4000: Cellular Therapy Essential Data Pre-Infusion

This form must be completed for all recipients of cellular therapy (non-HCT) where it is the first indication for treatment (no prior hematopoietic cell transplant), when a post-HCT cellular therapy event (e.g. DCI, CAR-T) is reported on an HCT follow up form, or when cellular therapy (non-HCT) is reported as a new indication following a marrow toxic injury (RITN patient) / non-cellular therapy (e.g. chemotherapy, immunotherapy).

For recipients of hematopoietic cellular transplants, complete the pre-TED Form 2400 and Disease Classification F2402.

This form reflects baseline recipient data and indication for a course of cellular therapy. All cellular therapies (non-HCT) are being collected on this form, including indications that reflect donor cellular infusions (DCI/DLI) done post-transplant, now referred to as “post-HCT cellular therapy”. A course of cellular therapy includes all infusions given per protocol, or when multiple infusions are given for the same indication using the same product/donor (e.g. post-HCT cellular therapy (DCI/DLI)). Multiple infusions of commercially available products require a separate Form 4000 for each infusion.

The use of cellular therapy is expanding. Treatment strategies include isolation and transfer of specific stem cell populations, administration of effector cells (e.g. cytotoxic T-cells), induction of mature cells to become pluripotent cells, and reprogramming of mature cells (e.g. CAR T-cells).

Links to sections of form:

Manual Updates:

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

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

Date	Manual Section	Add/ Remove/	Description

		Modify	
11/13/2020	4000:Cellular Therapy Essential Data Pre-Infusion	Modify	Clarified the time period for reporting co-morbid conditions prior to a cellular therapy infusion: Added the following guidance on answering question 37: Additionally, for the purposes of this manual, the term “at the time of patient assessment” is defined as the pre-infusion evaluation period performed with 6 months prior to the start of the lympho-depleting or preparative regimen.
10/23/2020	4000:Cellular Therapy Essential Data Pre-Infusion	Add	Added the following guidance on answering question 37: *Question 37 has been “hidden” in FormsNet3 for the current revision of this form. If an NMDP donor ID had been previously entered, this field will not be hidden and can be edited as needed. However, if an NMDP donor ID has not been entered yet, this field will be hidden and skipped until the form is revised and the question is removed from the form.*
9/23/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Corrected the formatting in the list of co-morbid conditions under question 115.
9/18/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Updated the instruction for reporting the new FDA approved product “Tecartus”: Please report the new FDA approved product ‘Tecartus (brexucabtagene autoleucel)’ as ‘Yescarta’. The products will be distinguished by the lymphoma histology. The new product name will be added to the option list in the next revision to be released in January 2021.
9/9/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Add	Clarification added on how to report ADD and ADHD as comorbidities to question 115: *Psychiatric disturbance – The presence of any mood, anxiety, or other psychiatric disorder requiring continuous treatment during the last four weeks. Examples include, but are not limited to, depression, anxiety, Attention-Deficit Disorder (ADD), Attention-Deficit Hyperactivity Disorder (ADHD), bipolar disorder, and schizophrenia requiring psychiatric consult or treatment in the last 4 weeks.*
8/26/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Add	Blue instruction box added above question 111 to clarify how to report the COVD-19 infections when diagnosed after the start of the lymphodepleting therapy: *Diagnosis of COVD-19 after the start of the lymphodepleting therapy: Questions 111 – 113 are intended to capture COVID-19 (SARS-CoV-2) infections diagnosed prior to the start of the lymphodepleting therapy / infusion. If a COVID-19 infection is diagnosed after the start of the lymphodepleting therapy, report the COVID-19 diagnosis on the post-infusion follow-up form (2450, 2100, and / or 4100).*
8/3/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Updated the instruction for reporting NCT ID: “All clinical trials are required to be registered on the clinicaltrials.gov website and will have an associated identification number. Report the number in question 12, do not include the letters “NCT” that precede the digits.”
7/29/2020	4000: Cellular Therapy Essential Data Pre-	Add	Added the following note box under question 49: Please report the new FDA approved product ‘Tecartus (brexucabtagene autoleucel)’ under “other product” and specify the name as ‘Tecartus’ in question 50 until the name can be added to the option list.

	Infusion		
6/9/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Add	Provided clarification (red text) on how to report heart valve comorbidity for question 115. Moderate or severe valve stenosis or insufficiency (mitral, aortic, tricuspid, or pulmonary) as determined by the most recent heart evaluation by an echocardiogram, prosthetic mitral or aortic valve, and / or symptomatic mitral valve prolapse. This does not include a documented medical history of heart valve disease.
6/8/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Add clarification: For the infusion being reported on this form, indicate if the recipient is a registered participant with BMT-CTN, RCI-BMT, USIDNET, COG, a Corporate / Industry trial, EudraCT, UMIN, an investigator initiated trial and/or another clinical trial sponsor, **regardless if that sponsor uses CIBMTR forms to capture outcomes data**.
5/21/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Q106- Clarified the instructions for reporting drug dose: Report the total ~~prescribed~~ dose that was actually given of the drug selected in question 104. Drug doses can be reported with one decimal place.
5/20/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Q104- Clarified the instructions for reporting drug dose: For each drug listed, checking the box will indicate it was given as part of the lymphodepleting therapy used prior to the cellular therapy infusion. Report the total ~~prescribed~~ dose of each drug that was actually given. Do not report the prescribed dose or the daily dose. The pharmacy record or Medication Administration Record (MAR) should be used for determining the exact total dose given.
5/11/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Add	Included instructions for questions that were added to the form (questions 111-113) intended to capture information on COVID-19 (SARS-CoV-2) infections.
4/7/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Add	For question 109-100, added the following guidance for Karnofsky/Lansky scores: **Documentation from an RN who has been trained and authorized to determine performance scores may also be used.**
1/24/2020	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Version 4 of the 4000: Cellular Therapy Essential Data Pre-Infusion section of the Forms Instruction Manual released. Version 4 corresponds to revision 6 of the form 4000.

Last modified: Nov 13, 2020

Q1-14: Recipient Data

Question 1: Ethnicity

The recipient's ethnicity is automatically populated based on the value reported on the CRID Assignment Form 2804. Verify that the recipient's ethnicity is correct. If an error is noted, correct Form 2804 and verify that the recipient's ethnicity has been updated on the Pre-CTED Form 4000.

Question 2: Race: (check all that apply)

The recipient's race is automatically populated based on the value reported on the CRID Assignment Form 2804. Verify that the recipient's race is correct. If an error is noted, correct Form 2804 and verify that the recipient's race has been updated on the Pre-CTED Form 4000.

Question 3: Has the recipient signed an IRB / Ethics Committee-approved consent form for submitting research data to the CIBMTR?

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

✻ **Reporting Consent Status for DCI and Other Post-HCT Cellular Therapies**
If this form is being completed for a DCI or other post-HCT cellular therapy reported on a Post-TED Form (Form 2450) or Post-HCT Follow-Up Data Form (Form 2100), report "not applicable" for question 3. The consent status will be reported on the Pre-TED Form (Form 2400) and should not be re- reported here. If the recipient's consent status has changed since the Pre-TED Form was completed, update the consent status on the Pre-TED Form (Form 2400).

When a recipient consents to participate in the Observational Database, their data are available in the CIBMTR's Observational Research Database and may be used for research. The database includes

recipient baseline and outcome data for related and unrelated allogeneic transplants from any cell source and for autologous transplants.

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

- How well recipients recover from their infusions
- How recovery after infusion can be improved
- What the long-term outcomes are after transplantation and cellular therapies
- How access to transplantation for different groups of recipients can be improved
- How well donors recover from collection procedures
- The application and success of transplantation in the management of marrow toxic injuries
- Cellular therapy
- Better understand new complications seen with infusion of certain cellular therapy products
- Compare outcomes of transplantation and cellular therapies between each other and to other therapies

Indicate if the recipient has signed an IRB-approved consent form to participate in the Observational Research Database. If “yes (patient consented),” continue with question 4. If “no” (patient declined)”, “not approached”, or “not applicable” (post-HCT scenario) continue with question 6. If the patient declines consent,or is not approached for consent, any data reported will not be used in observational studies.

