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*Sharing Knowledge.
Sharing Hope.*

CIBMTR Registration Forms Pre-TED and Post-TED

This draft manual provides updated information regarding the latest version of the TED forms, the pre-TED and the post-TED. It is labeled as a draft document as it will be incorporated into a larger formal manual covering all of the CIBMTR forms over the course of 2008, including the Report Forms. Please consider this document to represent interim guidance until the comprehensive manual can be completed and published.

This Manual will receive updates as identified. Please send any reporting questions or comments about this manual to dknutson@mcw.edu

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Commonly Used Abbreviations/Definitions

Please note a list of abbreviations on paper version page two of Pre-TED. These are used throughout all the Forms and in this document. New commonly used abbreviations proposed for use on future forms may be submitted to: dknutson@mcw.edu

| | |
|---|---|
| YYYY = 4 digit year | FGF = Fibroblast Growth Factor |
| MM = 2 digit month | FISH = Fluorescent In-situ Hybridization |
| DD = 2 digit day | FN2 = FormsNet2 |
| AHOP = Adult, Hematology, Oncology or Pediatric Unit (select only one) | FU = Follow-up |
| ALLO = Allogeneic | GVHD = Graft versus Host Disease |
| ANC = Absolute Neutrophil Count | HSCT = Hematopoietic Stem Cell Transplant |
| AUTO = Autologous | HCT = Hematopoietic Cell Transplant |
| BM = Bone Marrow | KGF = Keratinocyte Growth Factor |
| BMT-CTN = Blood & Marrow Transplant Clinical Trials Network | NMDP = National Marrow Donor Program |
| CIBMTR = Center for International Blood & Marrow Transplant Research | NOS = Not Otherwise Specified |
| CIC = Center Identification Code | NST = Non-myeloablative Stem Cell Transplant |
| CMV = Cytomegalovirus | PBSC = Peripheral Blood Stem Cells |
| CR = Complete Remission | PCL = Plasma Cell Leukemia |
| cRF = Comprehensive Report Form = "Research" Report Form | PHI = Protected Health Information |
| 2000 Baseline | Product Form = This was a transitional term used to temporarily describe the form pieces that came out of the '95/'02 CIBMTR Graft insert. The three Forms are IDM, HLA & INF. The term "Product Form" may have appeared in communication from Summer 2007; it is being retired. |
| 2004 IDM / 2005 HLA / 2006 INF | ProMiSe = Electronic data collection system for EBMT |
| 20xx Disease (pre-HSCT) | PTLD = Posttransplant lymphoproliferative disorder |
| 2100 Day-100 | RBC = Red Blood Cell |
| 2200 Six month- two year | RCI-BMT = Resource for Clinical Investigations in Blood & Marrow Transplant |
| 2300 Greater than two year | RIC = Reduced Intensity Conditioning |
| 21xx Disease Follow-Up (Post-HSCT) | SCTOD = Stem Cell Therapeutic Outcomes Database |
| 2046 FNG / 2047,2147 HEP / 2048,2148 HIV | TBI, TLI, TNI = Total (Body, Lymphoid, Nodal) Irradiation |
| 2900 Death | U = Unclassifiable |
| CTN = Blood & Marrow Transplant – Clinical Trials Network | UCB = Umbilical Cord Blood |
| d-0 = Day zero, a.k.a. Date of HSCT | UIA Form = Unique ID Assignment Form |
| DCI = Donor Cellular Infusion | Unit = Adult, Hematology, Oncology, Pediatric (AHOP) Note: select only one. |
| DLI = Donor Lymphocyte Infusion | VOD = Veno-occlusive disease |
| EBMT = European Group for Blood & Marrow Transplantation | |
| EBV = Epstein Barr Virus | |
| FACT = Foundation for the Accreditation of Cellular Therapy | |
| FDR = Forms Due Report | |

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CIBMTR HSCT Recipient Registration

If you are new to submitting data to CIBMTR this Manual will assist you in completing the Registration Forms: Pre-TED and Post-TED. If you are a seasoned CIBMTR data collector, these two Forms **replace** the previous Registration system of Pre-Reg, M-TED, TED and TEDFU, effective December 3, 2007. As of then, all types of HSCT (allo and auto) and all types of CIBMTR Centers* (Registering only, CTN and comprehensive Report Form->cRF Center) will all complete the *same* set of Forms** on the *same* schedule. But before explaining the new process, there is one very new, important FIRST step to be aware of: Unique ID Assignment.

* *Note: NMDP Transplant Centers are now included as CIBMTR Centers.*

***See Registration Forms Completion: Post-TED for details.*

FormsNet™ 2.0

FormsNet™ 2.0 (FN2) is the official Web-based data entry tool created by the NMDP. Centers will receive a packet with information regarding how to access the application as well as secure identification tokens that are necessary to be able to log-on. Refer to the instructions often until you are comfortable with the new system.

The primary contact at your transplant center can set up new users with FN2 access in a two-step process:

- (1) Request a FN2 account under "Personnel Change Forms" under the "Data Management" section on the CIBMTR website, and
- (2) After the request is complete, the primary contact needs to activate the new user by assigning a role to them in the application itself. This is located under the "Maintenance" tab in FN2.

The on-line version of FN2 has a slightly different appearance than the version used for paper submission, which is more compact to minimize the amount of paper faxed/stored. References to "page number" in this manual refer to the pages of the paper version available on www.cibmtr.org.

Forms Due Report (FDR)

Information on which forms are due is provided via the "Patient Forms Due" and "Center Forms Due" screens from within the FN2 application and also by a weekly E-mail report. "Patient Forms Due" provides a way to view forms due for a specific patient. "Center Forms Due" provides a way to view forms due at the center level. Both provide filters to customize the results. You may always contact your liaison to determine which Forms are due or for direction as to which recipient Forms should be done first.

Override Codes

If none of the available answer options appear appropriate, first check with someone at your center to see if a possible solution can be found (e.g. lab units are different and that is why the value is registering as an error). If no appropriate answer option exists, "override" the error (e.g. 'not tested', 'unknown', 'verify correct'). The frequency of override codes will be monitored. We will contact centers with higher than expected usage of override codes.

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Unique ID Assignment – UIA (2804)

The first step when starting to provide data for a new transplant recipient is the assignment of the Unique ID (CIBMTR Recipient ID, CRID). This will be done for patients electronically using the initial screen of FN2, or by providing a unique ID assignment form (Form 2804). Patients who have already been registered with the CIBMTR or NMDP will have a CRID assigned by the system. FN2 contains a look-up tool to find the CRID or contact your liaison. As more recipients receive care from more than one Center and the data is reported to more than one registry, it is increasingly important to make sure that each recipient is represented only once in a database, hence the need for an ID number that stays with the recipient no matter where they receive their care. Prior to completing any Forms for a first HSCT the procedure to obtain a Unique ID is as follows:

Electronically via FN2:

Log onto FN2 with your secure ID card

Or via fax request to your assigned campus (unable to access FN2):

Enter:

CIBMTR Center number

Today's Date

Recipient data

Table 1 Recipient data:

| <i>Must Enter</i> | Either/or groupings need A, B, C or D. | Field name | Tied to another field = need entire group | Q# |
|-------------------|--|------------------------------|---|----|
| | A | First name | Last name | 1 |
| | A | Last name | First name | 2 |
| yes | | DOB | | 3 |
| | B | Birth city | Birth State, Country | 4 |
| | B | Birth State | Birth city, Country | 5 |
| | B | Birth Country | Birth city, State | 6 |
| yes | | Gender | | 7 |
| | C | Social Security # | not US citizen, not apl. | 8 |
| | Optional | NMDP-RID | not apl. | 9 |
| | Optional | EBMT-ID | not apl. | 10 |
| | Optional – E* | IUBMID | CIBMTR Team # | 11 |
| | Optional – E* | Team ID (Team #) | CIBMTR IUBMID | 12 |
| | D | Mother's maiden name | | 13 |
| yes | | Primary disease group | | 14 |
| yes | | Tentative HSCT date | | 15 |
| yes | | Prior HSCT | | 16 |
| If Q16 | | Prior date | Source, product | 17 |
| If Q16 | | Prior cell source | Date, product | 18 |
| If Q16 | | Prior product | Date, source | 19 |

The ID server will assign a unique number that stays with the recipient for life and should be shared if the recipient's care transfers to another Center.

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* “Optional / Optional E”: Centers that wish to cross reference IUBMID with CRID must also enter the former CIBMTR Team number field with the IUBMID, or NMDP RID or EBMT CIC on the UIA Form.

Faxed requests will receive an E-reply containing the following information:

- CIBMTR Recipient ID (CRID)
- Year of birth
- Gender
- Anticipated Infusion date
- Disease

The system may determine that a recipient already exists in the Unique ID server that may match the recipient you are generating a new number for. You may be prompted for additional investigation to make sure no duplicate recipients get into the database.

This communication was previously sent to your center on November 29, 2007, to help explain the association between PHI and CRID:

FROM: J. Douglas Rizzo, MD MS
Associate Scientific Director, CIBMTR
Roberta J. King, MPH
Vice President, CIBMTR Minneapolis
RE: Collection of Protected Health Information to establish a unique identifier
Date: November 29, 2007

CIBMTR will be collecting protected health information, including identifiers such as name, social security number (SSN), mother’s maiden name and birth information in order to create a universal unique ID system for the C.W. Bill Young Transplantation Program (Program) established by the Stem Cell Therapeutic and Research Act of 2005 (Public Law 109-129). Careful consideration of this issue, by CIBMTR staff, an external Data Advisory Group and representatives of the Health Resources and Services Administration (HRSA) led to this decision. CIBMTR will request this information from transplant centers upon first notification of a transplant recipient to the CIBMTR, to create a unique ID for each patient. Patients already known to CIBMTR and NMDP will have a unique ID assigned to them using available information, including the IUBMID. Direct identifying information collected to establish the unique ID **will not be disclosed** to investigators for research purposes, it is for CIBMTR use only.

Several important security concerns have been addressed by the CIBMTR regarding the collection of these data.

- CIBMTR and NMDP have been designated as Public Health Authorities in their capacity of collection and use of the data for the SCTOD, addressing HIPAA privacy regulations.
- The electronic systems that will collect and house the protected health information (PHI) are very secure. The server holding the direct identifiers is separate from the outcomes database, and access to these data is highly restricted within CIBMTR. The electronic systems used for acquisition and generation of unique ID numbers have undergone rigorous certification and authorization from HRSA’s Office of Information Technology and comply with all federal regulations relevant to security of electronic data in federal databases.

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- Transmission of these data from transplant centers may occur electronically, but will be protected by double authentication entry requirements (login/password and SecurID card) for all system users who enter the data. Electronic transmission will be protected by SSL technology.
- Once the data are entered into the web-based system by the transplant center and a unique ID is assigned, the data are no longer visible to the transplant center. The PHI used to create the unique ID will not appear on any subsequent forms or correspondence. Centers wishing to confirm a unique ID will be able to re-enter data into one-way look-up tables, however PHI will not be displayed by the system. This security measure will prevent inappropriate revealing of PHI in the event that an unauthorized individual accesses the system. In cases where centers provide the information required to establish the unique ID using paper forms, the data is entered from the forms at the CIBMTR, the forms are securely destroyed, and centers are notified of the unique ID using email containing the unique ID, the year of birth, and date of transplant.
- Centers participating in the Program will need to take appropriate measures at their site to secure the PHI used to generate the unique ID. However, data collected to establish the ID need not be maintained by the site.

The use of PHI to uniquely identify patients who are included in the Program is needed for several reasons. A system to uniquely identify patients is important for the center-specific outcomes reporting required for the Program as administered by HRSA. Such a system will avoid duplication of patient records across transplant programs, particularly when situations exist where sequential transplants occur at different programs. This will also facilitate knowledge of previous autologous HCTs that may not be reported by a center performing an allogeneic HCT and adjusting the expected outcomes accordingly for the center-specific outcome reporting.

Uniquely identifying recipients will facilitate use of the National Death Index to determine completeness of reporting of survival and establish lack of bias in reporting deaths as lost to follow-up when performing center specific analyses and other long-term follow-up studies. Similarly, collection of these data will allow CIBMTR to help centers re-establish contact with patients who have been lost to follow-up but have not deceased, using databases available in the public and private sector. Data used to generate a unique ID may be used to increase the value of the Stem Cell Therapeutics Outcomes Database (SCTOD) by acquiring matching data from other Federal government databases for government reports or research about the Program. And, generation of a unique ID is essential to determining that all allogeneic HCT recipients in the US are reported to the SCTOD.

SSN and date of birth have been routinely collected by the National Marrow Donor Program and the U.S. solid organ transplant program (UNOS) since the early 1990s. The information is used for purposes similar to those described above, in the context of their government reporting functions.

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Finally, in the event of a state law or IRB policy that supersedes federal statute, centers may opt out of providing some of these data. Date of birth and gender are considered essential. If a SSN is not provided, full name of the patient and mother's maiden name are an alternative that will establish a unique ID. The unique ID system will be able to assign an ID when a few items are missing, however that will increase the risk of duplicate reporting of cases.

We hope that this memo provides clarity regarding the uses, values, and security of establishing unique ID numbers for the SCTOD program. If you have additional concerns, please contact Roberta King, Vice President, CIBMTR Minneapolis by phone at 612-627-5807 or by email at rking@nmdp.org.



EBMT Centers: If your data is submitted electronically to CIBMTR from ProMISe, you do NOT need to obtain a Unique ID, it will be assigned at the time EBMT transmits a file to CIBMTR. Centers that have only one CIC, but two or more CIBMTR Center numbers must complete the field 'unit', which will be added to the CIC to make it unique (for use in the look up table and data transfer). We are working on a system to inform you of the CRID assigned after your EBMT data is loaded to our database. Once it has been communicated to you, please use the CRID when communicating with CIBMTR. Other identifying numbers may be included if they are clearly labeled.

Log of Appended Documents – Log (2800)

Certain questions in the Forms may ask for specified medical record pages to be copied, de-identified and submitted along with the Form (or faxed/mailed separately) for electronic Form submission. There are several advantages to submitting additional records with the forms. These include: better substantiation of important medical complications, facilitation of additional training regarding complicated scenarios, and reducing the need for CIBMTR to contact centers to resolve discrepancies and query "outlier" values reported by a center that trigger error checking. Before de-identifying a copy of the document be sure to print the CIBMTR Center ID, CRID and note which Form and question the documentation references.

