNM system. The letter *T* refers to *Primary Tumor, N* refers to *Lymph Node,* and *M* refers to *Distant Metastasis.* The additional letters or numbers appearing after T, N, and M provide more details about the tumor, lymph nodes, and metastasis:

- The letter T followed by a number from 0 to 4 describes the tumor's size and spread to the skin or to the chest wall under the breast. Higher T numbers indicate a larger tumor and/or wider spread to tissues near the breast.
- The letter N followed by a number from 0 to 3 indicates whether the cancer has spread to lymph nodes near the breast and, if so, how many lymph nodes are affected.

The letter M followed by a 0 or 1 indicates whether the cancer has spread to distant organs—for example, the lungs or bones.

Stage	Definition
0	Carcinoma in situ. • **Lobular carcinoma in situ (LCIS):** Abnormal cells are in the lining of a lobule • **Ductal carcinoma in situ (DCIS):** Abnormal cells are in the lining of a duct. DCIS is also called intraductal carcinoma

Stage	Definition
I	The tumor is no more than 2 cm (¾ inch) across, **and** the cancer cells have not spread beyond the breast (T1, N0, M0).
II	**One** of the following criteria must be met: • The tumor is no more than 2 cm (¾ inch) across. The cancer has spread to the lymph nodes under the arm (T1, N1, M0). • The tumor is between 2 cm and 5 cm (¾ inch and 2 inches). The cancer has not spread to the lymph nodes under the arm (T2, N0, M0). • The tumor is between 2 cm and 5 cm (¾ inch and 2 inches). The cancer has spread to the lymph nodes under the arm (T2, N1, M0). • The tumor is larger than 5 cm (2 inches). The cancer has not spread to the lymph nodes under the arm (T3, N0, M0).
III	**NOTE** The Pre-TED does not collection the detail of Stage III. Locally advanced cancer. Stage III is generally divided into Stage IIIA, IIIB, and IIIC. **Stage IIIA** - **One** of the following criteria must be met: • The tumor is no more than 5 cm (2 inches) across. The cancer has spread to underarm lymph nodes that are attached to each other or to other structures. Or the cancer may have spread to lymph nodes behind the breastbone (T0-2, N2, M0). • The tumor is more than 5 cm across. The cancer has spread to underarm lymph nodes that are either alone, attached to each other, or attached to other structures. Or the cancer may have spread to lymph nodes behind the breastbone (T3, N1-2, M0).

Stage	Definition
III (cont.)	**Stage IIIB** - A tumor of any size has grown into the chest wall or the skin of the breast. It may be associated with swelling of the breast or with nodules (lumps) in the breast skin (T4, N0-2, M0). • The cancer may have spread to lymph nodes under the arm. • The cancer may have spread to underarm lymph nodes that are attached to each other or other structures. Or the cancer may have spread to lymph nodes behind the breastbone. • Inflammatory breast cancer is a rare type of breast cancer. The breast looks red and swollen because cancer cells block the lymph vessels in the skin of the breast. When a doctor diagnoses inflammatory breast cancer, it is at least Stage IIIB, but it could be more advanced. **Stage IIIC** - A tumor of any size has spread in one of the following ways (T0-4, N3, M0): • The cancer has spread to the lymph nodes behind the breastbone and under the arm. • The cancer has spread to the lymph nodes above or below the collarbone.
IV	Distant metastatic cancer. The cancer has spread to other parts of the body (including the ipsilateral supraclavicular lymph nodes).

Question 265: Metastases
Indicate whether the recipient's disease has metastasized beyond the breast and/or lymph nodes. Metastatic disease (M1) confirms that the disease has spread to the distant organs and is considered stage IV.

Questions 266-271: Status at Transplant
Indicate the recipient's disease status immediately prior to the start of the preparative regimen.

Disease Status	Definition
Adjuvant **(Stage II, III only)**	Adjuvant therapy uses chemotherapy drugs, radiation, hormone therapy, targeted therapy, or a combination of these to help destroy any cancer cells that were not removed during the breast cancer operation. Its goal is to decrease the risk of the breast cancer coming back.