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

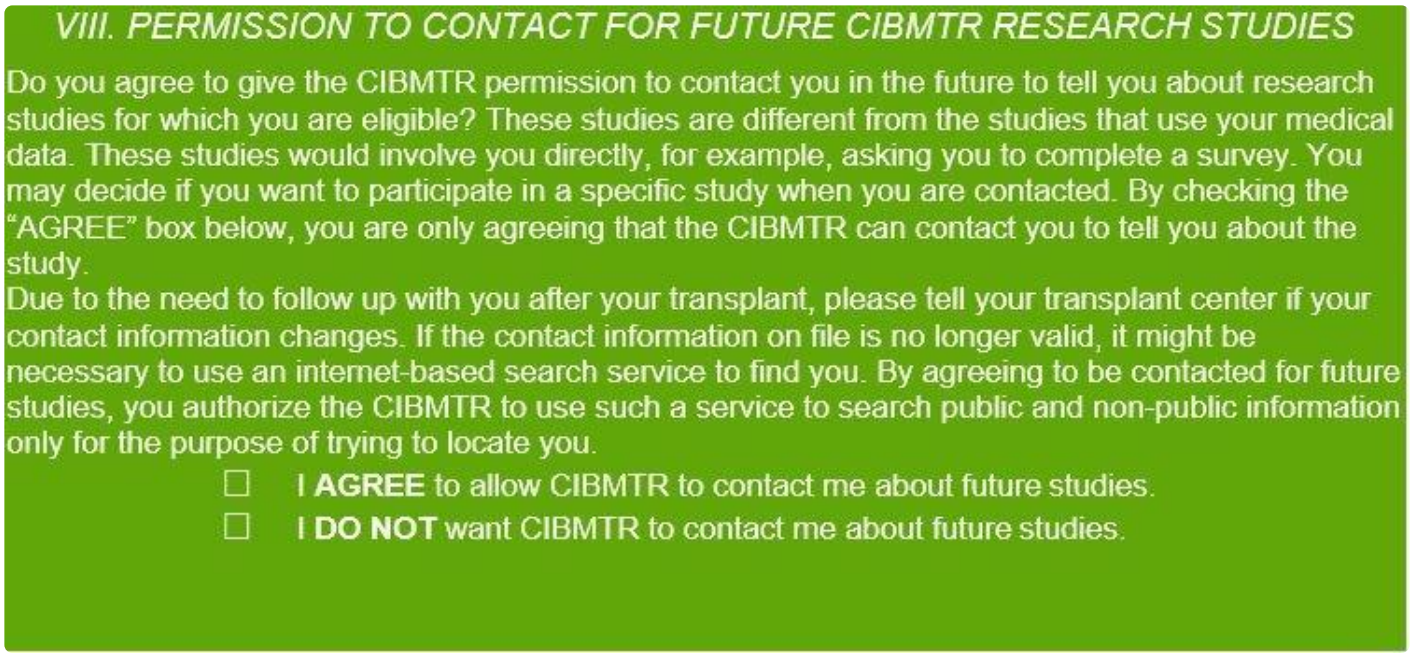
Recipients who transfer to another facility for a subsequent infusion
Any time a recipient transfers to another transplant center, an IRB approved research database consent would need to be obtained at the new center before data could be reported to the CIBMTR.

Question 4: Did the recipient give permission to be directly contacted by CIBMTR for future research?

Indicate if the recipient has given permission to be directly contacted by the NMDP / CIBMTR for future research as documented on the research database consent form. If “yes (patient provided permission),” continue with question 5. If “no (patient declined)”, continue with question 6.

If “yes (patient provided permission),” is selected, the Recipient Contact Information Form (2820) will also need to be completed.

Below is an example of this permission found in the NMDP/CIBMTR Research Database for Hematopoietic Cell Transplantation and Cellular Therapy Consent Form (Version 10.0).



VIII. PERMISSION TO CONTACT FOR FUTURE CIBMTR RESEARCH STUDIES

Do you agree to give the CIBMTR permission to contact you in the future to tell you about research studies for which you are eligible? These studies are different from the studies that use your medical data. These studies would involve you directly, for example, asking you to complete a survey. You may decide if you want to participate in a specific study when you are contacted. By checking the "AGREE" box below, you are only agreeing that the CIBMTR can contact you to tell you about the study.

Due to the need to follow up with you after your transplant, please tell your transplant center if your contact information changes. If the contact information on file is no longer valid, it might be necessary to use an internet-based search service to find you. By agreeing to be contacted for future studies, you authorize the CIBMTR to use such a service to search public and non-public information only for the purpose of trying to locate you.

☐ I **AGREE** to allow CIBMTR to contact me about future studies.

☐ I **DO NOT** want CIBMTR to contact me about future studies.

Question 5: Date form was signed:

Report the date (YYYY-MM-DD) the research database consent form was signed by the recipient. Do not report the date that the witness or healthcare professional signed the consent form.

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

> **!** Products that are commercially available are no longer under a clinical trial. However, if a commercial product is being used within the context of a clinical trial for a new indication, report the clinical trial in this question.

For the infusion being reported on this form, indicate if the recipient is a registered participant with BMT-CTN, RCI-BMT, USIDNET, COG, a Corporate / Industry trial, EudraCT, UMIN, an investigator initiated trial and/or another clinical trial sponsor, **regardless if that sponsor uses CIBMTR forms to capture outcomes data**. If "yes," continue with question 7 to report the sponsor. If "no," continue with question 13. If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.

- BMT-CTN: Blood and Marrow Transplant Clinical Trials Network
- RCI-BMT: Resource for Clinical Investigation in Blood and Marrow Transplant
- USIDNET: United States Immunodeficiency Network
- COG: Children's Oncology Group
- Corporate / Industry
- EudraCT: European Clinical Trials Database

- UMIN: University Hospital Medical Information Network Center
- Investigator initiated

Questions 7 – 12 Reporting Participation in More Than One Study
FormsNet3SM application: Complete questions 7 – 12 for each study the recipient is participating in by adding an additional instance in the FormsNetSM application.
Paper form submission: Copy questions 7 – 12 and complete for each study the recipient is participating in.

Question 7 – 12: Study sponsor:

Select the study sponsor of the clinical trial the recipient is participating in. Click on the link above for more information about each organization.

If the study sponsor is reported as "**BMT-CTN**", "**RCI-BMT**", "**USIDNET**", "**COG**", or "**Investigator initiated**" in question 7, specify the ClinicalTrials.gov identification number in question 12. Investigator initiated trials include those that are initiated and managed by a non- pharmaceutical/company researcher (e.g. individual physicians or cooperative groups) and center specific trials or multi-center trials. Continue with question 15.

If the recipient is participating in **corporate / industry** sponsored trial, indicate the study sponsor as "Corporate/Industry" in question 7, specify the name of the Corporate or Industry sponsor in question 8 and report the clinicaltrials.gov ID number in question 12. Corporate/Industry examples include, but are not limited to, Atara Biotherapeutics, Bellicum Pharmaceuticals, BlueBird Bio, Celgene, Juno Therapeutics, Kite Pharma, Mesoblast, and Novartis. Continue with question 15.

If the recipient is participating in a **European Medicines Agency** clinical trial, indicate the study sponsor as "EudraCT" in question 7 and specify the Study identification number in question 9 (not the recipient ID). The European Union Drug Regulating Authorities Clinical Trials is the European Clinical Trials Database of all clinical trials of investigational medicinal products with at least one site in the European Union commencing 1 May 2004 or later. See link for more information. The EudraCT number has the format YYYY-NNNNNN-CC, where YYYY is the year in which the number is issued, NNNNNN is a six digit sequential number, and CC is a check digit. Continue with question 13.