Recipient Transfers – Recip Transfers (2801)

For either subsequent HSCT or follow-up, if the recipient transfers their care to another center, a Recipient Transfer Form should be completed and submitted to the designated CIBMTR campus. The request can be initiated by either center, but must be approved by both to take effect.

Lost to Follow-Up Declaration – LtFU (2802)

Contact your liaison for suggestions on how to track recipients that are difficult to locate for annual follow-up. If no contact has been made for the annual follow-up, submit Form 2802. This Form must be completed each year or until the recipient is found or death is documented; then submit a Post-TED or cRF. The LTF designation on Post-TED will be replaced by this Form; please use Form 2802 instead of reporting LTF on Post-TED.

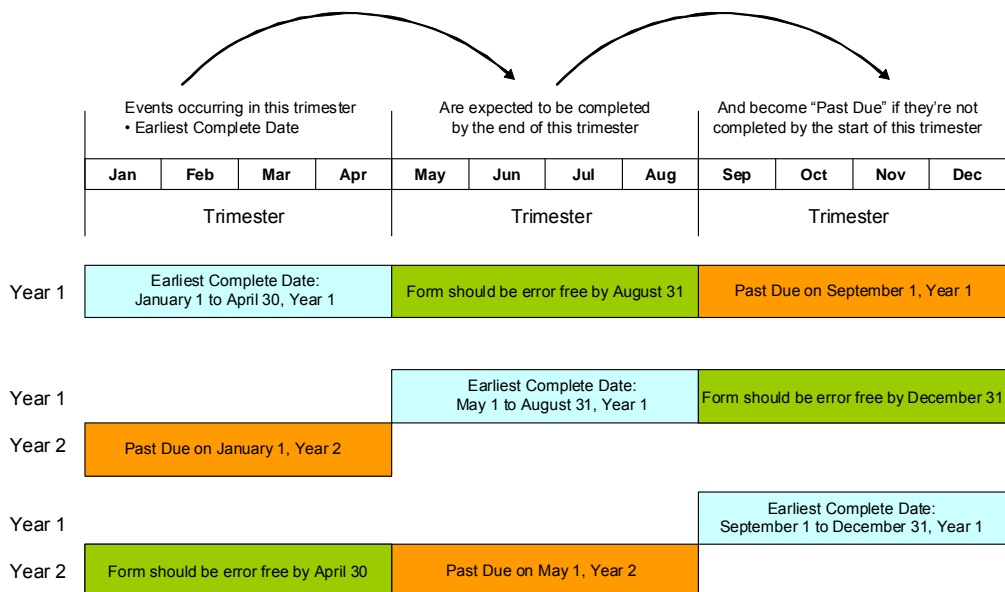
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Continuous Process Improvement (CPI)

All Forms are subject to the quality control/assurance system referred to as CPI. The Program remains unchanged and is in full effect for existing and new recipients utilizing an NMDP donor. All other recipients (existing CIBMTR and new related donor, non-NMDP unrelated donor and autologous HSCT recipients will be gradually phased in between May 2008 and April 2009).

Table 2

CPI Goal: 90% of Forms Completed for Each Trimester



November 2007

1

Please contact your liaison for questions regarding CPI.

*** All Form pieces must be 'error free' as determined by FN2.

Consent (IRB) documents must be current & on file with CIBMTR Minneapolis Data Transmission Agreement in effect.

Registration Forms Completion

Pre-TED may be completed up to two weeks prior to the start of the preparative regimen (if that is helpful to your Center), but must be completed and received by CIBMTR no later than the date of HSCT (d-0).

Post-TED is completed post-HSCT on approximately d-100, at 6 months, 1 year and annually on the HSCT anniversary as long as the recipient is alive, unless another reportable HSCT occurs, then the "clock" starts over with a new Pre-TED. CTN and Research centers will not complete Post-TED; complete a cRF for recipients on a BMT-CTN trial or those selected for comprehensive forms. If the recipient is not seen on the actual anniversary date, use the visit closest to the HSCT anniversary.

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Under new federal legislation, the SCTOD is *required* to collect outcomes data on all allogeneic transplants, related and unrelated. To meet the federal requirements, the Transplant Essential Data (TED) form has been expanded to include all necessary data elements. This revision was conducted in collaboration with the EBMT to facilitate more robust data sharing opportunities worldwide. December 3, 2007, Pre and Post-TED will be required for all related and unrelated donor transplants in the United States. Additionally, unrelated adult donor and unrelated cord blood transplants that are facilitated by the Program will require some or all of the following forms: HLA typing (HLA), graft characteristics (INF) and donor infectious disease markers (IDM). Table 3 below indicates the situations where the latter forms will require data submission directly from the transplant team, and situations where the data will be obtained from existing systems at the NMDP. These data will be used for evaluation of the Program operations, including federally required research such as analyses of center-specific outcomes and optimal registry/cord blood bank size. When appropriate, CIBMTR will share data from these forms with another registry, such as the National Cord Blood Inventory banks.

Table 3

| Situation | IDM Form | HLA Form | INF Form |
|---|------------------|--------------------------|-----------------|
| NMDP selected for cRF (any graft) | Via 'search' | Via 'search' | Yes |
| NMDP participating in the repository | Via 'search' | Via 'search' | Yes |
| NMDP UCB (TED or cRF track) | Via 'search' | Via 'search' | Yes |
| Non-NMDP selected for cRF (any graft) | Yes | Yes | Yes |
| Non-NMDP participating in repository | Yes | Yes | Yes |
| Non-NMDP unrelated adult donor U.S. citizen | Yes | Yes | Yes |
| Non-NMDP UCB (TED or cRF track) | Yes: maternal | Yes: recipient + cord | Yes |

When required, HLA and IDM Forms may be sent with Pre-TED or they can be sent with INF as a “package”, no later than two weeks post-HSCT.

Some of the sections/questions are designated as “**optional for non-U.S. Centers**”. These questions are additional to what is collected via the EBMT. We do appreciate non-U.S. centers supplying these data, if possible. MED-A contains a separate sheet for these data.

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Pre-TED

Center Identification

CIBMTR Center #: This new 5-digit number *replaces* the former 3-digit CIBMTR *Team number* and NMDP *TC code*. There is a look-up tool in FN2 to assist you if you know the old number, but not the new one. EBMT Teams submitting data via FN2 should include their CIC # (Center Identification Code) so we may cross reference both center numbers to ensure accuracy.

Hospital refers to the name of your Hospital or Transplant Center. For communication purposes it is important that you only use the official name.

Unit The letters A,H,O, & P are defined in the abbreviations on the Pre-TED Form, p2: Adult, Hematology, Oncology, Pediatric and “other”. If your center has more than one type of unit submitting data and you wish to be able to distinguish between them, tick or circle the **one option** that most differentiates their status. Only one choice should be selected. There are no definitions – it is for you to decide. You may leave this field blank if it serves no purpose.

Special information for EBMT Centers who allow transmission of MED-A data to CIBMTR: If your center has one CIC number with EBMT , but more than one CIBMTR Center number, you will need to consistently use the ‘unit’ field on MED-A as that is how your EBMT data will map to the proper recipient file in the CIBMTR database.

Contact information: The **contact person** should be the person who completed this Form or who will be able to answer queries about the data submitted. Please keep **phone #, fax #** and **E-mail address** accurate and up-to-date. We may need to contact your Center to clarify data submitted before or after we process it. On the paper version of the Form use the tick box for “**changed**” to indicate a change to one of these four fields. FN2 also contains a mechanism for updating contact changes.

Date of this Report (DOR): This represents the date the Form is in a “ready to send” state. All questions should be completed unless instructed otherwise. *Time-saving tip:* having another person look over the Form before sending will eliminate obvious errors. Note: it is no longer necessary to have the same DOR on each Form type (former CIBMTR rule) which served as the link between Form pieces to create a cRF. The HSCT number now links the pre-HSCT Forms and the indicator for follow-up period will link the post-HSCT Forms.

CIBMTR Use Only

If submitting this Form via paper (mail or fax), do not write anything in this box. We will note the date received. You will access the Forms Due Report (FDR) to determine whether a cRF is due “yes” or “no”. Please see prior section for FDR details. BMT-CTN study participants and HSCT utilizing UCB are currently *always* comprehensive Form due “yes”. (This box does not appear on FN2 screens.)

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Recipient Identification

Universal recipient ID #: This number is also known as the CIBMTR Recipient ID# (CRID) (see top of the paper version - pages 2-10). The CRID is meant to be a lifelong ID number that is used across the entire CW Bill Young system.

Recipients existing in the CIBMTR or NMDP database as of December 2, 2007 have a CRID assigned to them; you do NOT need to obtain one. To look up the new CRID use the look-up tool in FN2, utilizing:

former CIBMTR Team number plus recipient IUBMID#
OR
NMDP RID

Until your center has been invited to open the FN2 application, you will need to obtain a CRID by completing Form 2804 (UIA) and faxing it to your assigned campus (Milwaukee or Minneapolis). The recipient year of birth, gender, tentative HSCT date, disease and CRID will be E-mailed back to you. Once your center is able to access FN2 you will obtain the CRID electronically. This number replaces the CIBMTR IUBMID #. Centers *may* still assign an IUBMID if used for other purposes. NMDP Recipient ID # *will* still be assigned by NMDP for the ‘search process’. There is a look-up tool in FN2 for use with existing recipients reported prior to Dec. 3, 2007 and new entries as well.

Do NOT use the old numbers (IUBMID/UPN) in the new CRID field.

Once the data used to create the unique ID is sent to the CIBMTR, whether on paper or electronically, the primary data cannot be shared back with the center. In situations where the center wishes to confirm the unique ID generated by the CIBMTR, they may re-submit the primary data and receive a unique ID for comparison. If the same data has been entered, a “fuzzy match” for ID will be generated for the center. To protect confidentiality of personal health information, CIBMTR employees will not have access to the primary identifiers used to determine the unique ID, and therefore will be unable to answer such requests.

We recognize and respect the sensitivity of the data that is utilized for the purpose of generating the CRID. This level of identifying data is necessary to ensure that recipients already existing in the system are not assigned another number when receiving care from another facility or receiving a subsequent HSCT. The identifying data used for generating the unique ID will be stored in a secure database separate from the outcomes database. Once assigned, the unique ID will be used in all data submissions to the SCTOD and CIBMTR.

If this is not the first HSCT for the recipient, and your center did not perform the previous transplants, find out if the recipient already had a number assigned. The easiest thing to do is ask the other center for the number. In situations where this is not possible or practical, the Unique ID system will generate a possible match, based on the identifying information provided for the transplant being registered. This number may then be used for this patient, if the match is confirmed. If the match is considered “fuzzy”, directions will be provided with the unique ID. There will be a tool in FN2 to determine if a recipient already has an ID number assigned. This number stays with the recipient no matter where or how many times they are transplanted or followed. Although identifying information is needed to make sure the recipient is ONLY

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assigned one ID, these data are kept on a secure server that is separate from the database server. Also refer to the prior section Unique ID Assignment.

ID is assigned by...: If the ID is assigned by using the CIBMTR secure ID assignment server tick ‘**CIBMTR**’. If the data submitted is via the EBMT data file the **EBMT CIC** is supplied and EBMT box is ticked. We do not anticipate any ‘**other**’ at this time, but will allow future use of this tick box on an as needed basis.

Study ID#: At this time we are only interested in tracking **BMT-CTN**, **NMDP**, **RCI-BMT** and **SCTOD** study numbers. The recipient may participate in studies from other organizations and companies, but we are not collecting those study ID numbers. If a study ID is involved, take care to associate the correct study ID# with the correct study group. For instance, if the study of interest is a BMT CTN study, please check this box on the form and indicate the study ID number. FN2 allows for multiple entries. Paper submissions should have multiples entries listed in the margin or on an attached sheet.

Six spaces are provided for the study ID, e.g.:

0601 BMT-CTN: enter 0601 and tick BMT-CTN.

No study ID exists for SCTOD at this time (tick SCTOD but leave study ID blank).

HCT recipients identified as having a donor, *related or unrelated*, who is a U.S. citizen are considered participants in the SCTOD. CIBMTR, as the contractor for the SCTOD, is required to collect Registration Forms on these recipients in a timely fashion. At this time, there are no specific study IDs that should be entered for SCTOD. However, SCTOD recipients may also participate in a CTN trial, in which case that information should also be provided. Each study group that the recipient is associated with should be marked.

Consented for Research: Has the recipient, or legal guardian, signed a consent *to use their data* for research?

Note: The Office of the General Counsel, U.S. Department of Health and Human Services has determined, with the concurrence of the Office of Civil Rights, that the CIBMTR meets the Privacy Rule’s definition of a public health authority (PHA) and is authorized by law to collect the information necessary to fulfill the legislated mandate to collect data needed to assess outcomes of hematopoietic cell therapy. It is therefore not a “covered entity” under HIPAA. Additionally, transplant centers who fit the definition of covered entities may disclose certain individually identifiable health information to the CIBMTR under 45 CFR 164.512 (Privacy Rule), which allows for the disclosure of an individual’s protected health information without the individual’s written consent or authorization when such a disclosure is made to a PHA that is authorized by law to collect information for the purpose of preventing or controlling disease, injury or disability. Further information is available upon request from CIBMTR.

CIBMTR has been implementing consent procedures for submission of data since Dec of 2007. Use of data for research must have oversight from the relevant authority at each institution. This function is performed by the IRB in the United States. Until U.S. transplant centers have implemented the consent procedures outlined by the CIBMTR in Dec of 2007, prior arrangements to provide data for research to CIBMTR should remain in force. Once new IRB approved consent procedures are in place at the center, the old arrangements (such as the “data

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use agreement”) will become obsolete for submission of new data. Data submitted for research on patients transplanted before approval of the new procedures is covered by the previous procedures in place at the centers, and should not require new consent arrangements. In general, these data collected for the CIBMTR included only ‘limited data sets’ and were collected from centers that had ‘Data Use Agreements’ which included IRB oversight. Data Transmission Agreements will replace DUA’s in the new program; however, as long as the DUA hasn’t expired it remains in effect until the new DTA is finalized.

Note: consent in the new program is specifically to use the data for research. If the recipient falls under the criteria of the SCTOD and declines consent for research, TED level data (Pre and Post) is still collected. The notation regarding no consent for research will inform CIBMTR that these data cannot be used for research studies, but the data will still be used to report transplant activity for the U.S. government.