Disease Status	Definition
Never Treated	Never treated indicates the recipient was not treated for breast cancer (including surgery such as lumpectomy or mastectomy) prior to the start of the preparative regimen. This disease status at transplant should be chosen rarely.
Primary Refractory	The response of the breast cancer to treatment is less than in a PR. This status would also include recipients who had achieved a prior PR (but never CR) but are not in either PR or relapse immediately prior to transplant.
Complete Remission* *If yes, also complete questions 267-268*	**CR Confirmed:** Disappearance of target lesions for a period of at least one month. **CR Unconfirmed:** Complete response with persistent imaging abnormalities of unknown significance.
1st Partial Response*	At least 30% decrease in the sum of the longest diameter of measured lesions (target lesions), taking as reference the baseline sum of longest distance. **Note: 1st Partial Response** For CIBMTR reporting purposes, this response is reserved for recipients who have **never** achieved CR, but a PR was achieved and maintained at the time of the preparative regimen.
Relapse *If yes, also complete questions 269-271*	Recurrence of the disease after CR. Can be local or metastatic.

*Source of disease response definitions: CIBMTR Pre-HSCT Breast Cancer Disease Form 2020

FOR CR

Question 267: CR, specify
Using the definitions listed above, indicate whether the CR was “confirmed” or “unconfirmed.” For the purposes of this manual, the term “confirmed” is defined as a laboratory and/or pathological radiographic determination. The term “unconfirmed” is defined as scan abnormalities of unknown significance that are not biopsied or otherwise evaluated.

Question 268: CR, number
Indicate the number of this response.

FOR RELAPSE

Question 269: Relapse, specify
Using the definitions below, indicate whether the relapse is "local" or "metastatic."

Local: Recurrence occurred in the same side breast or local lymph nodes.

Metastatic: Recurrence occurred anywhere in the body other than the same side breast or local lymph nodes.

Question 270: Relapse, number
Using the guidelines below, indicate the number of this relapse.

1st relapse: one prior complete remission

2nd relapse: two prior complete remissions

3rd or higher: three or more complete remissions followed by relapse.

Do not include PRs when calculating the number of relapses.

Question 271: Relapse, sensitivity to chemotherapy*
Sensitivity is measured based on the last chemotherapy given prior to HSCT; chemotherapy must include ≥ 2 cycles of treatment given ≤ 6 months prior to HSCT. Indicate the sensitivity to chemotherapy using the following guidelines:

Sensitive: ≥ 50% reduction in the bi-dimensional diameter of all disease sites with no new sites of disease

Resistant: < 50% reduction in the diameter of all disease sites or development of new disease sites

Untreated: if last treatment was not chemotherapy

Unknown: only if there no documentation of the recipient's response following treatment

"Other" Disease

Question 272: Specify
Before using this category, check with a transplant physician to determine whether the disease can be classified as one of the listed options on the Disease Classification Sheets. Examples include: Composite Lymphoma (e.g., both active NHL and HL), Erythropoietic Protoporphyria (EPP), and Dystrophic Epidermolysis Bullosa (DEB).

Question 273: For any "other" disease: Is a pathology report attached to this form?
Indicate if a pathology report is attached. Attaching a pathology report will help the CIBMTR confirm reported data and reduce data queries. Attach a copy of the pathology report using the Log of Appended Documents (Form 2800).

NOTE: Alternative HCT
The CIBMTR is currently in the process of updating the Pre-TED form to remove questions 274-275. Cellular therapies for regenerative medicine (i.e., alternative HCT) are now captured on Form 4000.

Questions 274-275: Alternative HCT:
Report the indication for this HSCT.

Other Malignancies

NOTE: Sarcoma
The names of the sarcoma subtypes have changed with the revised Pre-TED form. If the sarcoma subtype documented in the recipient's medical record is not one of the listed options, consult with a transplant physician for assistance, as the name of the subtype may have changed.

Questions 276-277: Classification
Most of the malignancies listed in this section are solid tumors. Germ cell tumors that originate in the ovary or testes should be reported as *Ovarian* or *Testicular*, respectively. If the subtype is not listed, report as "other, solid tumor" and specify the reported malignancy. If a certain disease becomes a common indication for HSCT, the CIBMTR will add the disease as a separate category.

Questions 278-279: Status at Transplantation
Indicate the recipient's disease status immediately prior to the start of the preparative regimen.