If the recipient is participating in a study with **UMIN**, indicate the study sponsor as "UMIN" in question 7 and specify the alpha-numeric study identification number in question 10 (not the recipient ID). UMIN was established in 1989 as a cooperative organization national medical school in Japan, sponsored by the Ministry of Education, Culture, Science, Sports and Technology (MEXT), Japan. Continue with question 13.

If the recipient is participating in a clinical trial and the study sponsor is not listed, select "other sponsor" in question 7, specify the sponsor name in question 11, and report the ClinicalTrials.gov identification number in question 12. Continue with question 15.

ClinicalTrials.gov Identification Number
All clinical trials are required to be registered on the clinicaltrials.gov website and will have an associated identification number. Report the number in question 12, do not include the letters “NCT” that precede the digits.

Question 13 – 14: Is the recipient receiving cellular therapy outside of the context of a clinical trial?

Indicate “yes” if the recipient is receiving cellular therapy in the setting:

Institutional guidelines/standard of treatment: Internal protocols at the center.

Hospital exemption: Applicable when giving cell therapy product without a clinical trial, the hospital that produces the cells must be the hospital that gives the cells.

Compassionate use: No protocol is available or approved by institution, the physician asks for a one-time use.

If the recipient is not receiving the cellular therapy outside the context of a clinical trial, select “no” and continue with question 15.

Last modified: Aug 03, 2020

Q15-29: Cellular Therapy and HCT History

Question 15: Is this the first application of cellular therapy (non-HCT)?

Indicate if this is the recipient's first non-HCT cellular therapy application. This is defined as the first application the recipient ever receives, not the first application the recipient receives at your facility. The intent is to capture the full picture of the recipient's treatment history.

If "yes" or "unknown", continue with question 24. If "no", continue with question 16.

Question 16: Were all prior cellular therapies (non-HCT) reported to the CIBMTR?

This should include any/all infusions not performed at your center. If the recipient is a transfer patient, you will be able to see all past infusion dates in the Recipient Information Grid in FormsNet3SM. Contact the CIBMTR Customer Service Center if there are questions.

If "yes" or "unknown", continue to question 24. If "no", continue with question 17.

Question 17: Specify the number of prior cellular therapies:

Enter the number of prior cellular therapies for the recipient. A "cellular therapy event" is defined as the infusion or administration of a cellular therapy product for treatment of a specific indication(s). Each infusion or administration of a cellular product should be counted separately. Include all infusions the recipient received, even if they were not performed at your center. The intent is to capture the full picture of the recipient's treatment history.

> **Questions 18 – 23 Reporting Prior Cellular Therapies**
> FormsNet3SM application: Complete questions 18-23 to report all prior cellular therapies that have not yet been reported to the CIBMTR by adding an additional instance in the FormsNet3SM application.
> Paper form submission: Copy questions 17-22 and complete for each prior cellular therapy that has not yet been reported to the CIBMTR.

Question 18: Date of the prior cellular therapy:

Report the date (YYYY-MM-DD) of the prior cellular therapy being reported in this instance. If the exact date is unknown and must be estimated, check the "date estimated" box.

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

Question 19: Was the cellular therapy performed at a different institution?

Indicate if the prior cellular therapy being reported in this instance was performed at another institution. If “yes”, report the name and address of the institution in question 20. If “no”, continue with question 21.

Question 20: Specify the institution that performed the prior cellular therapy:

Report the name, city, state, and country of the institution where the recipient’s prior cellular therapy being reported in this instance was performed. These data are used to identify and link the recipient’s existence in the database and, if necessary, obtain data from the other institution where the previous treatment was administered.

Question 21 – 22: Specify the indication for the prior cellular therapy:

Select the indication for the prior cellular therapy being reported in this instance. Any indication that is followed by “(post-HCT)” or “(with HCT)” requires that a prior HCT also be reported to CIBMTR.

If the indication for the prior cellular therapy is not listed, select “other indication” and specify the indication in question 22. If the indication for the prior cellular therapy is not documented, select “unknown”.

Question 23: What was the cell source for the prior cellular therapy? (check all that apply)

Indicate the cell source(s) for the prior cellular therapy being reported in this instance. If the product is “off the shelf” or a “third party donor” product obtained from pharmaceutical companies or other corporate entities, donor type should still be identified.

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

An unrelated donor (allogeneic, unrelated) is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or step-parents/children.

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

Questions 24 – 29 HCT History
For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2400 and F4000. To reduce the reporting burden, duplicated questions on the Cell Therapy forms are disabled. This includes HCT History reported in Q24-29.

Question 24: Has the recipient ever had a prior HCT?

Include all HCTs in the recipient’s history, even if the transplants were not performed at your center. The intent is to capture the full picture of the recipient’s treatment history.

If “yes” continue with question 25. If “no” or “unknown”, continue with question 30.

Question 25: Were all prior HCTs reported to the CIBMTR?

This should include any/all HCTs not performed at your center. If the recipient is a transfer patient, you will be able to see all past infusion dates in the Recipient Information Grid in FormsNet3SM. Please submit any questions via Center Support in the ServiceNow application.

If “yes” or “unknown”, continue with question 30. If “no”, continue with question 26.

Question 26: Date of the prior HCT:

Report the date (YYYY-MM-DD) of the prior HCT being reported in this instance.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 27: Was the HCT performed at a different institution?

Indicate if the prior HCT being reported in this instance was performed at another institution. If “yes” report the name and address of the institution in question 28. If “no” continue with question 29.

Question 28: Specify the institution that performed the prior HCT:

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

Question 29: Specify the HSC source(s) for the prior HCT: (check all that apply)

Indicate the applicable cell source(s) for the prior HCT being reported in this instance.

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

An unrelated donor (allogeneic, unrelated) is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or step-parents/children.

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

Last modified: Jan 27, 2020

Q30-54: Product Identification

Question 30: Are any of the products associated with this course of cell therapy genetically modified?

Genetically modified products include any product that was manipulated to alter its gene expression through the insertion of different genes, or editing of genes. An example of a genetically modified product is the manipulation of T-lymphocytes to express Chimeric Antigen Receptors (CAR T-cells) directed towards specific tumor targets (antigens). If more than one product is being infused, indicate if any of the products are genetically modified. This question is used to determine the follow up schedule of the cellular therapy.

Questions 31-50 Reporting Donor Information
FormsNet3^{SM} application: Complete questions 31-50 to report all donors, per protocol, by adding an additional instance in the FormsNet3^{SM} application.
Paper form submission: Copy questions 31-50 and complete for all donors, per protocol.

Question 31: Specify donor:

Indicate the donor type for this product. If the product is “off the shelf” or a “third party” donor, product obtained from pharmaceutical companies or other corporate entities, donor type should still be identified.

An autologous product has cells collected from the recipient for his/her own use. Continue with question 33.

A related donor (allogeneic, related) is a blood-related relative. This includes syngeneic, monozygotic (identical) twins, non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc. Do not include adoptive parents/children or stepparents/children.
Continue with question 32.

An unrelated donor (allogeneic, unrelated) is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or stepparents/children.
Continue with question 32.

Question 32: Did NMDP/Be the Match facilitate the procurement, collection, or transportation of the product?

Distinguish if the product from the donor being reported in this instance is an NMDP product or a non-NMDP product. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank, Anthony Nolan, and StemCyte International Cord Blood Center. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation.

Question 33: Was the product a cord blood unit?

Indicate “yes” if the product was a cord blood unit.

- If the product was an **autologous** cord blood unit, continue with question 39 to report the non-NMDP CBU ID.
- If the product was a **related** cord blood unit, continue with question 39 to report the non-NMDP CBU ID.
- If the product was an **NMDP unrelated** cord blood unit, continue with question 36 to report the NMDP CBU ID.
- If the product was a **non-NMDP unrelated** cord blood unit, continue with question 39 to report the non-NMDP CBU ID.