In situations where non-SCTOD recipients (e.g. autologous transplants, non-U.S. recipients or donors) decline to provide consent for research, the CIBMTR still requests that minimal data be provided by the HCT center regarding the patient. This information is very important to maintain the epidemiologic integrity of the database, and does NOT require provision of any significant personal health information that could identify the patient. The requested data are: Year of birth, diagnosis, transplant type and date of transplant

Consented for CIBMTR Related Specimen Repository: Initially this repository will involve only seven centers piloting the program. The recipient and/or donor can consent; it does **not** have to be both. If your center is not involved in the program, always answer this question ‘no’.

Gender/Date of Birth: Indicate gender as applicable, male or female. Please note the order for reporting dates: **year, month, day (yyyy/mm/dd)**.

These pieces of data are extremely valuable for helping to make sure subsequent Forms are entered to the correct recipient file. DOB likely will appear on later Forms as a means of double checking the Universal/CRID # is correct.

Ethnicity: The United States Office of Management and Budget has defined ethnicity as culturally or geographically determined, and race as inherited genetic characteristics. The distinction between Hispanic and non-Hispanic is for the purpose of the U.S. census and reporting of Program data. According to the OMB, “Hispanic” is an ethnic designation based upon where someone (or their ancestors) were raised (e.g. “Latin America”). Hispanic people can be white, black/African American, and/or native; hence the separate data field for race.

Race: The easiest and most accurate way to collect these data may be to allow the recipient to self designate this answer rather than trying to extract from the patient chart. Some Centers obtain the answer to this question and other socio-economic questions found in the cRF by grouping them into a separate sheet and giving to the recipient to complete, at their discretion, during the meeting to sign consent Forms. The reason these data are collected is to analyze access to HSCT for all people. Multi-racial people can tick all options that apply.

The detailed list from the Baseline Form is included to assist in categorizing the recipient’s race. These grouping were created by the U.S. Office of Management and Budget (OMB) for the purpose of collecting census data. For consistency of data collection, please assign the major

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race category according to the subcategories as listed even if you would have placed the subgroup in a different major category.

Table 4

| | | | |
|--|--|--|---|
| <p>White</p> <p>1 <input type="checkbox"/> Eastern European</p> <p>2 <input type="checkbox"/> Mediterranean</p> <p>3 <input type="checkbox"/> Middle Eastern</p> <p>4 <input type="checkbox"/> North Coast of Africa</p> <p>5 <input type="checkbox"/> North American</p> <p>6 <input type="checkbox"/> Northern European</p> <p>7 <input type="checkbox"/> Western European</p> <p>8 <input type="checkbox"/> White Caribbean</p> <p>9 <input type="checkbox"/> White South or Central American</p> <p>10 <input type="checkbox"/> Other White</p> | <p>Black or African American</p> <p>11 <input type="checkbox"/> African (both parents born in Africa)</p> <p>12 <input type="checkbox"/> African American</p> <p>13 <input type="checkbox"/> Black Caribbean</p> <p>14 <input type="checkbox"/> Black South or Central American</p> <p>American Indian or Alaska Native</p> <p>15 <input type="checkbox"/> Alaskan Native or Aleut</p> | <p>16 <input type="checkbox"/> North American Indian</p> <p>17 <input type="checkbox"/> American Indian, South or Central America</p> <p>18 <input type="checkbox"/> Caribbean Indian</p> <p>Asian</p> <p>19 <input type="checkbox"/> South Asian</p> <p>20 <input type="checkbox"/> Filipino (Pilipino)</p> <p>21 <input type="checkbox"/> Japanese</p> <p>22 <input type="checkbox"/> Korean</p> <p>23 <input type="checkbox"/> Chinese</p> | <p>24 <input type="checkbox"/> Vietnamese</p> <p>25 <input type="checkbox"/> Other Southeast Asian</p> <p>Native Hawaiian or Other Pacific Islander</p> <p>26 <input type="checkbox"/> Guamanian</p> <p>27 <input type="checkbox"/> Hawaiian</p> <p>28 <input type="checkbox"/> Samoan</p> <p>29 <input type="checkbox"/> Other Pacific Islander</p> <p>Decline</p> <p>30 <input type="checkbox"/> Patient declines to provide race</p> |
|--|--|--|---|

Some regional differences in reference to race and ethnicity exist around the world. Centers are requested to use their best judgment with regard to regional differences in language when completing this form. For example, Asian may be considered synonymous with Oriental in some countries.

Disease Classification

Most of the time only one **Disease Classification** sheet will be submitted. It represents the disease for which the HSCT was performed. If the recipient has more than one diagnosis that is treatable by HSCT please refer to the Table 5 to determine how to report ‘disease’, e.g. if a patient has MDS that evolves into AML before transplant, then indicate MDS subtype, transformed to AML, and AML subtype. The date of diagnosis should reflect the date for the disease that is most proximate to the date of the transplant. In this example, the date of AML should be reported in the date of diagnosis field.

Table 5

| Diagnosis combo or transforms to: Indicate as primary disease | Send these Disease Classification Sheets | Date of diagnosis |
|--|--|-----------------------|
| MDS/MPS to AML | MDS/MPS & AML | AML |
| NHL to another NHL subtype | 1 Lymphoma (transformed subtype) | 1 st NHL |
| CLL to Richter syndrome (DLCL) | Other Leukemia & Lymphoma | CLL |
| SAA and MDS/AML | Anemia/hemogl., MDS &/or AML | MDS, unless AML |
| FAN and MDS/AML | Anemia/hemogl., MDS &/or AML | MDS, unless AML |
| MYE and AMY | 1 Plasma Cell Disorders | MYE |
| CML & ALL (“blast crisis of CML”) | CML | CML |
| Indication | Include with this group | CIBMTR DX code |
| Dyskeratosis Congenita | other constitutional anemia | 319 |
| | | |
| | | |

1. Date of diagnosis of primary disease for HSCT: The date should be the first date of pathologic confirmation as most physicians will not begin treating the disease until at or after that time. The date is important when the interval between diagnosis and HSCT is significant for the prognosis.

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It may be difficult to get the precise date if it is a disease the recipient has had for a long time (e.g. 10 years). The farther away the date is, the less important a precise “day” (or sometimes even month) is. A general “date” rule for statistical purposes: if only month and year are known, use the default “day” of “15”, but only if it fits with other known data (e.g. DOB, start of treatment, etc.). If only “year” is known, use “June 15”, again only if it “fits”.

If the HSCT is a subsequent transplant for a new malignancy (or other new indication), please report the new date of diagnosis and complete a Disease Classification Sheet for the new indication. On the Post-TED there is a new, separate box to report the disease status of the first indication (only for malignant disease). Answer the more detailed disease response questions for the new indication, if malignant; no response is collected for non-malignant diseases.

EBMT Teams: please refer to the EBMT Manual for instruction regarding creating month and day when the precise date is not known.

Hematopoietic Stem Cell Transplant (HSCT)

2. Date of this HSCT: If the infusion begins one day and ends on the next, report the date of the day it was started, not ended (even if one minute before midnight). Some Centers are experimenting with combinations of cellular therapy and stem cell infusions. The first date any cellular product is infused, even if it is not the product intended for engraftment, should be the date of this HSCT. Please contact your liaison if there is any question as to what date should be the “Date of this HSCT”.

What to do when the date changed between Form submissions?: If the only Form submitted is the UIA Form, there is a process to change the date. Once Pre-TED is submitted, the date reported on Pre-TED is entered as the correct date. On occasions when Pre-TED is submitted before d-0, the infusion date that was planned may change. In this circumstance, for paper Form submission, the actual infusion date should be provided on Post-TED in the following way:

Yes No 100 Day Report Only

Is 'Date of HSCT' same as date given on Pre-TED?

Tick ‘no’ and date of HSCT will be updated to the date reported on Post-TED.

3. Chronological number of this HSCT

Note: new instructions, different from prior versions of CIBMTR, IBMTR and NMDP Report Forms:

- ◆ Count only infusions of stem cell “events”; e.g. stem cells infused on d-0, d+1 and d+2 is one HSCT event, not 3.
- ◆ NMDP used to start the Forms over any time the donor was re-collected. That will only be true in the current system if it was not part of the original “plan” as mentioned previously
- ◆ If more cells are infused after d-0 that were not part of the original plan, e.g. concern that there were not enough cells given and counts are slow to recover (“pokey graft”), this type of infusion, or “boost”, must be reported as a separate HSCT event resulting in the “HSCT clock” starting over, *unless* these cells were autologous (autologous rescue, see “reasons” 1-3 below).

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- ◆ It may be helpful to consider how the ‘reason for subsequent HSCT’ question on Form 2100 would be answered, if you had to answer it. Options 8-9 below require some caution as many times DCI is used for those indications rather than HSCT.

What was the indication for subsequent HSCT?

Subsequent autologous HSCTs performed for engraftment reasons (op be completed. All other subsequent HSCTs will require a separate follo

- 1 no hematopoietic recovery
- 2 partial hematopoietic recovery
- 3 graft failure / rejection after achieving initial hematopoietic recovery
- 4 persistent primary disease
- 5 recurrent primary disease
- 6 planned second HSCT, per protocol
- 7 new malignancy → **Complete the section on New Malignancy (**
- 8 stable, mixed chimerism
- 9 dedining chimerism
- 10 other →

| |
|----------------|
| Specify: _____ |
|----------------|

4-5. If >1, most recent previous HSCT, Date & Type: CIBMTR requests a Pre-TED for each HSCT that any given recipient received; that is why only the most recent is requested, but there may be circumstances where prior data is not known. At a minimum, we need the date and type of transplant for HSCT #1 to appropriately account for recipient’s status in our database.

6-9 Institution where previous HSCT was performed, if different from current: This information is needed to try to determine if the recipient already exists in our database. If a recipient receives two HSCTs, each at a different center and those two centers report the same person with a different CRID#, these HSCTs are not linked, creating a “duplicate” patient in the database. Please help us avoid this. We use the contact information to 1) search our database, and 2) contact the other Team for data if we do not have it. The more detailed contact information you provide, the more likely we are to ensure no duplicates exist.

10-14 Cell source for this HSCT: The three tissue types listed here *all contain stem cells*. Some refer to HSCT with peripheral blood as “peripheral blood stem cell transplant” (**PBSC**), and shorten it further to “stem cell transplant”. The distinction was created as stem cells are not normally found in the peripheral blood. Typically something must be given to the donor (allo or auto) to cause the stem cells in the bone marrow (**BM**) to “spill” into the blood for collection. That is the purpose of “priming”.

More than one tissue type may be infused in the same HSCT “procedure”, as well as combinations of cellular therapy (**Other**, specify). Please contact your liaison regarding the details when more than one cell type is infused in a short period of time (e.g. less than two weeks) if you are not certain how to record the events.

15-16 Allo HSCT – donor gender: Auto HSCT skips this question. Indicate the donor as male or female. Multiple donor-HSCT with one at least female and one male donor will check both boxes or FN2 entry check both ‘yes’.

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17-24 Donor Type: Other terms for the listed options:

17. Autologous: The recipient is their own donor.

18. Multiple: Typically multiple cords, but also could be different tissue types.

19-20 Allogeneic: The donor is a different person from the recipient.

Syngeneic: monozygotic twin (one zygote or egg, paternal twin), identical twin (not to be confused with the term HLA-identical sibling).

Web sites re: paternal twins:

<http://www.medicinenet.com/script/main/art.asp?articlekey=53949>

<http://answers.yahoo.com/question/index?qid=20061128181248AArxQ3P>

HLA-identical sibling: may include non-monozygotic twin (a.k.a. dizygotic, fraternal twin). Also includes siblings (birthdates NOT the same), BUT must have identical HLA types. Do not include half-siblings even if their HLA typing appears to be identical- report them as 'HLA matched other relatives' (if their HLA is a match), "mismatched relative" if it does not match.

HLA-matched other relative: includes all other relatives (e.g. parents, aunts, uncles, children, cousins) who are completely HLA matched. This category does NOT include adoptive or step-parents/step children (unless somehow related through DNA).

HLA-mismatched relative: includes siblings that are not HLA-identical, and all other relatives (e.g. parents, aunts, uncles, children, cousins) who have at least one HLA mismatch.

Haploidentical (haplo.) means that one half of the HLA type matches the recipient; which is extremely common between parents and children, and does NOT include adoptive or step-parents/ step children (unless somehow related through DNA).

Unrelated donor: shares no known DNA with the recipient, and is usually found through an unrelated donor registry.

21 Registry or UCB Bank: At the present time the Bone Marrow Donors Worldwide (www.bmdw.org) code has been adopted to avoid submitting the entire name and address of the registry. If completing paper Forms please visit the www.bmdw.org or use the on-line appendix for the code. FormsNet includes a drop down listing of donor registry codes.

22. Other, specify: If a code does not exist for the donor's registry, write out the proper name for the registry (suggestion: please check their Web site for the correct registry name). Supply contact information for the cord blood bank that supplied the umbilical cord blood (UCB).

23., 24. HLA A->HLA-DPB1: under the given HLA type indicate the *number of mismatches* for each HLA type (Note: a "match" = "0" mismatches). Please use the specific separate lines for testing by serology (23. antigenic) and by DNA (24. allelic). If you are not familiar with HLA typing and the terminology, there may be individuals at your center willing to act as a resource to help you understand this very important section. If not, contact your liaison for assistance.

If multiple donors are used for this HSCT, leave this section blank, *but be sure to answer donor type and the registry from which they are from.*

25. Was there Ex Vivo Graft Manipulation: other than for RBC removal or volume reduction? Ex vivo refers to "outside the body"; do not record things *done to the recipient* to affect the graft. If the only purpose of the graft manipulation was to reduce the volume of the collection (plasma

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removal) or to remove RBC's (ABO incompatibility, prevent hemolysis), tick "No" even though this is a type of graft manipulation.

26. T-cell depletion: removes some or all of the T-cells to minimize GVHD. These T-cells may be infused at a later date. Methods of T-cell depletion may include the use of antibodies. For more detail regarding methods of T-cell depletion please refer to the CIBMTR Infusion Form (2600). This method is generally only used for allo HSCT.

27. Tumor purging: removes malignant cells from the collected product. This method is only used for auto HSCT.

28. Other negative selection: removal of cells by means other than T-depletion or tumor purging; 29. specify what was done.

30. CD34 selection: also known as 'positive selection', collects cells with a CD34+ marker on the surface, as stem cells are known to be CD34+. This is commonly done with a CliniMACS/CliniMax or Isolex machine.