Disease Status	WHO Definition	RECIST Definition
Adjuvant	Treatment given after the primary cancer treatment to increase the chances of a cure. Adjuvant cancer therapy may include chemotherapy, radiation therapy, hormone therapy, or biological therapy.	Not applicable

Disease Status	WHO Definition	RECIST Definition
Never Treated	Never treated indicates the recipient was not treated for the malignancy prior to the start of the preparative regimen. This disease status at transplant should rarely be used.	Not applicable
Complete Response (CR)	Complete disappearance of all known disease for ≥ 1 month. Includes disappearance of all signs and symptoms of disease with normalization of all biochemical and radiologic parameters, as well as a negative repeat biopsy.	Disappearance of all target lesions for a period of at least one month.
Complete Response Unconfirmed (CRU)	Disappearance of all signs and symptoms of disease with normalization of all biochemical and radiologic parameters, but with persistent, unchanging imaging abnormalities of unknown significance.	Complete response with persistent imaging abnormalities of unknown significance.
Partial Response (PR) **Partial Response (PR) (cont.)**	Decrease of ≥ 50% in total tumor load of the lesions that have been measured for at least 4 weeks. Partial response may be represented as PR1, PR2, etc. There are differing interpretations of what the number after "PR" represents, and this can be confusing. What is important to CIBMTR data analysis is to distinguish the type of PR as either: "**without** prior CR" or "**with** prior CR."	At least a 30% decrease in the sum of the longest diameter of measured lesions (target lesions), taking as reference the baseline sum of longest diameter.
	Question 279: Specify If the recipient is in a partial response, indicate whether there was a previous CR.	

Disease Status	WHO Definition	RECIST Definition
No Response/Stable Disease (NR/SD)	Disease has been treated and the size of one or more lesions has neither increased 25% or more in the size of one or more lesions, nor has total tumor size decreased 50% or more.	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum of the longest diameter of measured lesions (target lesions), since the treatment started.
Progressive Disease (PD)	Increase of ≥ 20% in the size of one or more measurable lesions, or the appearance of new lesions.	At least a 20% increase in the sum of the longest diameter of measured lesions (target lesions), taking as reference the smallest sum longest diameter recorded since the treatment started or the appearance of one or more new lesions.
Relapse (untreated)	The reappearance of disease after complete recovery. Should be determined by one or more diagnostic tests.	Not applicable.

Question 280: Was Response Evaluation Criteria in Solid Tumors (RECIST) criteria used for this status evaluation?
Check “yes” or “no” to indicate whether the RECIST disease response definitions were used to evaluate the recipient’s status. For more information regarding RECIST criteria, see Appendix N.

Question 281: Number (complete for CR, CRU or relapse)
Indicate which number the response represents.

Question 282: REL, sensitivity to chemotherapy (complete only for relapse)
Indicate if the disease is sensitive to chemotherapy. Sensitivity is measured based on the last chemotherapy given prior to HSCT; chemotherapy must include ≥ 2 cycles of treatment given ≤ 6 months prior to HSCT. Indicate the sensitivity to chemotherapy using the following guidelines:

Sensitive: ≥ 50% reduction in the bi-dimensional diameter of all disease sites with no new sites of disease

Resistant: < 50% reduction in the diameter of all disease sites or development of new disease sites

Untreated: if last treatment was not chemotherapy

Unknown: only if there no documentation of the recipient's response following treatment

NOTE: Malignant vs. Non-Malignant
Malignant diseases involve cells dividing without control, which can spread to other parts of the body through the blood and lymph systems. These diseases are usually characterized by unlimited, aggressive growth; invasion of surrounding tissues; and metastasis.

Non-malignant diseases involve cell overgrowth, but lack the malignant properties of cancer.

The diseases listed in the following section are **non-malignant.**

Anemia/Hemoglobinopathy

Questions 283-287: Classification
Indicate the disease classification at diagnosis.

Platelet Disorders

Questions 288-289: Classification
Indicate the disease classification at diagnosis.

Histiocytic Disorders

Questions 290-291: Classification
Indicate the disease classification at diagnosis.

Inherited Disorders of Metabolism/Osteopetrosis

Questions 292-293: Classification
Indicate the disease classification at diagnosis.