Indicate “no” if the product was not a cord blood unit.

- If the **autologous** product was not a CBU, continue with question 48.
- If the product was **related** and not a CBU, specify the related donor type in question 34 then continue with question 43 to report donor date of birth.
- If the unrelated donor was **NMDP** and not a CBU, report the NMDP donor ID in question 37.
- If the unrelated donor was **non-NMDP and** not a CBU, report the non-NMDP unrelated donor ID in question 38.

Question 34: Specify the related donor type:

Indicate the relationship and match between the recipient and the related donor being reported in this instance.

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

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

HLA-matched other relative:
Includes: All blood relatives, other than siblings, who are HLA matched (e.g., parents, aunts, uncles, children, cousins, half-siblings). The patient and donor will be allele-level matched at HLA-A, B, C, and DRB-1.
Does not include: Adoptive parents/children or step-parents/children who are HLA matched.

HLA-mismatched relative:
Includes: Siblings who are not HLA-identical and all other blood- relatives who have at least one HLA

mismatch (mismatch can be at the antigen or allele level) (e.g., parents, aunts, uncles, children, cousins, half-siblings). The patient and donor will be allele-level mismatched at one or more loci (HLA-A, B, C, or DRB-1).
Does not include: Adoptive parents/children or stepparents/children.

Question 35: Was this donor used for any prior cellular therapies or HCT? (for this recipient)

Indicate if the allogeneic unrelated or related donor being reported in this instance was used for prior cellular therapies or HCT for this recipient. Do not answer this question for autologous donors. If this is the recipient's first infusion, select "no".

Question 36: NMDP Cord Blood Unit:

Report the NMDP unrelated cord blood unit ID. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation. The ID is always numeric and begins with "9" (e.g., 9000-0000-0). If the product ID does not begin with a "9," the product may not be an NMDP cord blood unit and the source of the product should be double-checked. Enter the NMDP unrelated cord blood unit ID. Continue with question 40.

> ! Question 37 has been "hidden" in FormsNet3 for the current revision of this form. If an NMDP donor ID had been previously entered, this field will not be hidden and can be edited as needed. However, if an NMDP donor ID has not been entered yet, this field will be hidden and skipped until the form is revised and the question is removed from the form.

Question 37: NMDP Donor ID:

Report the NMDP Donor ID (e.g., 0000-0000-0). This ID is unique for each donor and is assigned by NMDP. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search/product documentation. Enter the NMDP Donor ID (e.g., 0000-0000-0). Continue with question 40.

Question 38: Non-NMDP unrelated donor ID: (not applicable for related donors)

Report the non-NMDP unrelated donor ID. Examples of non-NMDP donor registries include, but are not limited to: Anthony Nolan, Australia Bone Marrow Donor Registry, and REDOME. This ID is often located on the product label, the paperwork accompanying the product, and registry-specific search/product documentation. Enter the non-NMDP unrelated donor ID. Continue with question 40.

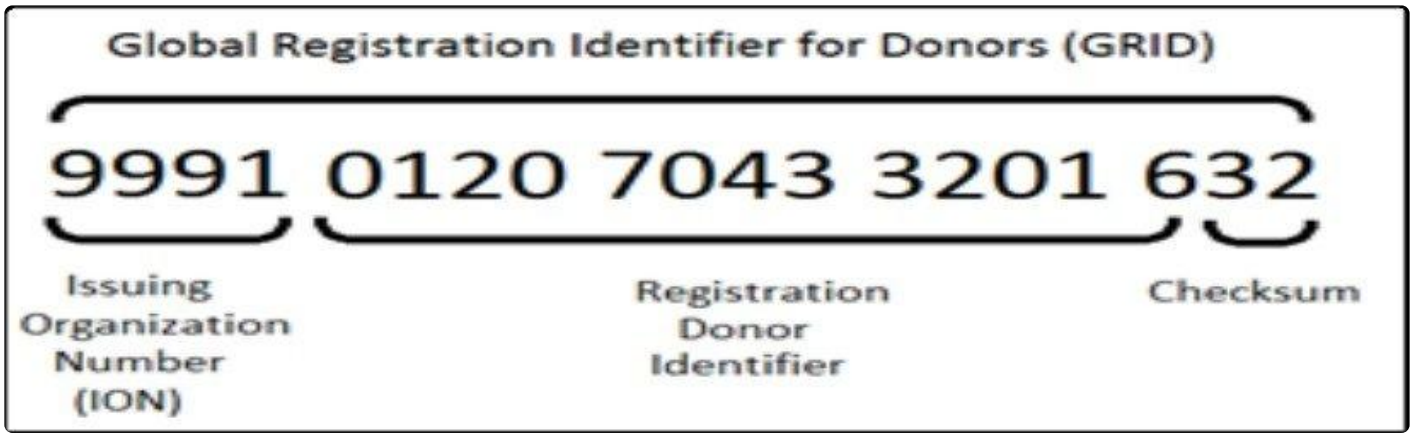
Question 39: Non-NMDP cord blood unit ID: (include related and autologous CBUs)

Report the non-NMDP cord blood unit ID. Examples of non-NMDP donor registries include, but are not limited to: St. Louis Cord Blood Bank and StemCyte International Cord Blood Center. This ID is often located on the product label, the paperwork accompanying the product, and registry-specific search/product documentation. Enter the non-NMDP cord blood ID. Continue with question 40.

Note that some cord blood banks can ship their units either through the NMDP or directly to the transplant center. Carefully review the accompanying documentation to determine which is appropriate for your unit. You may wish to consult with your center's Transplant Coordinator, as he or she will have insight as to how the product was acquired.

Question 40: Global Registration Identifier for Donors (GRID):

The Global Registration Identifier for Donors (GRID) was developed by the WMDA to ensure secure, reliable and unambiguous assignment of unrelated donors. The GRID standard is a 19-character donor identifier composed of three elements: Issuing Organization Number (ION), Registration Donor Identifier, and Checksum (shown below). This standard will ensure each donor ID is globally unique and will reduce the risk of misidentification of donors or their donations.



https://www.wmda.info/professionals/optimising-search-match-connect/why-global-identifier/

Question 41-42: Registry or UCB Bank ID:

Specify the registry used to obtain the adult donor or umbilical cord blood unit and continue with question 48. The Bone Marrow Donors Worldwide (BMDW) codes have been adopted to avoid submitting the entire name and address of the donor registry. Some common banks that do not list with BMDW have been added to the FormsNet list, including St Louis Cord Blood Bank (SLCBB) and Viacord (VIAC).

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

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

If the BMDW website does not list a match code for the adult donor registry or cord blood bank, provide the registry's official name in the question 42.

Please ensure that the registry you are entering under "other" is not already listed in the pull-down list for

question 41. For example, NMDP adult donors, NMDP cords, and New York Cord Bank each have their own entries above in the registry or UCB Bank ID drop down menu.

Question 43-44: Date of birth (donor / infant):

For related or non-NMDP donors only, report if the donor's/infant's date of birth is "known" or "unknown" for question 43. If the donor's/infant's date of birth is known, report the date of birth (YYYY-MM-DD) in question 44 and continue with question 47. If the donor's/infant's date of birth is unknown, continue with question 45.

Question 45-46: Age (donor / infant):

For related or non-NMDP donors only, if the DOB is unknown, report if the donor's/infant's age is "known" or "unknown" for question 45. If the donor's/infant's age is known, report the donor's/infant's age at the time of product collection in question 46. Report the age in months if the recipient is less than 1 year old, otherwise report the age in years. If the donor's/infant's age at collection is unknown, continue with question 47.

Question 47: Sex (donor / infant):

For related or non-NMDP donors only, indicate the donor's biological sex as "male" or "female." For cord blood units, report the infant donor's sex.