31. Ex vivo expansion: technique to increase the quantity of stem cells.

32. Other, 33. specify: the other 'positive selection method:

34., 35. Performance Score: 34. Indicate which scale was used. If the recipient is <16 years, please use the Lansky Play-Performance Scale for Children; if age ≥16 use Karnofsky. 35. If performance status is not quantified in the medical record, ask the physician responsible for the recipient's care. Data professionals should not attempt to assign the performance score using available medical records, but are advised to review these data with physician staff caring for the patient. Other performance score scales should be reclassified to Karnofsky-Lansky.

36., 37. CMV-antibodies: Cytomegalovirus is a viral entity to which a large proportion of the population has been exposed and which remains dormant in tissues following acute infection. Primary infection with this virus, or reactivation, can lead to significant infections and substantial complications for transplant recipients. Prior exposure to this virus, and therefore potential for reactivation, is usually tested during the pre-transplant patient and donor evaluation. 50-90% adults test + for CMV antibody but are asymptomatic. This testing is usually conducted by determining antibody titers. Positive result = 'reactive', negative = 'non-reactive', 'not done' means the test was not performed, and 'unknown' indicates you can't find the answer ("unknown" may be re-requested in the future for this question). Occasionally, reports show a specific antibody titer, which requires comparison to the reported standards for reactive or non-reactive at the center. If multiple donors are used for this HSCT, and at least one is positive, report 'reactive' on the donor line, even if the other/s donor is/are not-reactive.

Preparative Regimen

38. Was a preparative regimen given?

This section collects data pertaining to the preparative regimen given for HSCT. Treatment for the recipient's disease should not be reported in this section.

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Typical reasons for no prep-regimen include:

- 1) Diagnosis for HSCT is an immune deficiency disease which doesn't require a prep-regimen.
- 2) It is a subsequent allogeneic HSCT and the reason for the HSCT pertains to the prior graft, e.g. no ANC recovery, poor ANC recovery or the recipient had ANC recovery $>0.5 \times 10^9/L$ for three consecutive lab values and then it fell below $0.5 \times 10^9/L$ (graft failure).

It usually does NOT include subsequent infusions for chimerism problems (mixed/stable or declining). Typically DCI (lymphocytes) is used to treat issues of chimerism. If you do not understand the difference consult with the HSCT physician or contact your liaison. This concept is very important to understand in order to accurately complete these Report Forms.

39, 41. Are radiation:

Total body irradiation (TBI): The entire body received radiation, although certain fields (vital organs) may have been blocked or shielded.

Limited field: **TLI** (total lymphoid irradiation), **TNI** (total nodal irradiation) or **TAI** (total abdominal irradiation)

40, 42. What was the total prescribed cumulative dose for the radiation?:

Record total quantity of radiation administered (not the dose of each fraction). If TBI is fractionated, the dose per fraction times number of fractions equals total dose. Select the correct units, Gy or cGy, to accurately describe the total dose.

43-109 Drugs: Accurate information regarding drugs used and dosage is crucial to the evaluation of transplant regimens. The therapy recorded here must be part of the patient's transplant protocol. When completing Pre-TED for a subsequent HSCT, do not report therapy that may have been given to treat the recipient's disease between transplants in this section.

Drugs go by many names; refer to the on-line appendix to identify alternate names or ask the transplant unit pharmacist. Anthracycline, monoclonal antibody and radiolabeled monoclonal antibody are broad categories with the specific drug names listed immediately after. Only use "other, specify" when the drug really isn't represented. Do not use abbreviations unless the on-line appendix includes that abbreviation.

44-110. Report the **total dose** to be *given as prescribed in the transplant protocol or standard of care*, not the daily dose. If the dose includes a decimal, please round down to the nearest whole number if <0.5 or less, round up if ≥ 0.5 . For paper submission do not modify the number of boxes nor include decimal values.

Indicate which **units** are appropriate for the dose. If available records do not list the units as indicated on Pre-TED, please consult with the transplant pharmacist.

If the intended dose does not turn out to be the actual dose, you will NOT have to send corrected information. If the recipient is selected for cRF the actual dose received is reported in the Baseline Form (2000).

112. Is the intent of the preparative regimen (allo only) myeloablative?

NOTE: the question on the previous versions of CIBMTR Registration Forms asked the exact opposite question.

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To date there are no published definitions of non-myeloablative/reduced intensity conditioning, there exists some diversity of opinion on the topic. Answer the question based on the belief of the physician overseeing the care of the recipient at your center.

If this is a traditional stem cell transplant, the purpose of the therapy reported here is to produce marrow ablation (pancytopenia) usually for >1 month, requires a stem cell transplant for marrow reconstitution and usually produces complete donor chimerism. If these criteria are met, answer “yes”.

Non-myeloablative (NST) transplants still utilize pre-transplant conditioning; however, the purpose is to prevent rejection and suppress the recipient’s hematopoietic immune system, but not eliminate it. In general, recipient autologous hematopoietic recovery would occur following NST within 1 month without a stem cell transplant, but with stem cell transplant typically produces mixed chimerism. If these criteria are met, answer ‘no’.

Reduced Intensity Conditioning (RIC) is generally considered to be any regimen not meeting the criteria for either myeloablative and non-myeloablative. Answer ‘no’.

113-118. Reason/s for NST/RIC: Common reasons for NST-RIC include:

113. recipient age (see date of birth), 114. co-morbid conditions (see Q119-140), 115 Prior HSCT (see Q3-9), 116 specified in the protocol to do so, “117 other”, if not one of the prior reasons, and 118 specify the “other reason”.

Co-Morbid Conditions

119. Is there a history of mechanical ventilation? May impact the recipient’s pulmonary function post-HSCT.

120. Is there a history of proven invasive fungal infection? Tick ‘yes’ only if the past fungal infections could be problematic during the HSCT (e.g. a minor nail infection from many years ago was probably not clinically significant.). When in doubt consult the transplant physician as to the appropriateness of reporting.

121-140. Were there clinically significant co-existing disease or organ impairment at time of patient assessment prior to the preparative regimen? The purpose of this question is to identify serious pre-existing conditions that may affect transplant outcomes. Examples of significant coexisting diseases include diabetes mellitus, stroke, or rheumatoid arthritis. Appendix 1, **HCT Co-morbidity Index (HCT-CI)** may be used by the clinician performing the pre-HSCT evaluation of the recipient to document co-morbid conditions for use in reporting. If you answer “yes” to the main question, you must answer each condition ‘yes’, ‘no’, or ‘not done’ (the organ system was not assessed).

Use the most specific category available; definitions are found to the left of the label. Many conditions listed in the recipient’s medical history may be completely resolved and unlikely to be of importance during or after the HSCT, e.g. appendectomy. Please do not report these historic conditions in “other”. If you are unfamiliar with the appropriateness of something listed, please consult with the transplant physician.

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Follow ‘skip’ direction if the main question is answered ‘no’: allo-HSCT skips to Box A: ‘GVHD Prophylaxis’; continue to Box B. Auto-HSCT skips to Box B: ‘Post-HSCT Disease Therapy Planned as of Day-0.’

138. ANY history of malignancy, other than the disease for which the patient is being transplanted, should be reported.

GVHD Prophylaxis (allo only)

141-158. Was GVHD prophylaxis planned/given? The therapy requested in this question refers to something that is done as a preventive measure. It typically is done to all recipients as outlined in their treatment protocol. Recipients of transplants from a syngeneic donor (monozygotic or identical twin) usually do not receive GVHD prophylaxis. If GVHD prophylaxis is used for an identical twin transplant, please fax or E-mail an explanation to the liaison and request it be scanned as part of the Form documentation. Do not report agents started *after* the development of Acute GVHD (therapy) in this section. Note, the list provided is the trade name of the drug. Refer to the on-line drug appendix to identify alternate names or ask the transplant unit pharmacist.

Post-HSCT Disease Therapy Planned As Of Day 0

159. Is this HSCT part of a planned multiple (sequential) graft/HSCT protocol? Also known as ‘tandem transplant’. If a second or subsequent HSCT is planned according to the protocol at time of first (or previous if more than two) HSCT answer ‘yes’, even if the recipient does not go on to receive the second or subsequent HSCT. The use of the word “planned” here *does not* mean “if the recipient relapses we plan to re-transplant them.”

160-169. Is additional post-HSCT therapy planned? If therapy is planned according to the protocol at time of first HSCT answer ‘yes’, even if the recipient does not go on to receive it. The use of the word “planned” here *does not* mean “if the recipient relapses we plan to treat them.” Refer to the on-line appendix to identify drug names or ask the transplant unit pharmacist.

Other Toxicity Modifying Regimen

171. Was KGF (palifermin, Kepivance) started or is there a plan to use it?

172. Was FGF (velafermin) started or is there a plan to use it?

These two newer drugs sound very much alike. If one was used, please confirm which one before ticking the box. If the recipient is part of a study for KGF or FGF, so you do not know if the recipient received the drug, something else or placebo, tick “masked trial”. Once the trial is over please update the field to what actually happened via the error correction process.

Disease Classification Sheet

173. Indicate the primary disease for which the HSCT was performed: Disease classification begins with the major category (Q173), then divides into sub categories/subtype.

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WHO disease classifications have been adopted with this version Form. If you have any questions about the correct category to tick, please first provide pertinent medical record data and a copy of this Form to the transplant physician for their opinion. For further clarification please do not hesitate to contact your liaison.

General information about Disease Response:

Definition for disease response terms:

'Primary refractory (less than PR to initial therapy)' is the equivalent choice for "never CR and less than PR at this time". If the recipient was in a PR at some point and are not in PR at the time of transplant and never achieved CR prior to the transplant, they are primary refractory.

PR (partial remission): May be represented as PR1, PR2, etc. There are differing interpretations of what the number after "PR" represents:

Table 6

| | CIBMTR interpretation | Other interpretation |
|-----|--|---|
| PR1 | Without prior CR: Recipient treated for the first time->achieves PR; includes progression->treated->achieves PR, is still PR1 | First PR no matter when it occurs: Recipient treated->achieves CR->relapsed->treated->achieve PR for the first time. |
| PR2 | With prior CR: At some point the recipient was in CR->relapsed->treated->achieves PR is PR2 | Recipient was in PR->progressed (was not in PR)->treated and is in PR again. |

To avoid confusion please 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. Report PR that included a prior CR in the relapse-sensitive category and indicate which relapse (number) the recipient is in.

Acute Leukemias

Q174 Classification acute leukemias:

AML: FAB classifications are included in {brackets} for reference. CIBMTR database code for diagnosis is a three digit code included in (###). No "other" category is defined by WHO for AML.

ALL

186. Classification: Divide between precursor B-cell and precursor T-cell. If cytogenetic abnormalities present at diagnosis are among the options listed, please also tick the appropriate sub-type. No "other" category is defined by WHO for ALL.

Ambiguous lineage

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193. Classification: Neither exclusively AML or ALL, but still acute leukemia. Note: bi-phenotypic means both AML and ALL present simultaneously.

194. Other acute leukemia, specify: This category should rarely be used. If you cannot find the appropriate subtype for the recipient, please gather pertinent medical record notes for the recipient, a copy of this Form and ask the transplant physician to help select the subtype. Providing supporting documentation for this category at the time of Registration may avoid triggering a data query. For further clarification please do not hesitate to contact your liaison.

175. Did AML transform from MDS or MPS? MDS and MPS are on a continuum of disease with AML being a more aggressive phase. The prognosis for someone with prior MDS/MPS is not as promising as de novo AML. That is why it is an important distinction.

Occasionally the physician does not know the actual onset of MDS/MPS, but enough information was available at the diagnosis of AML to know that it arose from MDS/MPS. If the physician is confident the AML arose from MDS/MPS, it is obvious MDS preceded the AML so tick 'yes' and indicate MDS/MPS was diagnosed on the same day as AML.

176. Was AML therapy related? Agents to treat other diseases can damage the marrow and lead to AML. Please indicate if treatment for a prior condition may have led to AML and indicate the possible source (177-179).

180., 187., 195. Was imatinib mesylate given for pretransplant therapy anytime prior to the start of the preparative regimen? Also known as Gleevec, Glivec.

181., 188., 196. Status at Transplantation Represents the response to all prior therapy: 'Never treated' may be appropriate if the recipient had a prior disease, a transplant was in the works, AML was discovered, and a decision was made to proceed to transplant instead of treating the AML.

PIF includes as many regimens as were unsuccessfully tried; it is NOT limited to just one regimen, but is limited to 'never CR'.

For CR and relapse indicate which **number**.

CR is defined as less than 5% blasts in a cellular marrow with a normal CBC and no other signs or symptoms of (extramedullary) disease, which must be maintained for a minimum of 1 month (or it doesn't "count").

Concern has been expressed about recipients who require more than one course of therapy (to many) in order to achieve CR. This detail of data is not collected in the Pre-TED Form at this time. It is collected in the cRF where number of courses (lines of therapy) and number of cycles are collected. If the recipient is in CR at the time of transplant as indicated above, report them as CR even if it took more than one course to achieve the CR. Do NOT report them as PIF. If the "4 week" criteria has not been met as there is not 4 weeks prior to HSCT, the status would have to be modified if in fact the recipient did not 'hold' the CR for the length of time post-HSCT to meet 4 weeks.

182-183, 189-190, 197-198 For hematologic CR indicate whether it included **cytogenetic or molecular remission**.

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184/185, 191/192, 199/200 For all CR's and relapses: indicate the **number**.

Chronic Myelogenous Leukemia (CML)

201. Classification CML: In the new WHO disease classification, the diagnosis CML must include evidence, found anytime between diagnosis and the start of the prep regimen, of either the:

Philadelphia chromosome: Ph+,_t(9;22)(q34;q11) [Note: 9 and 22 refer to chromosomes and q34 and q11 refer to the breakpoints of the long arms of chromosome 9 and 22 respectively.]

Complex variation: three or more chromosomes involved in the translocation, one of which must be #22, e.g. t(3; 9; 22)

Variation form: any translocation involving 22q11 or 22.q11.2 in which CML is the suspected diagnosis, e.g. t(13; 22)(p3;q11)

OR demonstrate **bcr/abl gene rearrangement**.

Tick the combination that best describes the abnormalities identified any time between diagnosis and the start of the preparative regimen. If none of those abnormalities are found, but CML is still suspected, report in the "Other Leukemias" group under 'Atypical CML'.

202. Did recipient receive treatment prior to this HSCT? If yes, tick yes or no to all questions indicating yes to the therapy that was used between the diagnosis of CML and the start of the preparative regimen for HSCT.