Immune Deficiencies

Questions 294-296: Classification
Indicate the disease classification at diagnosis.

Autoimmune Disorders

NOTE:
For all recipients with autoimmune disease, the Pre-TED form should be submitted at the time of mobilization.

Question 297: Autoimmune Deficiencies, Specify
Indicate the disease classification at diagnosis.

Systemic Sclerosis (Connective Tissue Disease)

Questions 298-321: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Questions 322-324: Miscellaneous Labs at Original Diagnosis
For each antibody listed, indicate whether the result was “normal,” “elevated,” or “not done.”

Systemic Lupus Erythematosus (Connective Tissue Disease)

Questions 325-351: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Questions 352-358: Miscellaneous Labs at Original Diagnosis
For each test listed, indicate whether the result was “normal,” “elevated or low,” or “not done.”

Sjögren Syndrome (Connective Tissue Disease)

Questions 359-371: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Polymyositis-Dermatomyositis (Connective Tissue Disease)

Questions 372-386: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Questions 387-390: Miscellaneous Labs at Diagnosis
For each test listed, indicate whether the result was “normal,” “elevated,” or “not done.”

Antiphospholipid Syndrome (Connective Tissue Disease)

Questions 391-406: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Questions 407-409: Miscellaneous Labs at Diagnosis
For each test listed, indicate whether the result was “normal,” “elevated,” or “not done.”

Other Connective Tissue Disease

Question 410: Other connective tissue disease, specify:
Specify the other connective tissue disease classification at the time of original diagnosis.

Wegener Granulomatosis (Vasculitis)

Questions 411-422: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Questions 423-427: Miscellaneous Labs at Diagnosis
For each antibody listed, indicate whether the result was “normal,” “elevated,” or “not done.”

Polyarteritis Nodosa, Classical and Microscopic (Vasculitis)

Questions 428-441: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Questions 442-444: Miscellaneous Labs at Diagnosis
For each test listed, indicate whether the result was “normal,” “elevated,” or “not done.”

Churg-Strauss, Giant Cell Arteritis, Takayasu, Behçet’s Syndrome, and Overlap Necrotizing Arteritis

If the recipient’s primary disease is listed in the box above, check the appropriate disease.

Other Vasculitis

Question 445: Other vasculitis, specify
Specify the other vasculitis disease classification at the time of original diagnosis.

Rheumatoid Arthritis

Questions 446-460: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Psoriatic Arthritis/Psoriasis

Questions 461-467: Involved Organs/Clinical Problem(s) and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problem(s) at the time of original diagnosis, and whether or not that involvement was the primary reason for the HSCT.

Juvenile Idiopathic Arthritis: systemic (Stills disease), Oligoarticular, Polyarticular

If the recipient's primary disease is listed in the box above, check the appropriate disease.

Juvenile Idiopathic Arthritis: Other

Question 468: Juvenile idiopathic arthritis: other, specify
Specify the other juvenile idiopathic arthritis disease classification at the time of original diagnosis.

Other Arthritis

Question 469: Other arthritis, specify
Specify the other arthritis disease classification at the time of original diagnosis.

Multiple Sclerosis

Questions 470-478: Involved Organs/Clinical Problem and Primary Reason(s) for Transplant
Indicate the involved organs and/or clinical problems at the time of original diagnosis, and whether that involvement was the primary reason for the HSCT.

Myasthenia Gravis

If the recipient's primary disease is Myasthenia gravis, check the box.

Other Autoimmune Neurological Disorder

Question 479: Other autoimmune neurological disorder, specify
Specify the other autoimmune neurological disorder at the time of original diagnosis.

Idiopathic Thrombocytopenic Purpura (ITP), Hemolytic Anemia, and Evan Syndrome

If the recipient's primary disease is listed in the box above, check the appropriate disease, and submit the form.

Other Autoimmune Cytopenia

Question 480: Other autoimmune cytopenia, specify
Specify the other autoimmune cytopenia disease classification at the time of original diagnosis.

Crohn's Disease and Ulcerative Colitis

If the recipient's primary disease is listed in the box above, check the appropriate disease.

Other Autoimmune Bowel Disorder

Question 481: Other autoimmune bowel disorder, specify
Indicate the disease at the time of original diagnosis.