Question 48: Specify the total number of products: (per protocol) (as part of this course of cellular therapy)

Report the number of products to be infused per protocol. This question is used to make the correct number of Cellular Therapy Product forms (Form 4003) come due. Each product must be part of the protocol and will be given regardless of disease response.

Example 1. A series of collections from the same donor that uses the same collection method even if the collections are performed on different days, should be considered a single cellular therapy product if only one set of manufacturing steps are applied to the collected material.

Example 2. Products from the same donor but obtained using different manufacturing steps are considered different products and require multiple product forms.

Example 3. If the cells were manipulated or modified by different methods and at the end of the manufacturing process are combined for a single infusion or administration, it will be considered a single product and it will require a single Form 4003.

Question 49-50: Name of product:

This question is limited to commercialized products and is used for study enrollment and validation. If the name of the product is not an option or if the product has no commercialized name (e.g. DCI/DLI product),

select ‘other product’ from the list.

> ✻ Please report the new FDA approved product ‘Tecartus (brexucabtagene autoleucel)’ as “Yescarta”. The different products will be distinguished by the lymphoma subtype. The new product name will be added to the option list in the next revision to be released in January 2021.

The product name selected here will be auto-populated onto subsequent forms and used to disable questions where the information is not made available to sites (i.e. manufacturing or cell dose).

Question 51: In what setting is this cell therapy product infusion being planned?

Indicate if this cell therapy product infusion will be administered as an inpatient or outpatient procedure.

Question 52: Is a subsequent HCT part of the overall treatment protocol?

This question intends to capture instances where the cellular therapy is administered in association with an HCT, either planned or dependent upon the response to the cellular therapy. If, at the time of the current infusion, a subsequent HCT is planned according to the protocol, check “yes” even if the recipient does not receive the planned subsequent HCT. The word “planned” should not be interpreted as: *if the recipient relapses, then the “plan” is to perform a subsequent HCT*. If “yes,” continue with question 53. If “no,” continue with question 55.

Question 53: Specify the HCT type:

Specify the type of the subsequent HCT that is planned as part of the overall treatment protocol.

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

An allogeneic product is from a donor who is not the recipient, either related or unrelated to the recipient.

Question 54: Specify the circumstances which the subsequent HCT will be performed:

Specify the reason for which the subsequent HCT will be performed as “regardless of response to cellular therapy”, “only if the patient responds to cellular therapy” or “only if the patient fails to respond or has an incomplete response”.

Last modified: Nov 11, 2020

Q55-69: Indication for Cellular Therapy

Question 55: Does your center consider this infusion to be a donor lymphocyte infusion (DLI)?

Indicate whether this course of cellular therapy is considered to be a DLI at your center. An infusion can be classified as a "DLI" when:

- The intent is something other than to restore hematopoiesis
- The infusion must be post-HCT, often by the same donor as the HCT
- Indication is suboptimal donor chimerism, immune reconstitution, GVHD treatment, prevent or treat disease relapse (as reported on F4000)
- Composition of cells is lymphocytes

Question 56-57: Is the cellular therapy being given for prevention?

If the cellular therapy is being given for prevention, indicate "yes" and specify the reason in question 57. Reasons for prevention include:

- GVHD prophylaxis (with HCT)
- Prevent disease relapse (post-HCT)
- Infection prophylaxis

If the indication is in the list above and the cell therapy is being given with HCT or post-HCT, no additional consent is required from the patient.
If the cellular therapy is not being given for prevention, indicate "no" and continue with question 58.

Question 58: What was the indication for performing treatment with cellular therapy?

From the list provided, select the indication for which the recipient is receiving the cellular therapy.

If the indication is in the list below and the cell therapy is being given with HCT or post-HCT, no additional consent is required from the patient:

- Suboptimal donor chimerism (post-HCT)
- Immune reconstitution (post-HCT)
- GVHD treatment (post-HCT)

The Disease Classification Form 2402 will come due if the indication is reported as "malignant hematologic disorder", "non-malignant disorder", or "solid tumor". This allows CIBMTR to capture disease specific information for cellular therapy utilizing an existing form to maintain consistency in data collection.

If the recipient is receiving post-HCT cellular therapy (e.g. DCI/DLI) for relapsed, persistent, or progressive disease, the indication should be recorded as "malignant hematologic disorders" and complete a new F2402 for the disease that has relapsed/persisted/progressed.

Disease Classification Questions
The newest versions of the TED forms use the World Health Organization (WHO) disease classifications. The disease classification questions contain all of the established WHO disease types and subtypes. The “other indication” category should be used only if the recipient’s disease is not one of the listed options. For more information regarding disease classification, consult a transplant physician, contact the CIBMTR Customer Service Center, or visit the WHO website.

Malignant vs. Non-Malignant
Malignant disease involve cells dividing without control that can spread to other parts of the body through blood and lymph systems. These diseases are usually characterized by unlimited, aggressive growth, invasion of surrounding tissues, and metastasis. Non-malignant tumors involve cell overgrowth, but lack the malignant properties of cancer. Non-malignant diseases include severe aplastic anemia, disorders of the immune system, inherited disorders of metabolism, etc. The CIBMTR database disease codes are represented in parentheses after the disease subtype on the Disease Classification questions and can be helpful in mapping diagnosis [e.g Myeloid Sarcoma (295)], and determining if the disease is malignant or non-malignant. Disease codes (10-299) indicate a malignant disease, with the exception of Paroxysmal Nocturnal Hemoglobinuria (PNH) (56). A disease code of (300) or above indicates a non- malignant disease, with the exception of disease code (900), which could indicate either a malignant or non-malignant disease.

Question 59: Date of diagnosis:

This question is answered if the indication for cellular therapy is cardiovascular disease, musculoskeletal disease, neurologic disease, ocular disease, pulmonary disease, infection treatment or other indication. The diagnosis date for malignant hematologic disorder, non-malignant disorder or solid tumor will be captured on the Disease Classification Form (Form 2402).

Report the date (YYYY-MM-DD) of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease for which the patient is receiving cellular therapy. Enter the date the sample was collected for examination. If the indication is infection, report the date of diagnosis as the collection date for the first positive microbiology culture. If the diagnosis was determined at an outside center, and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.

If the recipient was diagnosed prenatally (in utero) or if the indication is a congenital disorder, report the date of birth as the date of diagnosis.

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

Question 60-62: Specify cardiovascular disease:

If cardiovascular disease is the indication for cellular therapy, indicate the specific disease in question 60. If “other cardiovascular disease” is selected, specify in question 61. If “other peripheral vascular disease” is selected, specify in question 62. Continue with question 103.

Question 63-64: Specify musculoskeletal disorder:

If musculoskeletal disorder is the indication for cellular therapy, indicate the specific disorder in question 63. If “other musculoskeletal disorder”, specify in question 64. Continue with question 103.

Question 65-66: Specify neurologic disease:

If neurologic disease is the indication for cellular therapy, indicate the specific disease in question 65. If “other neurologic disease”, specify in question 66. Continue with question 103.

Question 67: Specify ocular disease

If ocular disease is the indication for which the recipient is receiving the cellular therapy, specify in question 67. Examples include treatment of glaucoma or photoreceptor degeneration. Continue with question 103.

Question 68: Specify pulmonary disease

If pulmonary disease is the indication for which the recipient is receiving the cellular therapy, specify in question 68. Examples include Chronic Obstructive Pulmonary Disease (COPD) or pulmonary fibrosis. Continue with question 103.

Question 69: Specify other indication

If the indication for which the recipient is receiving the cellular therapy is “other indication” because it does not fit into a category listed above, specify the indication in question 69. An example is treatment of autism by cellular therapy. Please submit any questions regarding the indication via Center Support in the ServiceNow application. Continue with question 103.

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Q70-76: Infection

This section to be completed when infection is the indication for the cellular therapy.

Question 70-76: Organism:

If treatment of infection is the indication for the cellular therapy, report the fungal or viral organism(s) for which the recipient is receiving the cellular therapy.