204-208. Some drugs are listed specifically.

203. Not listed but is chemotherapy- "combination chemotherapy."

209-210. Does not appear on the list, is "other" and specify.

211/217. Status at Transplantation Represents the response to all prior therapy, indicate type of response and number of that response.

212. CML disease status before treatment that achieved this CR? For hematologic CR the status just prior to the start of the therapy that achieved the CR is of interest.

213, 215 Cytogenetic remission: For CR and CP only, tick whether the recipient was in complete cytogenetic remission, was not in cytogenetic remission or it is unknown (e.g. not tested).

214, 216 Molecular remission: For CR and CP only, tick whether the recipient was in molecular remission, was not in molecular remission or it is unknown (e.g. not tested).

Myelodysplastic or Myeloproliferative Diseases

218-250 Classification MDS/MPS: This disease contains a continuum of disorders and may transform from one subtype to another during the course of the disease; therefore the subtype at first diagnosis and the subtype present just prior to the start of the preparative regimen is requested. If the disease has transformed to AML, the date of diagnosis reported on paper

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version page one should be that of AML. The **MDS/MPS** diagnosis date should be reported in Q251 and also complete the **AML Disease Classification Sheet**.

Other diagnosis: **CMML** and **JMML** are reported here.

No “other” disease classification was indicated by WHO. If you cannot find the appropriate subtype for the recipient, please gather pertinent medical record notes for the recipient, a copy of this Form and ask the transplant physician to select the subtype. Providing supporting documentation for this category at the time of Registration may avoid triggering a data query. For further clarification please do not hesitate to contact your liaison.

252. Was Janus kinase 2 (jak2) gene mutation positive at any time between diagnosis and the start of the preparative regimen. This question applies to chronic myeloproliferative diseases {MPS} **Q235-250**. Jak2 is a protein tyrosine kinase of the non-receptor type that associates with the intracellular domains of cytokine receptors; JAK2 is the predominant JAK kinase activated in response to several growth factors and cytokines such as IL-3, GM-CSF and erythropoietin; it has been found to be constitutively associated with the prolactin receptor and is required for responses to gamma interferon. More information can be found at: (<http://atlasgeneticsoncology.org/Genes/JAK98.html>)

253. Was MDS/MPS therapy related? Agents to treat other diseases can damage the marrow and lead to MDS/MPS. Please indicate if treatment for a prior condition may have led to MDS/MPS and indicate the possible source **254-256**.

257. Status at Transplantation Represents the response to all prior therapy. Categories are mutually exclusive.

259/260. Indicate the number for both CR and relapse.

- 1 complete remission (CR) — requires all of the following, 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 $\geq 1000 / \text{mm}^3$ without myeloid growth factor support; platelets $\geq 100 \times 10^9/\text{L}$ without thrombopoietic support; 0% blasts
- 2 hematologic improvement (HI) — requires one measurement of the following, maintained for ≥ 8 weeks without ongoing cytotoxic therapy; specify which cell line was measured to determine HI response:
 - 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
 - HI-P — for pre-treatment platelet count of $> 20 \times 10^9/\text{L}$, platelet absolute increase of $\geq 30 \times 10^9/\text{L}$; for pre-treatment platelet count of $< 20 \times 10^9/\text{L}$, platelet absolute increase of $\geq 20 \times 10^9/\text{L}$ and $\geq 100\%$ from pre-treatment level
 - HI-N — neutrophil count increase of $\geq 100\%$ from pre-treatment level and an absolute increase of $\geq 500 / \text{mm}^3$
- 3 no response / stable disease (NR / SD) — does not meet the criteria for at least HI, but no evidence of disease progression
- 4 progression from hematologic improvement (Prog from HI) — requires at least one of the following, in the absence of another explanation (e.g., infection, bleeding, ongoing chemotherapy, etc.):
 - $\geq 50\%$ reduction from maximum response levels in granulocytes or platelets
 - reduction in hemoglobin by ≥ 1.5 g/dL
 - transfusion dependence
- 5 relapse from complete remission (Rel from CR) — requires at least one of the following:
 - return to pre-treatment bone marrow blast percentage
 - decrease of $\geq 50\%$ from maximum response levels in granulocytes or platelets
 - transfusion dependence, or hemoglobin level ≥ 1.5 g/dL lower than prior to therapy
- 6 progression to AML (AML) — $\geq 20\%$ blasts in the bone marrow

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261. JMML has a separate response list:

- complete response — normalization of WBC and organomegaly
- partial response — ≤ 50% reduction in WBC and/or organomegaly
- marginal response — between 25% and 50% reduction in WBC and organomegaly ~ or ~ partial response in WBC but no change in organomegaly ~ or ~ partial response in organomegaly but no change in WBC
- stable disease — ≤ 25% reduction in WBC and/or organomegaly
- progressive disease — increase in WBC and/or organomegaly

Other Leukemias

262. Classification Other Leukemias: Includes: atypical CML (see CML for explanation), CLL, PLL, hairy cell leukemia, and other leukemia (263. specify what the “other” is).

If you cannot find the appropriate subtype for the recipient, please gather pertinent medical record notes for the recipient, a copy of this Form and ask the transplant physician to select the subtype. Providing supporting documentation for this category at the time of Registration may avoid triggering a data query. For further clarification please do not hesitate to contact your liaison.

264. Status at Transplantation Represents the response to all prior therapy.

- complete response — no lymphadenopathy; no organomegaly; neutrophils > 1.5 x 10⁹/L; platelets > 100 x 10⁹/L; hemoglobin > 11g/dL; lymphocytes < 4 x 10⁹/L; bone marrow < 30% lymphocytes; absence of constitutional symptoms
- nodular partial response — complete response with persistent lymphoid nodules in bone marrow
- partial response — ≥ 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; one or more of the following: neutrophils ≥ 1.5 x 10⁹/L or 50% improvement over baseline, platelets > 100 x 10⁹/L or 50% improvement over baseline, hemoglobin > 11.0 g/dL or 50% improvement over baseline
- stable disease — no change; not complete response, partial response, nor progressive disease
- progressive disease — 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 10⁹/L; transformation to a more aggressive histology
- untreated — no chemotherapy given in the 6 months prior to HSCT

2013-CLL

Lymphomas

265/271. Classification Lymphoma: Both Hodgkin Lymphoma (HL) and Non-Hodgkin Lymphoma (NHL) subtypes are from WHO disease classification. NHL can transform from one NHL subtype to another, but HL does not “transform” to NHL. When NHL transforms, report the date of diagnosis as the first date of diagnosis, but the subtype is the last transformed type prior to the start of the preparative regimen. If the recipient has HL and develops NHL an important distinction is whether both diseases are considered active. If HL is believed to be in remission, then it is appropriate to report NHL the same as though the recipient had any other prior malignancy in a historical sense. If both are “active” this is one example of an appropriate use of the diagnosis code “900” (see paper version page 6)

| |
|-----------------------------|
| “OTHER” DISEASE |
| <i>Specify (900):</i> _____ |

Note: Waldenstrom Macroglobulinemia previously had been collected in the PCD section. It now is listed with Lymphoma. It is the same disorder, just a new location.

If you cannot find the appropriate subtype for the recipient, please gather pertinent medical record notes for the recipient, a copy of this Form and ask the transplant physician to select the

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subtype. Providing supporting documentation for this category at the time of Registration may avoid triggering a data query. For further clarification please do not hesitate to contact your liaison.

266/275. Status at Transplantation Represents the response to all prior therapy, through all transformations.

Never treated = disease untreated

Primary refractory (less than PR to initial therapy) = PIF res

Partial response (PR)- see explanation at beginning of Disease Classification section (just after Q173).

276. Without prior CR. With prior CR = relapse sensitive- indicate as Rel-sens and indicate which number relapse.

CR confirmed

277. Number = CR1, CR2, CR3+

CR unconfirmed (CRU- complete response with persistent scan abnormalities of undetermined significance)

277. Number = CRU1, CRU2, CRU3+

Rel (relapse)

278. Number

279. Sensitivity to chemotherapy- see detailed definitions below.

Sensitivity to chemotherapy is defined as:

sensitive – $\geq 50\%$ reduction in the bidimensional 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 res, REL res*)

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

unknown (*PIF unk, REL unk*)

It is measured based on the last therapy given. If the last therapy was not chemo, it should be reported as PIF/relapse “untreated” (by chemotherapy).

disease untreated

PIF res Primary induction failure – resistant: NEVER in COMPLETE remission but with stable or progressive disease on treatment

PIF sen / PR1 Primary induction failure – sensitive: NEVER in COMPLETE remission but with partial remission on treatment

PIF unk Primary induction failure – sensitivity unknown

CR1 1st complete remission: no bone marrow or extramedullary relapse prior to transplant

CR2 2nd complete remission

CR3+ 3rd or subsequent complete remission

CRU1 1st complete remission undetermined: as above with the exception of persistent scan abnormalities of unknown significance

CRU2 2nd complete remission undetermined

CRU3+ 3rd or subsequent complete remission undetermined

REL1 unt 1st relapse-untreated: includes either bone marrow or extramedullary relapse

REL1 res 1st relapse-resistant: stable or progressive disease with treatment

REL1 sen 1st relapse-sensitive: partial remission (if complete remission was achieved, classify as CR2, code 6)

REL1 unk 1st relapse-sensitivity unknown

REL2 unt 2nd relapse-untreated: includes either bone marrow or extramedullary relapse

REL2 res 2nd relapse-resistant: stable or progressive disease with treatment

REL2 sen 2nd relapse-sensitive: partial remission (if complete remission achieved, classify as CR3+, code 7)

REL2 unk 2nd relapse-sensitivity unknown

REL3+ unt 3rd or subsequent relapse-untreated: includes either bone marrow or extramedullary relapse

REL3+ res 3rd or subsequent relapse-resistant: stable or progressive disease with treatment

REL3+ sen 3rd or subsequent relapse-sensitive: partial remission (if complete remission achieved, classify as CR3+, code 7)

REL3+ unk 3rd relapse or greater-sensitivity unknown

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Plasma Cell Disorders

280. Classification Plasma Cell Disorders: Please report the appropriate plasma cell disorder subtype. If the recipient had more than one disorder, either sequentially or at the same time, see Table 7 and, please report the most recent (multiple myeloma = MYE):

Table 7

| Diagnosis combination: | Report as: | Date Diagnosis |
|----------------------------------|-------------------|-----------------------|
| Plasmacytoma first, now has MYE | MYE | MYE |
| MYE + plasma cell leukemia (PCL) | PCL | PCL |
| MYE + amyloidosis | MYE | MYE |

Report the heavy chain sub-type (IgG, IgA, IgD, IgE, or IgM)

281. light chain (kappa or lambda). “Light chain only” disease will be kappa or lambda, but not one of the “Ig’s”.

“Non-secretory” will not show either an Ig or kappa/lambda.

“Primary Amyloidosis” Use only if the recipient has NO evidence of multiple myeloma.

In *very rare* instances a recipient could have two heavy chain types. That is a proper use of **287.**

“other PCD”. If this is a subsequent HSCT and the two subtypes did not exist prior to the first HSCT, double check with the transplant physician as this could represent oligoclonal reconstitution, not a second sub-type.

If you cannot find the appropriate subtype for the recipient, please gather pertinent medical record notes for the recipient, a copy of this Form and ask the transplant physician to select the subtype. Providing supporting documentation for this category at the time of Registration may avoid triggering a data query. For further clarification please do not hesitate to contact your liaison.

Stage at diagnosis:

You may report either

282-283. Salmon & Durie or the newer

284-286. I.S.S. (International Staging System). If I.S.S., report either the lab values (284-285) from diagnosis or the stage (286) based upon those values.

Status at Transplantation

288-289. Represents the response to all prior therapy

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Response Codes

Stringent complete response (sCR) — CR as defined below, plus:

- normal free light chain ratio, and
- 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 made at any time before the institution of any new therapy, and no known evidence of progressive or new bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy sCR requirements.

Complete response (CR) — negative immunofixation on serum and urine samples, and disappearance of any soft tissue plasmacytomas, and $\leq 5\%$ plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed).

CR requires two consecutive assessments made at any time before the institution of any new therapy, and no known evidence of progressive or new bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy CR requirements.

Very good partial response (VGPR) — serum and urine M-protein detectable by immunofixation but not on electrophoresis, or $\geq 90\%$ reduction in serum M-protein and urine M-protein level < 100 mg/24 hours

VGPR requires two consecutive assessments made at any time before the institution of any new therapy, and no known evidence of progressive or new bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy VGPR requirements.

Partial response (PR) — $\geq 50\%$ reduction in serum M-protein, and reduction in 24-hour urinary M-protein by $\geq 90\%$ or to < 200 mg/24 hours.

If the serum and urine M-protein are unmeasurable (i.e., do not meet any of the following criteria: • serum M-protein ≥ 1 g/dL • urine M-protein ≥ 200 mg/24 hours • serum free light chain assay shows involved level ≥ 10 mg/dL, provided serum free light chain ratio is abnormal), a $\geq 50\%$ decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria. If serum and urine M-protein are unmeasurable, and serum free light assay is also unmeasurable, a $\geq 50\%$ reduction in plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was $\geq 30\%$. In addition to the above listed criteria, a $\geq 50\%$ reduction in the size of soft tissue plasmacytomas is also required, if present at baseline.

PR requires two consecutive assessments made at any time before the institution of any new therapy, and no known evidence of progressive or new bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy PR requirements.

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Stable disease (SD) — not meeting the criteria for CR, VGPR, PR or PD.

SD requires two consecutive assessments made at any time before the institution of any new therapy, and no known evidence of progressive or new bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy SD requirements.

Progressive disease (PD) — requires any one or more of the following:

Increase of $\geq 25\%$ from baseline in:

- serum M-component and/or (absolute increase ≥ 0.5 g/dL) (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient to define relapse if the starting M-component is ≥ 5 g/dL)
- urine M-component and/or (absolute increase ≥ 200 mg/24 hours)
- for recipients without measurable serum and urine M-protein levels: the difference between involved and uninvolved free light chain levels (absolute increase > 10 mg/dL)
- bone marrow plasma cell percentage (absolute percentage $\geq 10\%$) (relapse from CR has a 5% cutoff vs. 10% for other categories of relapse)
- 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
- 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 made at any time before classification as disease progression, and/or the institution of any new therapy.