Organism:
From Table 1 entitled “Codes for Commonly Reported Organisms”, select the code corresponding to the identified organism as indicated on the microbiology report, laboratory report, or other physician documentation. Report the code in the boxes provided on the form.

Fungal infections: Note the inclusion of Pneumocystis (formerly found under parasites). The most commonly found fungal infections are Candida (C. albicans), Aspergillus (A. fumigatus), and Fusarium sp.

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

Table 1: Codes for Commonly Reported Organisms

201 *Candida albicans*	301 Herpes Simplex Virus (HSV)	323 Influenza A Virus
208 Candida non-albicans	302 Varicella Virus	324 Influenza B Virus
210 *Aspergillus*, NOS	303 *Cytomegalovirus* (CMV)	325 Enterovirus (ECHO, Coxsackie)
211 *Aspergillus flavus*	304 *Adenovirus*	326 Enterovirus (polio)
212 *Apergillus fumigatus*	306 Hepatitis A Virus	327 Enterovirus D68 (EV-D68)
213 *Aspergillus niger*	307 Hepatitis B Virus	328 Enterovirus NOS
214 *Aspergillus ustus*	308 Hepatitis C Virus	340 Hepatitis E
215 *Aspergillus terreus*	309 Human Immunodeficiency Virus 1 or 2	341 BK Virus
221 *Cryptococcus neoformans*	310 Influenza, NOS	342 JC Virus (Progressive Multifocal Leukoencephalopathy (PML))
222 *Cryptococcus gattii*	311 Measles Virus (Rubeola)	343 Human metapneumovirus
230 *Fusarium* (all species)	312 Mumps Virus	344 *Coronavirus*

240 *Zygomycetes*, NOS	314 Respiratory Syncytial Virus (RSV)	345 *Norovirus*
241 *Mucorales* (all species)	315 Rubella Virus	346 Dengue Virus
242 *Rhizopus* (all species)	316 Human Parainfluenza Virus (all species)	347 Chikaugunya virus
260 *Pneumocystis* (PCP / PJP)	317 Human herpesvirus 6 (HHV-6)	348 West Nile Virus (WNV)
261 *Histoplasma* (capsulatum)	318 Epstein-Barr Virus (EBV)	349 Human T-lymphotropic Virus 1 or 2
270 *Blastomyces* (dermatitidis)	320 *Rotavirus* (all species)	503 Suspected fungal infection
271 *Coccidioides* (all species)	321 *Rhinovirus* (all species)	777 Other organism
272 *Scedosporium* (all species)	322 *Human Papillomavirus* (HPV)	

Last modified: Jan 27, 2020

Q77-102: Disease Assessment at Last Evaluation Prior to Cellular Therapy

Disease Assessment
These questions are for malignant disease indications with relapsed, persistent or progressive disease only. This section should not be completed if the indication for cellular therapy is reported as one of the following: Suboptimal donor chimerism (post-HCT), Immune reconstitution (post-HCT), GVHD prophylaxis (with HCT), GVHD treatment (post-HCT), Prevent disease relapse (post-HCT), Infection treatment, or Infection prophylaxis

All values reported in questions 77-102 must reflect the most recent testing prior to the start of systemic therapy (or infusion if no therapy was given). If the disease was not assessed prior to the infusion, report “no” and continue with question 103. If it is not known if the disease was assessed prior to the infusion, report “unknown” and continue with question 103.

Question 77: Was the disease assessed prior to the cellular therapy?

Indicate if the disease status was assessed prior to the cellular therapy. If “yes”, continue with question 78. If “no”, continue with question 103.

Method of Disease Assessment:
This section should be completed for every malignant disease. Not all diseases have molecular and / or cytogenetic / FISH abnormalities to monitor disease status. If a disease assessment was done, but has always been normal, report the disease status as “not applicable”. In some circumstances, disease may be detected by molecular or cytogenetic testing, but may not be considered a relapse or progression. Test results should still be reported.

Question 78: Was the disease status assessed by molecular testing (e.g. PCR)?

Molecular assessment involves testing blood, bone marrow, tumor or other source for the presence of known molecular markers. Molecular assessments are the most sensitive test for genetic abnormalities and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control. RFLP testing (with PCR amplification) is an example of a molecular test method used to detect BCR/ABL.

Report “yes” if a molecular method was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 79. If a molecular method was not used to determine disease status, check “no” and continue with question 82.

Report “no” if a molecular testing was not performed or could not be used to determine disease status and continue with question 82.

Report “unknown” if testing was not performed near the start of the systemic therapy / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable) and continue with question 82.

Report “not applicable” if molecular studies were never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary disease for transplant and continue with question 82. Report “unknown” if testing was not performed near the start of the systemic therapy / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable).

Question 79: Date sample collected:

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by molecular method. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy infusion (the earliest date reported in question 107).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 80: Was disease detected?

Report whether the recipient’s primary disease was detected by molecular testing on the date reported in question 79. In order to be considered positive for disease, the assay must detect a number of copies of the molecular marker exceeding the threshold for sensitivity of the assay, for a quantitative study. However, do note that the presence of only a single marker amongst numerous tested is sufficient to indicate disease detected.

If the recipient’s primary disease was detected by the molecular assessment reported in question 79, report “yes” and continue with question 81.

If the recipient’s primary disease was not detected by the molecular assessment reported in question 79, report “no” and continue with question 82.

Question 81: Was the status considered a disease relapse or progression?

If the physician believes the test results indicate disease relapse or progression, report “yes.” If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression (e.g., a recipient transplanted for CML exhibits such a low level of BCR-ABL positivity post-cellular therapy that the physician does not believe is disease), report “no”.

Question 82: Was the disease status assessed via flow cytometry (immunophenotyping)?

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where

cell surface markers can be quantified on cellular material.

Report “yes” if flow cytometry was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 83.

Report “no” if flow cytometry was not performed or could not be used to determine disease status and continue with question 86.
Report “uknown” if testing was not performed near the start of the systemic therapy / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable) and continue with question 86.

Report “not applicable” if flow cytometry was never performed (since diagnosis) or has never shown abnormalities associated with the recipient’s primary disease for transplant and continue with question 86.

Question 83: Date sample collected:

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by flow cytometry. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy infusion (the earliest date reported in question 107).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 84: Was disease detected?

Report whether the recipient’s primary disease was detected by flow cytometry on the date reported in question 83. In order to be considered positive for disease, an abnormal cell population associated with the recipient’s primary transplant disease must be detected regardless of the sensitivity of the flow cytometry panel performed. This means an abnormal cell population detected by MRD flow cytometry would be reported in the same way as an abnormal cell population detected by a standard flow cytometry assay.

If the recipient’s primary disease was detected by the flow cytometry assessment reported in question 83, report “yes” and continue with question 85.

If the recipient’s primary disease was not detected by the flow cytometry assessment reported in question 83, report “no” and continue with question 86.

Question 85: Was the status considered a disease relapse or progression?

If the physician believes the test results indicate disease relapse or progression, report “yes.” If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression, report “no.”

Question 86: Was the disease status assessed by cytogenetic testing (karyotyping or FISH)?

Cytogenetic studies involve the study of chromosomes, typically through one of two methods: karyotyping or fluorescence in situ hybridization (FISH). Blood, bone marrow, or tissue preparations may be tested by either of these two methods. Karyotyping is both less sensitive and less specific than FISH testing; FISH studies identify only abnormalities detectable by the employed probe set, and cannot provide information about the presence or absence of chromosomal abnormalities or markers outside the specific probe set utilized. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same. For more information of cytogenetic assessments, see Appendix C.

Report “yes” if cytogenetic testing was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 87.

Report “no” if cytogenetic testing was not performed or was not used to determine disease status and continue with question 95.
Report “uknown” if testing was not performed near the start of the systemic therapy / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable) and continue with question 95.

Report “not applicable” if cytogenetic testing was never performed (since diagnosis) or has never shown abnormalities associated with the recipient’s primary disease for transplant and continue with question 95.

Question 87: Was the disease status assessed by karyotyping?

Karyotyping is performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

Report “yes” if karyotyping was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 88.

Report “no” if karyotyping was not performed or was not used to determine disease status and continue with question 91.
Report “uknown” if testing was not performed near the start of the systemic therapy / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable) and continue with question 91.

Report “not applicable” if karyotyping was never performed (since diagnosis) or has never shown abnormalities associated with the recipient’s primary disease for transplant and continue with question 91.

Question 88: Date sample collected:

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by karyotyping. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy infusion (the earliest date reported in question 107).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 89: Was disease detected?

Report whether the recipient's primary disease was detected by karyotyping on the date reported in question 88. Do not include clinically insignificant polymorphism, or chromosomal abnormalities of no known significance as disease detected. This includes anomalies such as age-dependent loss of the chromosome Y.

If the recipient's primary disease was detected by the karyotyping assessment reported in question 88, report "yes" and continue with question 90.

If the recipient's primary disease was not detected by the karyotyping assessment reported in question 88, report "no" and continue with question 91.

Question 90: Was the status considered a disease relapse or progression?

If the physician believes the test results indicate disease relapse or progression, report "yes". If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression, report "no."

Question 91: Was the disease status assessed by FISH?

Fluorescence in situ hybridization (FISH) studies identify only abnormalities detectable by the employed probe set, and cannot provide information about the presence or absence of chromosomal abnormalities or markers outside the specific probe set utilized.

Report "yes" if FISH was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 92.

Report "no" if FISH studies were not performed or used to determine disease status or "unknown" if it is not known if FISH studies were performed, and continue with
question 95.

Report "unknown" if testing was not performed near the start of the systemic therapy / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable) and continue with question 95.

Report “not applicable” if FISH studies were never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary disease for transplant and continue with question 95.

Question 92: Date sample collected:

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by FISH. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy infusion (the earliest date reported in question 107).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 93: Was disease detected?

If the recipient’s primary disease was detected by the FISH assessment reported in question 92, report “yes” and continue with question 94.

If the recipient’s primary disease was not detected by the FISH assessment reported in question 92, report “no” and continue with question 95.

Question 94: Was the status considered a disease relapse or progression?

If the physician believes the test results indicate disease relapse or progression, report “yes”. If the recipient has a positive test result, but the physician does not believe the result represents relapse or progression, report “no”.

Question 95: Was the disease status assessed by radiological assessment? (e.g., PET, MRI, CT)

Radiologic assessments are imaging techniques used to assess disease response to transplant, typically for lymphomas or solid tumors, though valuable in some less common presentations of disease, such as leukemia cutis. Imaging techniques used to evaluate disease response typically include PET, CT, or MIBG, but may include x-ray, skeletal survey, or ultrasound in some cases.

Report “yes” if a radiologic assessment was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 96.

Report “no” if a radiologic assessment was not performed or used to determine disease status or “unknown” if it is not known if a radiological assessment was performed, and continue with question 98.

Report “unknown” if testing was not performed near the start of the systemic therapy / infusion (within approximately 30 days) and after the most recent line of therapy (if applicable) and continue with question 98.

Report “not applicable” if radiologic assessments were never performed (since diagnosis) or have never shown abnormalities associated with the recipient’s primary disease for transplant and continue with

question 98.

Question 96: Date assessed:

Indicate the date (YYYY-MM-DD) the disease was assessed by radiological assessment. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy infusion (the earliest date reported in question 107).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 97: Was disease detected?

If the recipient's primary disease was detected by the radiologic assessment reported in question 96, report "yes".

If the recipient's primary disease was not detected by the radiologic assessment reported in question 96, report "no".

Question 98: Was the disease status assessed by clinical / hematologic assessment?

Clinical / hematologic assessments are the least sensitive method of disease detection. Examples include circulating blasts in the bloodstream for AML or enlargement of a malignant mass for lymphoma / solid tumor as determined by physical exam. Every recipient who has an evaluation by a physician has a "clinical" assessment.

Report "yes" if a clinical / hematologic assessment was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 99.

Report "no" if a clinical / hematologic assessment was not performed or used to determine disease status or "unknown" if it is unknown if a clinical/hematologic assessement was performed, and continue with question 100.

Question 99: Date assessed:

Indicate the date (YYYY-MM-DD) the disease was assessed by clinical/hematologic assessment. The sample collection or clinical examination date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy infusion (the earliest date reported in question 100).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 100: Was disease detected?

If the recipient's primary disease was detected by the clinical / hematologic assessment reported in question

99, report “yes”.

If the recipient’s primary disease was not detected by the clinical / hematologic assessment reported in question 99, report “no”.

Question 101: What was the recipient’s disease status immediately prior to the cellular therapy?

Indicate the disease status of the primary transplant disease immediately prior to the cellular therapy. Disease response criteria vary by disease, and are outlined in the CIBMTR Forms Instruction Manual.

Question 102: Date assessed:

Indicate the date (YYYY-MM-DD) of the disease status reported in question 101. The date assessed should be prior to the start of any systemic therapy given immediately prior to the cellular therapy infusion (the earliest date reported in question 107).

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Last modified: Jan 27, 2020

Q103-107: Systemic Therapy Prior to Cellular Therapy

Question 103: Was lymphodepleting therapy given prior to the infusion? (does not include lines of therapy given for disease treatment, bridging therapy, or maintenance)

Lymphodepleting therapy is given to destroy lymphocytes and T cells.

Do not report bridging therapy in this section. Bridging therapy, therapy given after leukapheresis up until the initiation of lymphodepleting chemotherapy for the purpose of disease control or management, should be reported on the disease specific form if applicable.

Do not report therapy given to treat disease, it should be reported on the disease specific form if applicable

✻ Copy and complete questions 104-107 to report all drugs given as lymphodepleting therapy.

Question 104-105: Specify lymphodepleting drugs:

The form lists each drug by the generic name.

For each drug listed, checking the box will indicate it was given as part of the lymphodepleting therapy used prior to the cellular therapy infusion. Report the total dose of each drug that was actually given. Do not report the prescribed dose or the daily dose. The pharmacy record or Medication Administration Record (MAR) should be used for determining the exact total dose given.

The “other drug” category should only be used if the drug is not one of the listed options. If more than one “other” drug is prescribed, list the generic name of the drugs in the space provided and attach a copy of the source document using the attachment feature in FormsNet3SM.

Question 106: Total dose:

Report the total dose that was actually given of the drug selected in question 104. Drug doses can be reported with one decimal place.

Question 107: Date started:

Report the date (YYYY-MM-DD) the drug was administered. If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Last modified: May 21, 2020

Q108-110: Functional Status

Specify the functional status of the recipient immediately prior to the cellular therapy.

Question 108: What scale was used to determine the recipient's functional status prior to the cellular therapy?

The CIBMTR uses the Karnofsky/Lansky scale to determine the functional status of the recipient immediately prior to the start of the cellular therapy. The Karnofsky Scale is designed for recipients aged 16 years and older, and is not appropriate for children under the age of 16. The Lansky Scale is designed for recipients one year old to less than 16 years old. For recipients less than one year old, questions 108-110 should be left blank.

Select the appropriate performance scale, Karnofsky or Lansky, based on the recipient's age.

Question 109-110: Performance score prior to the cellular therapy:

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. The CIBMTR uses the Karnofsky/Lansky scale to determine the functional status of the recipient immediately prior to the start of the lympho-depleting or preparative regimen. For the purposes of this manual, the term "immediately prior" represents the pre-infusion work-up phase, or approximately one month prior to the start of the lympho-depleting or preparative regimen.

Select the appropriate performance scale, Karnofsky or Lansky, based on the recipient's age. Using this scale, select the score (10-100) that best represents the recipient's activity status immediately prior to the start of the preparative regimen. For an example of the Karnofsky/Lansky scale, see Appendix L.