Clinical relapse (CRel) — requires one or more of the following:

Direct indicators of increasing disease and/or end organ dysfunction (CRAB features) listed below; for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient to define relapse if the starting M-component is ≥ 5 g/dL.

- development of new soft tissue plasmacytomas or bone lesions
- definite increase in the size of existing plasmacytomas or bone lesions. A definite increase is defined as $\geq 50\%$ (and at least 1 cm) increase as measured serially by the sum of the products of the cross-diameters of the measurable lesion.
- hypercalcemia (> 11.5 mg/dL or 2.65 mmol)
- decrease in hemoglobin of ≥ 2 g/dL or 1.25 mmol
- rise in serum creatinine by ≥ 2 mg/dL or 177 $\mu\text{mol/L}$

CR requires two consecutive assessments made at any time before classification as relapse, and/or the institution of any new therapy.

Relapse from CR (Rel) — requires one or more of the following:

- reappearance of serum or urine M-protein by immunofixation or electrophoresis
- development of $\geq 5\%$ plasma cells in the bone marrow (relapse from CR has a 5% cutoff vs. 10% for other categories of relapse)
- appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia)

Rel requires two consecutive assessments made at any time before classification as relapse, and/or the institution of any new therapy.

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Breast Cancer

290. Classification, Breast Cancer: An important characteristic for disease prognosis is whether the breast cancer is inflammatory (dermal/lymphatic invasion) or not. If not readily documented, please ask the transplant physician, who likely knows and append the medical record.

- Inflammatory (251)
- Non-inflammatory (252)

291. Stage at Diagnosis: This staging system was designed by the American Joint Committee on Cancer (1988) and is found on the cRF Breast Cancer Pre-HSCT Disease Form. The letters T, N, M refer to Primary Tumor, Lymph Node location and Distant Metastasis. The subscript numbers represent the code for the individual measurements for TNM, and when combined reveal the stage: I-IV. On Pre-TED if Stage IV is indicated at diagnosis, skip “stage” and report as metastatic in the next question..

- 0 In situ
- 1 I - $T_1 N_0 M_0$
- 2 II - $T_{0,1} N_1 M_0$ or $T_2 N_{0,1} M_0$ or $T_3 N_0 M_0$
- 3 IIIA - $T_{0-2} N_2 M_0$ or $T_3 N_{1-2} M_0$
- 4 IIIB - $T_4 N_{Any} M_0$, $T_{Any} N_3 M_0$, Inflammatory
- 5 IV - $T_{Any} N_{Any} M_1$

292. Metastases M1 = distant metastasis (includes metastasis to ipsilateral supraclavicular lymph nodes) = metastatic, all others = no distant metastasis.

293. Status at Transplantation Represents the response to *all* prior therapy

Adjuvant is appropriate only when diagnosed as Stage II or III, surgery removed all known disease and no relapse occurred prior to the start of the preparative regimen.

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, which should be fairly rare.

Primary refractory means a complete remission was never achieved no matter how many lines of therapy were used and is analogous to ‘no response’ below.

Complete remission is complete disappearance of all known disease for ≥ 4 weeks and is synonymous with complete response.

294. CR specify:

CR confirmed- all known sites of disease are gone.

CR unconfirmed – stands for complete response with persistent scan abnormalities of unknown significance. This means something still appears on a pathology report, however it is small, not growing and is being given the benefit of the doubt that it is scar tissue, which will likely never go away.

295. CR Number

1st = 1st CR

2nd = 2nd CR

3rd or higher = 3rd CR or more.

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First partial response (PR1) is reserved for “never in CR”, but a PR was achieved and maintained at the time of the preparative regimen. $\geq 50\%$ reduction in greatest diameter of all sites of known disease and no new sites of disease for ≥ 4 weeks. Please review explanation in the General information about Disease Response section just after Q173.

Relapse should only be used after CR is achieved.

296. Relapse Specify

The site of the relapse present just prior to the start of the preparative regimen was local (same side breast or local lymph nodes) or metastatic (body part other than the same side breast or distant lymph nodes).

297. Relapse Number

1st relapse indicates one prior CR, 2nd relapse indicates two prior CR's, 3rd or higher – three or more CR's followed by relapse. Do not include the status of PR when calculating the number of relapses.

298. Sensitivity to chemotherapy is defined as:

What was sensitivity of breast cancer to chemotherapy prior to conditioning? (*Response to last chemotherapy given prior to transplant; chemotherapy must include ≥ 2 cycles treatment given ≤ 6 months prior to transplant*)

- 1 Sensitive: $\geq 50\%$ reduction in bidimensional diameter of all disease sites with no new sites of disease
- 2 Resistant: $< 50\%$ reduction in diameter of all disease sites or development of new disease sites
- 3 Untreated
- 8 Unknown

It is measured based on the last therapy given. If the last therapy was not chemo, it should be reported as “untreated” (by chemotherapy).

Complete response: complete disappearance of all known disease for ≥ 4 weeks

Complete response with persistent bone scan/x-ray abnormalities of unknown significance

Partial response: $\geq 50\%$ reduction in greatest diameter of all sites of known disease and no new sites of disease for ≥ 4 weeks

No response: $< 50\%$ reduction in greatest diameter of all sites of known disease and no new sites of disease

“Other” Disease

299. Classification: Other disease specify: This category should be used very infrequently such that we ask you: *Before using this category, please check with transplant physician whether the diagnosis can be classified among options on Disease Classification Paper version pages 3-10.* If the indication is “alternative HCT” check the appropriate box in Q301 and leave Q299 blank.

300. For any "other" disease: Is a pathology report attached to this form? Appending pathology documents will minimize our need to contact you in the future regarding the diagnosis of this recipient. All patient identifiers should be masked (covered or marked out) prior to sending, however, be sure to note your CIBMTR Center Number and the recipient's Unique ID. Do not mask dates.

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301. Alternative HCT: If the cell infusion is for one of the newer “alternative” uses of cell therapy, please indicate the purpose: _____

Alternative HCT:

- Cardiac regeneration
- Neurologic regeneration
- Tolerance Induction Pre-solid Organ Transplant
- Other, specify: _____

Cardiac regeneration may restore heart muscle after heart attack, neurologic regeneration may restore brain function or tolerance induction, e.g. giving some donor stem cells from the donor of some other solid organ to minimize graft rejection and immunosuppressive therapy.

Other Malignancies

303. Classification, Other Malignancies: Most of these malignancies are solid tumors, the most common indications represented. Very rare indications should be reported as “other”. Over time if they become common they will be added as a separate category. The sarcoma group has undergone some updating. Germ cell tumors that originate in the ovary or testes should be reported as Ovarian or Testicular, respectively. Breast Cancer is not included here as it has its own section. If you do not find the sarcoma subtype listed in the recipient’s medical record among this list, please double check with the physician before using “other”; the subtype may just have a new name.

304. Classification, Other Malignancies Specify: If you cannot find the appropriate subtype for the recipient, please gather pertinent medical record notes for the recipient, a copy of this Form and ask the transplant physician to select the subtype. Providing supporting documentation for this category at the time of Registration may avoid triggering a data query. For further clarification please do not hesitate to contact your liaison.

305. Status at Transplantation Represents the response to *all* prior therapy. Please check the definitions (BOTH RECIST and not) provided in the appropriate Disease Form at www.cibmtr.org

306. Status at transplantation, PR, specify: Without prior CR or with prior CR. Please see section at General information about Disease Response (just after Q173).

307. Response Evaluation Criteria in Solid Tumors (RECIST) was used for this status evaluation? Some disease categories have changed to using RECIST criteria, which is listed for your convenience. Please tick ‘yes’ if the status you are indicating represents RECIST criteria.

308. Number (complete for CR, CRU and relapse).

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309. Sensitivity to chemotherapy, complete only for relapse is defined as:

Sensitive: $\geq 50\%$ reduction in bidimensional diameter of all disease sites with no new sites of disease

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

Untreated

Unknown

It is measured after the last chemotherapy given. If the last therapy was not chemo, it should be reported as “untreated” (by chemotherapy).

Non-Malignant Disorders

Classification:

Only the disease subtype is reported. No status of disease pre-HSCT or post-HSCT is collected for non-malignant disease; just a few test results for some of the autoimmune diseases.

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Post-TED

General Information

Post-TED paper version contains an important instruction in the header:

Post-Transplant Essential Data

Note: “>100 Days Report” answer *since last report*

= symbol for answer that is only valid on >d100 evaluation.

As this single Form is used for time points after d-100 there are some answers that are not appropriate for the first time follow-up is submitted. On the paper version these answers are designated by a circle instead of a square tick box.

Optional for non-U.S. Centers

Some of the sections/questions are designated as “optional for non-U.S. Centers”. These questions are additional to what is collected via the EBMT. We do appreciate non-U.S. centers supplying these data if possible.

Center Identification

See Pre-TED section.

When to submit?

This single Form is used for ‘TED track only’ or ‘No cRF due’ recipients at three time points post-HSCT:

Day-100

6 months (new for CIBMTR for HSCT on or after Dec 3, 2007)

Annual, specify year (HSCT anniversary)

The paper version of Post-TED contains an extra box “FU visit” which should not be used.

Note: the structure of TED data is such that it should fit on a timeline with a distinct start and stop date that does not over lap another Form, with one exception: in the event of a subsequent HSCT (Pre-TED), e.g. post-HSCT period for HSCT X will overlap with the patient status evaluation just prior to HSCT Y.

Did the recipient receive a subsequent HSCT since the date of contact from the last Report?

The only subsequent infusion that will NOT start the TED Forms over is an autologous re-infusion for a reason relating to the graft, e.g. no ANC recovery, poor ANC recovery (>0<500) or loss of ANC recovery (achieved >500 ANC for 3 consecutive labs, but fell below for 3 consecutive labs (a.k.a. graft failure). These infusions are not intended to treat the recipient’s disease but rather to buy time (also known as autologous rescues). All other subsequent infusions will be reported by completing a new Pre-TED Form. The most recent HSCT date will be used to determine when subsequent Follow-up Forms are due.

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CIBMTR Use Only

See Pre-TED section.

Recipient Identification

See Pre-TED section.

Disease: Please make sure the diagnosis reported here is the same one used on the Pre-TED Form. The CIBMTR database code for diagnosis is included after the disease label. e.g.

AML with t(8;21)(q22;q22), (AML1/ETO) (281) . You may use the diagnosis code (e.g. 281) instead of writing out the diagnosis. FN2 will provide a drop down box.

Hematopoietic Stem Cell Transplant (HSCT)

Donor type: Indicate whether the type of HSCT for the current Post-TED was allo or auto.

Chronological number of this HSCT# DCI#:

Past reporting for CIBMTR chronologic HSCT # included the count of DCI as that was the only way to include DCI reporting in the database. That has been resolved thus the count should now be separated.

Once a recipient receives at least one dose of the preparative regimen, a Post-TED Form must be completed, even if the recipient does not go on to be infused, receives a subsequent HSCT or dies before day-100. Contact your liaison for instructions when the recipient starts the prep regimen but the infusion is postponed.

The only subsequent infusion that will NOT start the TED Forms over is an autologous re-infusion for a reason relating to the graft, e.g. no ANC recovery, poor ANC recovery (>0<500) or loss of ANC recovery (achieved >500 ANC for 3 consecutive labs, but fell below for 3 consecutive labs (a.k.a. graft failure). These infusions are not intended to treat the recipient's disease but rather to buy time (also known as autologous rescues).

How to count the number of DCI's? Look at paper version page two in the DCI section. From Q76 "Total # DCI in 10 weeks" add all the DCI's that would be reported from each DCI reporting box, e.g. DCI infused at 80 and 90 days post-HSCT (from Day-100 Report) and again at 380 and 390 days (from 2nd year Report) = 4 DCI [not 2] on 2nd year Report.

Date HSCT for follow-up: Report the date of the HSCT represented for this follow-up Form. When a subsequent HSCT takes place, the last contact date for the Post-TED prior to the new HSCT should be one day prior to the start of the preparative regimen for the next HSCT or one day prior to the subsequent HSCT when no preparative regimen is used. Follow-up reporting for the prior HSCT is then complete; continue follow-up reporting only on the latest HSCT. Be sure to use the correct HSCT date for the time period you are reporting on.

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100 Day Report Only

1. Is 'Date of HSCT' same as date given on Pre-TED? The time line for reporting a recipient begins with the first dose of the preparative regimen. As centers are able to register recipients prior to the start of the preparative regimen (if it benefits your center to do so), we understand that occasionally the transplant will be delayed or not take place altogether. This is the mechanism to convey when there has been a change. The date does not need to be corrected in the Unique ID Assignment section as it will only be compared to the Pre-TED.

2. Was HSCT Infusion given? If No.: If yes, continue to "Initial ANC Recovery" section Q.6. If no, next question.

3. At least 1 dose of the prep regimen was given? If Yes.:

If no, stop completing the Form and submit. If yes, continue with remaining questions Q's to # 4-7:

Patient died during prep regimen?

This HSCT is cancelled?

This HSCT is postponed?

New estimated date: _____ - _____ - _____
 YYYY MM DD

If (Q4,5) recipient died/HSCT cancelled, skip to Q26-39 (survival and COD) and submit the Form.

If (Q6) HSCT is postponed and it is HSCT #1, go to Q26/27 and submit Form. If the recipient goes on to have the infusion, an adjustment in HSCT number will be made to indicate the new HSCT is HSCT#1. The portion of prep. regimen given for the abandoned HSCT will be collected as treatment for disease (if comprehensive Report Form is collected). Date prep regimen began becomes the date for the regimen given for the HSCT the recipient actually received.

If (Q6) HSCT is postponed and it is \geq SCT #2, complete post-HSCT information as usual for prior HSCT.

Initial ANC Recovery

ANC refers to the Absolute Neutrophil Count, a subset of the granulocytes, demonstrated in peripheral blood (CBC). Commonly reported units are $500/\text{mm}^3 = 0.5 \times 10^9/\text{L}$. ANC recovery is defined as achieving $>0.5 \times 10^9/\text{L}$ neutrophils ("segmented neutrophils + band neutrophils", or "segs & bands") for three (3) consecutive labs tested on different days*.

Calculating the absolute count from a differential:

Differential: the relative number of each type of white blood cell in the blood sample typically expressed as a percentage. Do not report the percentage values from a differential. If the absolute neutrophil count is not given, convert the differential as follows:

(% neutrophils times total WBC) divided by 100 = absolute neutrophils. If the segs and bands are reported individually, add them together before doing the calculation:

$\text{WBC } 5,400/\text{mm}^3$ with 70% segs + 3% bands = $0.73 \times 5.4 = 3.942 \times 10^9/\text{L}$ ANC.

*Traditionally, the definition of neutrophil engraftment required selecting the first date of three consecutive days in which the recipient's ANC was $\geq 500/\text{mm}^3$ ($0.5 \times 10^9/\text{L}$). For various reasons

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it may not be possible to obtain daily lab values. Under those circumstances you may report neutrophil recovery based upon three consecutive lab values that are more than a day apart as long as the counts show a continual increase, not counts going up and down.

The count may reflect stimulation from growth factors, or irradiated granulocytes, but any infusion intended to “boost” the hematopoietic recovery should be reported as a subsequent HCT.

8. Initial ANC recovery- Was $>0.5 \times 10^9/L$ achieved for 3 consecutive labs?: ‘Yes’

9. First date of 3 labs’ If $\geq 0.5 \times 10^9/L$ is met by the stated criteria, tick ‘yes’ and report the first date of the three consecutive labs.

‘No’

10. Last assessment’ If not met, tick ‘no’ and report the latest date of assessment.

‘Never below’

Once the preparative regimen is started, it takes some time for the recipient’s counts to drop; be sure to locate the lowest count (nadir) before checking the lab reports for recovery. If the recipient was transplanted for an Immune Deficiency or the preparative regimen was non-myeloablative (NST) or reduced intensity (RIC), the counts may never have been below $0.5 \times 10^9/L$. However, if the ANC was ever less than 500, this option must not be checked.

‘Previously reported’

Once $\geq 0.5 \times 10^9/L$ has been achieved and reported the tick circle ‘previously reported’ may be used. If the level has not been achieved, continue to tick ‘no’ and report the latest date assessed.

‘Unknown’

As ANC recovery is fundamental to successful HSCT, this answer should rarely be used. It is imperative that every effort be made to track these data for the recipient.

Engraftment: to demonstrate *engraftment* for allogeneic recipients, particularly non-ablative or reduced intensity approaches, chimerism tests must be done. These measure the quantity of donor cells compared to host (recipient) cells. While ANC usually represents donor cells in allogeneic HCT, it cannot be proven without chimerism studies.

11. Did graft failure occur? Graft failure is defined as a decline in ANC to $<500/mm^3$ ($0.5 \times 10^9/L$) for three consecutive days. It may be due to drugs, infection (especially CMV), GVHD and other etiologies. (Note: “failure to engraft”, which is slightly different, is represented by answering ‘no’ to *initial ANC recovery*.)

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Initial Platelet Recovery

(Optional for non-U.S. centers)

12. Initial platelet recovery- Was $\geq 20 \times 10^9/L$ achieved for 3 consecutive labs, with no platelet transfusions in the prior 7 days?: Platelets, also a subset of WBC, derived from megakaryocytes in the bone marrow, are the cells responsible for blood coagulation, hemostasis and blood thrombus formation. This section refers to the first time (“initial”) ≥ 20 is achieved, NOT subsequent recovery after a drop. This recovery may take place after the recipient has returned back to the care of their referring physician; therefore, a relationship should be established in advance such that the physician understands the importance of collecting and sharing this data with your center.

‘Yes’

13. Date platelet $\geq 20 \times 10^9/L$ achieved must be at least seven days following the last platelet transfusion and the first date of three consecutive lab values tested on different days that show that level was achieved and maintained.

‘No’

14. Date of last assessment if not achieved, unsupported by platelet transfusions as described in Q12.

‘Never below’

Once the preparative regimen is started, it takes some time for the recipient’s counts to drop; be sure to locate the lowest count (nadir) before checking the labs for recovery. If below for just 1 reading you may not use this option.

‘Previously reported’

Once $\geq 20 \times 10^9/L$ has been achieved *and reported* the ‘previously reported’ option may be used. If the level has not been achieved, continue to tick ‘no’ and report the latest date assessed.

‘Unknown’

It is imperative that every effort be made to track this data for the recipient.

GVHD (allo only)

Graft versus host disease (GVHD) is an immunological phenomenon resulting from the reaction of donor immune cells against major or minor histocompatibility antigens of the recipient. It is primarily mediated by donor derived T cells. Very rarely, GVHD may occur due to autologous reactivity (autologous GVHD), third party transfusions, or with identical twin transplantation. Factors influencing the severity of GVHD are related to three main categories: donor/graft, recipient and treatment-related. The most influential donor/graft factor is the degree of genetic disparity between the donor and the recipient (HLA), but other risk factors include female donor to male recipient, parity, older donors, and T-cell dose. The occurrence of aGVHD becomes a risk factor for the development of cGVHD. Recipient age is also a factor along with prior infections. The treatment related factors include an intense preparative regimen and inadequate post-HSCT immune suppression (GVHD prophylaxis).

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In the past, GVHD was classified into acute or chronic on the basis of its time to diagnosis following transplant, and other clinical and histological (biopsy or post-mortem) features. Today there has been increased recognition that acute and chronic GVHD are not dependent upon time since HCT, so determination of acute or chronic should rest on clinical and histologic features. However, organ staging and overall grade should only be calculated from the clinical picture, not histology.

Acute GVHD usually begins between 10 and 40 days after HSCT but can appear earlier or later. It occurs in 20-40% of non-T-cell depleted HLA identical sibling transplants. The rate is higher for transplants from mismatched family donors and unrelated donors. The organs usually affected are the skin, gut or liver although other sites (e.g. conjunctiva) may be involved.

15. Maximum grade of acute GVHD: Please note: this scale is based on *clinical evidence* (physician observation), not histology. If there is a difference in the clinical grade recorded by the physician and a histologic report, use the data from the clinical documentation noting the difference as a ‘Report Note’ if you wish. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, *overall grading remains clinical* and is based on the criteria published by Thomas et al, N Engl J Med 1975. Report the maximum grade of aGVHD present during the reporting period represented by this Post-TED, not the maximum ever. If aGVHD was present, but the maximum grade was not documented, tick **present** (but) **grade unknown**. Please make sure referring physicians understand the importance of conveying these data to your Center.

16. Maximum extent of chronic GVHD during this period: Chronic GVHD can occur following acute GVHD or *de novo* (without prior evidence of aGVHD) and affects 25-50% of long-term survivors of allogeneic transplants. It usually develops after day 100, but has been documented as occurring as early as day 60 and as late as day 400 post-HSCT. The mechanism of tissue damage differs from acute GVHD and a greater variety of organs are affected. There is a simple staging system for grading severity as limited or extensive.

Although according to strict criteria, recipients must have at least skin and/or liver involvement to be considered “extensive”, involvement of any other target organ has generally also met the definition. For example, a recipient with only eye involvement or only mouth involvement would still be considered “extensive.” Note that recipients with limited chronic GVHD can **ONLY** have skin and/or liver involvement since other manifestations make them “extensive.”

Reporting Stage of Chronic GVHD (Blood 1981; 57:267) KM Sullivan

Limited: Localized skin involvement resembling localized scleroderma with or without liver involvement; no other organ involvement.

Extensive: Generalized skin and/or multiple organ involvement

17. Date of diagnosis of chronic GVHD: Report the date of clinical diagnosis recorded in the recipient’s medical record, or if not recorded, you may use the date of histologic confirmation. The date of diagnosis is not necessarily the same as the date that symptoms began. Between recipient visits the symptoms of GVHD may change from those of acute GVHD to chronic. Best efforts should be made to assign the date of diagnosis, as this is an important outcome.

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If this is a Follow-Up Report Form and the recipient had chronic GVHD that resolved for at least 30 days, but has reactivated (“flair”); report the new episode and list the new date of diagnosis.

18. Continued from last report: If the episode continues from one report to another tick ‘continued from last report.’

Did A New Malignancy, Lymphoproliferative or Myeloproliferative Disorder Occur?

19. Did a new malignancy, lymphoproliferative or myeloproliferative disorder occur? Different from the disease for which HSCT performed (not recurrence of transformation).

20. Date of diagnosis: Should be the date of the pathology report confirming the new malignancy.

21. New malignancy diagnosis: Please be sure to differentiate between disease that has relapsed and a *de novo* (“first time”) malignant process diagnosed post-HSCT. Do not report a history of a malignancy diagnosed before the first transplant and now relapsed. Report all new cancers including skin cancers (basal, squamous, melanoma,) new leukemia, myelodysplasia, solid tumor and lymphoproliferative disorders. Cytogenetic abnormalities that appear post-HSCT, but are known to be associated with the pre-HSCT diagnosis should be reported as relapse of the disease and not as a new malignancy for this question. For breast cancer found in the contralateral breast, please report as “relapse of breast cancer” as that is where we will look for these recipients at the time of any studies. Note: PTLN (posttransplant lymphoproliferative disorder) is collected in lymphoma or lymphoproliferative disease, not “other”.

Paper submission of new malignancy: if >1 new malignancy occurred in a single reporting period (e.g. basal cell carcinoma), copy the page and report individually as many times as occurred, labeling 2nd, 3rd, etc.

22. Other leukemia (including ALL) specify. Do not report AML/ANLL here.

23. Is the tumor EBV positive?

24. Other malignancy specify. Review specific subtype options. If specific option cannot be located check with physician who oversaw care of recipient and ask them to determine if specific subtype is listed. Only use this option if a more appropriate answer is not available.

25. Copy of pathology report/documentation attached? Prior studies of second cancers required confirmation that the reported new malignancy was in fact new. Attaching a copy of the de-identified pathology report from the new malignancy diagnosis assists this confirmation. Be sure to re-label the top of the page with CIBMTR Center # and CRID. If using FN2 for data submission please submit the copy via fax or postal mail.

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Survival

26. Survival status at latest follow-up: If only month and year are known, you may estimate the “day” or use “15” (but only if it is compatible with other known dates). If only year is known use “June 15” (but only if it is compatible with other known dates) and tick “Date estimated”.

Alive:

27. Latest follow-up: Date of last actual contact with recipient to determine medical status for this report should be based upon physician contact, which includes the transplant center, referring physician, or other physician currently assuming responsibility for the recipient’s care. We understand this may become difficult the further out from HSCT the recipient becomes.

- If an evaluation was not actually performed on Day 100, 6 months or HSCT anniversary by the transplant center or the physician assuming the recipient’s care, choose the visit as close to Day-100, 6 months or HSCT anniversary as possible.
- Questions referring to “current” data should be interpreted as “current for the reporting period represented by the Form.”
- Information after the last contact date for this Report Form should be recorded on the next Form.

Dead:

28. Latest follow-up: Report the date of death. If precise date is not known please contact your liaison who may be able to utilize resources to find the date.

Lost-to-Follow-Up: Note this status will be removed from Post-TED

29. Last known date alive.

- Information up to the date last known alive should be reported on Post-TED. After that point utilize Lost to Follow-Up Form 2802. Renew 2802 annually as long as appropriate.
- Recipient’s with this status remain on the “Forms Due – yes” report as a reminder should any additional information become available.

30. If dead: Main cause of death:

Cause of death (COD): Only **one primary** cause of death may be specified. If relevant, multiple contributing causes may be listed. If the COD is truly not known, indicate as such. **Do not report the final medical event**, “cardiac and/or respiratory arrest”, as the primary COD or summarize as “multi-organ failure”, rather investigate what led up to the recipient’s death (for example, fungal pneumonia as the cause rather than the final medical event of “respiratory failure”) In most cases the physician’s determination as reported on the death certificate will be useful for this purpose.

Primary and contributing cause of death (COD). For the purpose of Registration, primary COD is summarized into three main categories: the disease for HSCT was present and is the primary COD, HSCT related COD, and new malignancy (not disease transformation or progression). Typically one of the three categories apply, but if not, use “other” and specify the other COD.

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Relapse/Progression/Persistent disease: Persistence or recurrence of underlying disease for which recipient was transplanted. Be sure the Post-HSCT disease evaluation reflects the presence of disease post-HSCT.

For Aplastic anemia report “rejection/poor graft function”.

HSCT related causes: Contributing cause of death (tick all that apply):

31. GVHD: Provide details aGVHD/cGVHD section as applicable.

32. Cardiac toxicity: Rarely a primary cause of death. If cardiac toxicity is proposed as the primary COD, confirmation from the transplant physician should be considered.

33. Infection: can be proven or suspected.

34. Pulmonary toxicity: Lung failure not from infection, includes bronchiolitis obliterans (if part of cGVHD it can also be reported here), radiation pneumonia, etc.

35. Rejection/poor graft function: Includes failure of marrow to achieve an ANC $0.5 \times 10^9/L$ (no engraftment or partial engraftment) or loss of graft. May also be recorded as bone marrow failure or aplasia (note: recipients transplanted for a disease other than Aplastic Anemia the term “aplasia” does not necessarily refer to the recipient developing SAA.).

36. (Hepatic) Veneno-Occlusive Disease: can be caused by chemo/radiotherapy. Consists of endothelial damage, micro thrombosis of the hepatic venules and sinusoidal fibrosis. It is more common in allogeneic transplants than autologous and typically occurs within 3 weeks of transplant. In the absence of a histological diagnosis, recipients must fulfill the criteria below for a diagnosis of VOD.

Clinical Criteria For Veneno-Occlusive Disease Of Liver Recipients reported as having veno-occlusive disease of liver based on clinical signs and symptoms **only** must have two or more of the following with no other identifiable cause for liver disease:

1. Jaundice (bilirubin ≥ 2 mg/dL or > 34 $\mu\text{mol/L}$)
2. Hepatomegaly with right upper quadrant pain
3. Ascites and/or weight gain ($>5\%$ over baseline, as generally accepted)

References: McDonald GB, et al. Hepatology 1984; 4:116-122

Jones RJ, et al. Transplantation 1987; 778-783

37. Other HSCT related COD

New malignancy: Must be diagnosed after the first transplant was performed, if prior, use “other”. Please be sure that the new malignancy differs from the malignant disease for which the transplant was performed (e.g. *de novo* leukemia, AML diagnosed many years after a transplant for ALL, not MDS transformed to AML).

Other: Please carefully consider whether the cause of death can be classified into one of the categories provided above. If this is not possible, then indicate and provide details.

Post-HSCT Therapy (Optional for non-U.S. Centers). This box collects data on specific therapies from current CIBMTR studies. It is not intended to collect every type of possible post-HSCT therapy.