If a Karnofsky/Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician's clinic note), data management professionals should not assign a performance score based on analysis of available documents. Rather, a physician or mid-level health care provider (NPs and PAs) should provide documentation of the performance score. Documentation from an RN who has been trained and authorized to determine performance scores may also be used.

The CIBMTR recognizes that some transplant centers prefer to collect and use the ECOG performance score as opposed to the Karnofsky/Lansky score. Although the ECOG and Karnofsky/Lansky performance score systems are based on similar principles, the scales are not the same. For example, the Karnofsky/Lansky scale is described in 11 categories, whereas the ECOG performance status is reported in six categories. Due to the overlap between the two systems, an ECOG score of "one" can represent either "80" or "90" on the Karnofsky/Lansky scale. For centers that collect only an ECOG performance score, CIBMTR will make the following accommodations when auditing the source data:

- Centers collecting ECOG scores should do so using standard practices to ensure accuracy.

- For the purposes of CIBMTR reporting, conversion of ECOG to Karnofsky/Lansky should follow a standard and consistent practice. This practice should be clear and reproducible.

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

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Q111-120: Comorbid Conditions

Diagnosis of COVD-19 after the start of the lymphodepleting therapy: Questions 111 – 113 are intended to capture COVID-19 (SARS-CoV-2) infections diagnosed *prior* to the start of the lymphodepleting therapy / infusion. If a COVID-19 infection is diagnosed *after* the start of the lymphodepleting therapy, report the COVID-19 diagnosis on the post-infusion follow-up form (2450, 2100, and / or 4100).

Questions 111-113 will be answered for all recipients.

Question 111: Has the patient been infected with COVID-19 (SARS-CoV-2) based on a positive test result at any time prior to the start of the preparative regimen / infusion

SARS-CoV-2 is a novel virus belonging to the coronavirus (CoV) family that emerged in December 2019. The disease caused by this new CoV is known as COVID-19 (coronavirus disease 2019). The new virus is highly contagious and was officially declared a pandemic in March 2020. Transmission is believed to be from person to person through respiratory droplets from coughing and sneezing . Testing for COVID-19 is generally performed on specimens collected from a nasal swab or sputum sample .

Indicate whether or not the recipient has ever had a known COVID-19 (SARS-CoV-2) infection, based on a positive test result, at any time prior to the start of the preparative regimen or infusion (if no preparative regimen was given).

If the recipient has had a documented COVID-19 (SARS-CoV-2) infection, report “yes” and continue with question 112.

If the recipient has not had a documented COVID-19 (SARS-CoV-2) infection, report “no” and continue with question 114.

Question 112: Did the patient require hospitalization for management of COVID-19 (SARS-CoV-2) infection?

Report “yes” if the recipient was admitted to the hospital for management of their COVID-19 (SARS-CoV-2) infection. This includes any regular hospital or intensive care unit (ICU) admissions. Otherwise, report “no” and continue with question 114.

Question 113: Was mechanical ventilation given for COVID-19 (SARS-CoV-2) infection?

The clinical spectrum of COVID-19 varies from asymptomatic or paucisymptomatic forms to clinical conditions characterized by respiratory failure that necessitates mechanical ventilation and support in an intensive care unit (ICU)1. Mechanical ventilation may impact the recipient’s pulmonary function post-infusion. Report “yes” if the recipient was placed on mechanical ventilation for COVID-19 and continue with question 114.

Questions 114-120 will be answered for malignant hematologic disorders and solid tumor indications only

Question 114: Were there clinically significant co-existing disease or organ impairment at the time of patient assessment prior to preparative regimen?

Hepatic and Renal Comorbidities[1]
In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities
Hepatic Comorbidity: The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the systemic therapy regimen. If no systemic therapy was given, then it would be day -24 and the cellular therapy infusion date. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.
Renal (Moderate/Severe) Comorbidity: Serum creatinine > 2 mg/dL or > 177 µmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the systemic therapy regimen. If no systemic therapy was given, then it would be day -24 and the cellular therapy infusion date. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.

Report “yes” to question 114 if the recipient has a documented history and/or current diagnosis of any of the following:

Documented Medical History
Arrythmia
Cardiac[2]
Cerebrovascular disease
Heart valve disease[3]
Inflammatory bowel disease
Peptic ulcer

Current Diagnosis at the Time of Pre-HCT Evaluation
Rheumatologic
Solid tumor, prior[4]
Diabetes
Hepatic, mild[5]
Hepatic, moderate/severe
Infection

Obesity
Psychiatric disturbance
Pulmonary, moderate
Pulmonary, severe
Renal, moderate/severe[6]

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

[3] Excluding asymptomatic mitral valve prolapse

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

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

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

Hepatic and Renal Comorbidities
Report all comorbidities including those that are considered complications of the primary disease for infusion. See examples below.

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

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

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

Additionally, for the purposes of this manual, the term "at the time of patient assessment" is defined as the pre-infusion evaluation period performed within 6 months prior to the start of the lympho-depleting or preparative regimen. If the recipient does not have a documented history of clinically significant disease(s) or organ impairment(s), check "no" and submit the form.

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

Appendix J.

Question 115: Co-existing diseases or organ impairments

Indicate if the recipient had any of the co-existing diseases or organ impairments listed below. The definitions for each of the categories below are taken from Sorror, M. L. (2013). How I assess comorbidities before hematopoietic cell transplantation. Blood, 121(15), 2854-2863.

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

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

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

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

Heart valve disease: Moderate or severe valve stenosis or insufficiency (mitral, aortic, tricuspid, or pulmonary) as determined by the most recent heart evaluation by an echocardiogram, prosthetic mitral or aortic valve, and / or symptomatic mitral valve prolapse. This does not include a documented medical history of heart valve disease.

Hepatic (mild): Chronic hepatitis, bilirubin > upper limit of normal to 1.5x upper limit of normal, or AST/ALT > upper limit of normal to 2.5x upper limit of normal, or any history of hepatitis B or hepatitis C infection. See note in question 114.

Hepatic (moderate/severe): Liver cirrhosis, bilirubin > 1.5x upper limit of normal, or AST/ALT > 2.5x upper limit of normal. See note in question 114.

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

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

Obesity: Patients with a body mass index > 35 kg/m2 or BMI-for-age ≥ 95% (pediatric recipients only) during pre-transplant work-up period.

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

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

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

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

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

Renal (moderate / severe): Serum creatinine > 2 mg/dL or > 176.8 µmol/L, or on any form of dialysis at transplant, or prior renal transplantation. See note in question 114.

If renal (moderate / severe) comorbidity is selected, complete question 116.

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

Prior malignancy, specify: Any solid tumor(s) and / or hematologic malignancy(ies) that have been treated at any time point in the patient's past history. A history of any benign tumor(s) should not be reported.

If the recipient is receiving a cellular therapy for a disease that has transformed from one disease to another, the original malignancy should not be reported in this section. Details regarding disease transformation will be captured on the Pre- TED Disease Classification Form (Form 2402). For more information regarding disease combinations and transformations, refer to the Common Disease Combinations and Common Disease Transformations tables in the Primary Disease for HCT / Cellular Therapy section of the Disease Classification Form (Form 2402).
If prior malignancy is selected, complete question 117.

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

Question 116: Was the recipient on dialysis immediately prior to start of lymphodepleting therapy?

Indicate if the recipient was dialysis, hemodialysis, or peritoneal dialysis dependent within approximately one month prior to the start of the lymphodepleting therapy.

Question 117-120: Specify prior malignancy (check all that apply)

Specify the recipient's prior solid tumor(s) and / or hematologic malignancy(ies). If "Other skin malignancy (basal cell, squamous" is selected, specify the skin malignancy in question 118. If "Other hematologic malignancy" is selected, specify the prior hematologic malignancy in question 119. If "Other solid tumor" is selected, specify the prior solid tumor in question 120.

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

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