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40-42. FGF (Velafermin), imatinib mesylate (Gleevec, Gilivec) or KGF (palifermin, Kepivance): Please indicate if any of the agents listed were used during the indicated reporting period. Masked trial refers to a study in which you do not know if the recipient is receiving the study drug, placebo or something else. Only tick ‘masked trial’ if one of the listed drugs is involved in the study. Once the trial is over, please send a correction and indicate whether the drug was used or not.

Note: KGF and FGF (palifermin and velafermin) sound a lot alike. Please record each of these very carefully.

HSCT For Non-Malignant Disease Only As there are no standard summary criteria for measuring non-malignant disease response no disease evaluation is collected.

43. DCI given in this period? If the recipient received a DCI in this reporting period answer ‘yes’ and continue with paper version page 2. If no DCI was given, the Post-TED is complete for recipients transplanted for non-malignant disease.

Malignant Disease Evaluation For This Hsct:

Note: if indication for HSCT was a non-malignant disease do not complete this disease evaluation section.

44. Was a CR Ever Achieved in Response to HSCT (including any therapy planned as of day 0, excluding any change in therapy in response to disease assessment)?

This section collects the data known as “best response to transplant” and is a widely misunderstood data point. **The purpose is to capture how well the recipient responded to ONLY the prescribed “transplant package”.** It never includes treatment given in response to a disease evaluation (e.g. treatment given for relapsed or persistent disease that was not planned before the HCT was executed). It often is achieved in the first 100 Days, but some diseases like MYE and CLL may take longer, typically 1 year, but possibly up to 2 years. After that the recipient has likely derived the most benefit that they will see from the HSCT. Once the recipient relapses or progresses, or receives therapy in response to a disease evaluation, the response to that additional therapy is NOT included in this data field. It will be collected in the ‘current disease status’ field.

There should not be any ambiguity in the answer to this question. If the recipient was in CR at the start of the preparative regimen, the best response is not applicable as CR had already been attained.

45. Yes, post-HSCT CR achieved, Date: If CR was achieved due to the effect of the HSCT/package (includes therapy planned as part of the HSCT, but not therapy in response to a disease evaluation) give the date CR established post-HSCT. Typically this date is less than 100 days post-HSCT, but could take up to one year (and rarely up to 2 years) post-HSCT. When this option is used, in subsequent reporting periods tick “First CR date reported previously”.

46. No, never in CR from HSCT, Date assessed: If the recipient has never been in CR from the effects of the HSCT and/or planned therapy, tick no and give the latest date assessed.

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If the recipient has relapsed, progressed, or received therapy in response to a disease evaluation, report the best response prior to the relapse, progression or start of treatment for disease.

If you have ANY questions about “best response” please contact your liaison.

First Relapse or Progression After HSCT

(in this period, *any* type, not persistent disease)

47. First relapse or progression after HSCT: There are three methods to evaluate disease. Not all diseases use all three methods, but every recipient who has an evaluation by a physician has a “clinical” assessment. If the recipient dies, but has not been in for a visit, a physician still must pronounce them dead, hence they have a “clinical” visit. If disease is discovered by autopsy, the date of the assessment should be reported as the date of death, not the actual autopsy date. No data for the recipient can exceed the date of death.

Each method can record relapse or progression, but only the FIRST instance for each method should be reported. Subsequent reporting periods should utilize the “previously reported” option if relapse/progression was already documented by that method.

48. Relapse / progression detected by molecular method:

Yes, 49. date (molecular marker) **first seen**, e.g. RFLP, STR, “PCR”.

No (molecular markers not found), **50. date of assessment**

Previously reported: use this option if disease was already found and reported post-HSCT by that method .

Not evaluated: Also used if disease does not have molecular markers.

51. Relapse / progression detected by cytogenetic / FISH method:

Yes, 52. date (cytogenetic / FISH) **first seen**, e.g. CML t(9;22).

No (cytogenetic / FISH not found), **53. date of assessment**

Previously reported: use this option if disease was already found & reported post-HSCT by that method .

Not evaluated: Also used if disease does not have cytogenetic / FISH markers.

54. Relapse / progression detected by clinical / hematologic method:

Yes, clinical / hematologic **55. date (first seen)**, e.g. physician assessment.

No (clinical / hematologic not found), **56. date of assessment**

Previously reported: use this option if disease was already found & reported post-HSCT by that method .

Not evaluated.

Additional Treatment?

57. Additional treatment (Post-HSCT for any reason)?

58. DCI (allo only) (If yes, also complete DCI section): is only appropriate for allogeneic HSC; the “D” represents the donor. Work is under way to prepare for the collection of other types of cellular therapy, including alternative uses in a future version of TED.

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59. Planned (given regardless of disease status/assessment post-HSCT): This is generally given within the first year or two post-HSCT as is part of the HSCT “package”. It does NOT mean the “recipient relapsed therefore we planned to treat them”. Please be aware of the distinction regarding planned and not planned therapy.

60. Not planned (given for relapse, progression, or persistent disease): refers to treatment given in response to a disease assessment.

Method of Latest Disease Assessment

(Record most recent of each)

This section should be completed for every malignant disease. Not all *diseases* have molecular and/or cytogenetic/FISH (fluorescent In-Situ Hybridization) abnormalities identified with which to monitor disease status. If none exist, tick “not evaluated”. If you don’t know whether the recipient is being monitored by these methods please ask someone at your Center.

61. (Method of latest disease assessment) **Molecular** testing:

62. Disease detected? Occasionally a recipient may have a positive test result, but the physician does not believe it represents “disease”. In that instance, tick “yes” to ‘disease detected’ but “no” to “Was the status considered a disease relapse or progression”.

63. If yes, was the status considered a disease relapse or progression? E.g. CML HSCT recipient exhibits a low level of BCR-ABL positivity post-HSCT (from molecular observation not FISH) that the physician does not believe represents disease and is not treating it.

64. (Molecular disease detected?) **Date latest assessed?**

65. (Method of latest disease assessment) **Cytogenetic/FISH** testing:

66. Disease detected? As with molecular testing, if a result is positive, but the treating physician does not believe it represents disease tick “yes” to ‘disease detected’ but “no” to “Was this status considered a disease relapse or progression”.

67. If yes, was the status considered a disease relapse or progression? E.g. CML HSCT recipient exhibits a low level of Philadelphia chromosome positivity post-HSCT that the physician does not believe represents disease and is not treating it.

68. (Cytogenetic/FISH disease detected?) **Date latest assessed?**

69. (Method of latest disease assessment) **Clinical/Hematologic**:

70. Disease detected? All recipients should have some type of medical contact and is reported in the “clinical” category. It does not have to be your transplant Center that did the assessment. Indicate whether disease was detected by clinical or hematologic means at the latest assessment.

71. (Clinical/Hematologic disease detected?) **Date latest assessed?**

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72. Was a previous HSCT performed for a different disease than this HSCT?

If this is the recipient's first HSCT – skip this box. If only applies if a subsequent HSCT is given for a “new malignancy”. Track the status of the first indication for HSCT in this box to ensure the Malignant Disease Evaluation section only collects response for the indication for HSCT.

73. (If a previous HSCT was performed for a different disease than this HSCT) Give status of original disease.

74. (status of original disease) Date determined?

Donor Cellular Infusion (DCI)

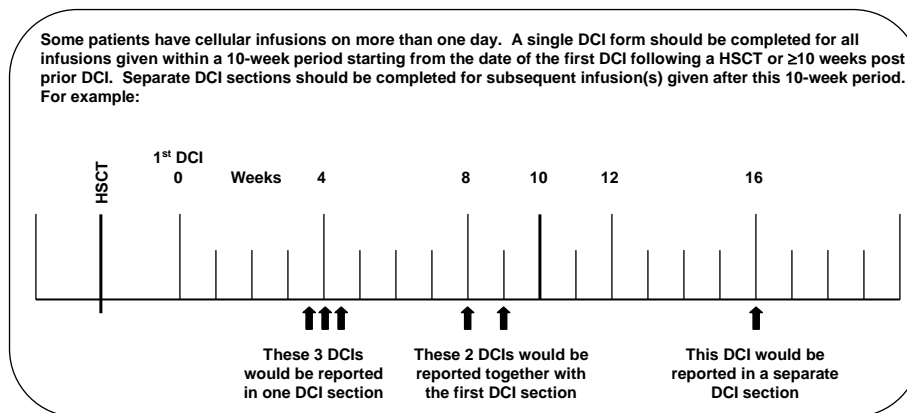
The paper version of Post-TED includes three sections in which to report DCI infusions without copying the page; while FN2 is virtual – complete as many as you need. The Manual only includes sections for the first reporting as instructions for subsequent sections would be identical.

Has the recipient received a DCI from the original donor? This section refers to cellular therapy from the original donor, lymphocytes, unstimulated peripheral blood mononuclear cells, dendritic cells, mesenchymal cells, etc. If a bag of cells saved from the HSCT are now infused without a preparative regimen and the reason for the infusion does not pertain to the prior graft (no engraftment, partial/poor engraftment or loss of the graft/late graft failure), please report as Donor Cellular Infusion.

If a different donor was used, report as a subsequent HSCT.

Some recipients have cellular infusions on more than one day. A single DCI section should be completed for all infusions given within a 10-week period, which is a change from the previous 002-Report Forms of 28 days. For example:

DCI Calculation Timeline



Please contact your liaison with any specific examples you wish to discuss. List the dates indicated on the timeline prior to contacting your liaison.

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75 [87 second, 99 third]. (DCI given in this period) **Date of first DCI** : In the example above, the first DCI is at approximately the two week mark – report that date. The second DCI “box” date would be the one at the 16 week mark.

76 [88, 100]. Total # DCI in 10 weeks (from the date of first DCI): In the example above the total number is 5.

77-82 [89-94, 101-106]. Types of cell(s) (infused during the 10 week period) (check all that apply):

The most common type of DCI is the DLI (Donor Lymphocyte Infusion), but as you can see from the list, there are other types of cellular therapy. On the paper version check all that apply; if using FN2 tick yes/no to each cell type.

83-84 [95-96, 107-108]. Indication (for the infusions within the 10 weeks period): What is the reason the cells are being infused? All of the known indications are listed at the moment. “Other” is to report novel uses; “engraftment” should NEVER be listed as a reason. If the recipient does not have a graft, stem cells are required to attain one and that is reported as a subsequent HSCT. If a new indication occurs within the 10 week period, please list in a new section.

85 [97, 109]. Maximum Grade of aGVHD: DCI can trigger aGVHD independent of the HSCT. See aGVHD section for details regarding GVHD.

86 [98, 110]. If another DCI was received in this reporting period, disease status before next DCI: the response to the DCI includes the grouping (if more than one) within the 10 week period and is only answered if you need to complete data in the next DCI box in this reporting period. “Current status” will collect the response if no additional DCIs were done.

111. Were there more than three instances of DCI infusions in this reporting period If yes, copy the paper version page and continue numbering the sections as 4th, 5th, etc. If no, submit Post-TED.

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Appendix 1 The Hematopoietic Cell Transplant-Co-morbidity Index (HCT-CI) Assign scores appropriately if the patient has any of these co-morbidities

UPN _____ CIBMTR Center # _____ CRID _____ Date _____

| Co-morbidity | Definition / compartments | Yes | Score |
|-------------------------------|--|---|---|
| 1. Arrhythmia | <ul style="list-style-type: none"> – Atrial fibrillation* – Atrial flutter* – Sick sinus syndrome* – Ventricular arrhythmia* | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | 1 |
| 2. Cardiovascular | <ul style="list-style-type: none"> – Coronary artery disease* – Congestive heart failure* – Myocardial infarction* – Ejection fraction \leq 50%§ | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | 1 |
| 3. Inflammatory bowel disease | <ul style="list-style-type: none"> – Crohn’s disease* – Ulcerative colitis* | <input type="checkbox"/> <input type="checkbox"/> | 1 |
| 4. Diabetes | – Treated with insulin or oral hypoglycemic drugs* | → | 1 |
| 5. Cerebro-vascular | <ul style="list-style-type: none"> – Transient ischemic attacks* – Cerebro-vascular ischemic or hemorrhagic stroke* | <input type="checkbox"/> <input type="checkbox"/> | 1 |
| 6. Depression / anxiety | – Requiring psychological consult and/or specific treatment§ | → | 1 |
| 7. Hepatic – mild | <ul style="list-style-type: none"> – Chronic hepatitis§ – Bilirubin $>$ULN- 1.5 X ULN§ – AST/ALT $>$ULN-2.5XULN§ | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | 1 |
| 8. Obesity | <ul style="list-style-type: none"> – Body mass index $>$35 (adults)§ – Body mass index-for-age \geq95% percentile (children)§ | <input type="checkbox"/> <input type="checkbox"/> | 1 |
| 9. Infection | – Requiring anti-microbial treatment before, during, and after The start of conditioning regimen§ | → | 1 |
| 10. Rheumatologic | – Required treatment* | → | 2 |
| 11. Peptic ulcer | – Confirmed by endoscopy and required treatment* | → | 2 |
| 12. Renal | <ul style="list-style-type: none"> – Serum creatinine $>$ 2mg/dl (or $>$177 μmol/L)§ – On dialysis§ – Prior renal transplantation* | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | 2 |
| 13. Pulmonary – Moderate | <ul style="list-style-type: none"> – DLco corrected for hemoglobin 66-80% of predicted§ – FEV₁ 66-80% of predicted§ – Dyspnea on slight activity§ | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | 2 |
| 14. Pulmonary – Severe | <ul style="list-style-type: none"> – DLco corrected for hemoglobin \leq 65% of predicted§ – FEV₁ \leq 65% of predicted§ – Dyspnea at rest or requiring oxygen therapy§ | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | 3 |
| 15. Heart valve disease | – Except asymptomatic mitral valve prolapse§ | → | 3 |
| 16. Prior solid malignancy | – Treated with surgery, chemotherapy, and/or radiotherapy excluding non-melanoma skin cancer* | → | 3 |
| 17. Hepatic – moderate/severe | <ul style="list-style-type: none"> – Liver cirrhosis§ – Bilirubin $>$1.5 X ULN§ – AST/ALT $>$2.5XULN§ | <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> | 3 |
| Total score | | | <div style="border: 1px solid black; width: 40px; height: 20px; margin: 0 auto;"></div> |

*Diagnosed at any time in the patient’s past history.

§Detected at the time of pretransplant assessment.

ULN indicates upper limit of normal; DLco, diffusion capacity of carbon monoxide; FEV₁, forced expiratory volume in one second; AST, aspartate aminotransferase; and ALT, alanine aminotransferase.