

4000: Cellular Therapy Essential Data Pre-Infusion

This form must be completed for all recipients of cellular therapy (non-HCT) with or without a prior HCT. Recipients of CAR T cells, donor lymphocyte infusions, tumor-infiltrating lymphocytes, cytotoxic T cells are common cellular therapies that should be reported using this form. Regenerative medicine indications can only be reported using this form with the exception of genetic modified hematopoietic stem cells to treat hematologic or other non-malignant indications. These infusions are considered transplants and should be reported using the Pre-Transplant Essential Data (Pre-TED) Form 2400.

For recipients of hematopoietic cellular transplants (HCT), complete the Pre-TED (2400) and Disease Classification (2402) forms.

This form reflects baseline recipient data and indication for a course of cellular therapy. All cellular therapies (non-HCT) are 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 Pre-Cellular Therapy Essential Data (4000) forms 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).



Consent Status and Baseline Forms

There has been a change to the functionality of submitting the Pre-Transplant Essential Data (2400), Pre-Transplant Essential Data Disease Classification (2402), and Pre-Cellular Therapy Essential Data (4000) forms. If a consent status has not yet been reported for a recipient, the edit form icon will appear disabled (see Figure 1 below). When the user hovers over the icon, it will display that consent has not yet been reported for that recipient (see Figure 2 below). The user should go to the Consent Tool (see [Navigation to the Consent Tool](#)) and document the recipient’s consent status in order to enable the edit icon and allow for completion of the form.

Figure 1. Disabled Edit Form Icon

Forms

Export to Excel

	Status ▼	Center ▼	Event ▼	Form ▼	Visit ▼	V
	DUE		2020-12-01	2400	Pre-TED	
	DUE		2020-12-01	2402	Pre-TED	

Figure 2. Hovered Text, Consent Not Yet Reported

	Status ▼	Center ▼	Event ▼	Form ▼	Visit ▼	V
	DUE		2020-12-01	2400	Pre-TED	
	Consent not yet reported		2020-12-01	2402	Pre-TED	

Links to sections of form:

- [Q1-17: Recipient Data](#)
- [Q18-32: Cellular Therapy and HCT History](#)
- [Q33-57: Product Identification](#)
- [Q58-77: Indication for Cellular Therapy](#)
- [Q78-84: Lymphodepleting Therapy Prior to Cellular Therapy](#)
- [Q85-88: Toxicity Prophylaxis](#)
- [Q89-99: Hematologic Findings Prior to Lymphodepleting Therapy](#)
- [Q100-102: Functional Status](#)
- [Q103-113: Comorbid Conditions](#)

Manual Updates:

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

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

Date	Manual Section	Add/ Remove/ Modify	Description
4/11/22	4000 Pre-CTED	Add	Clarification added on what to report if vaccine brand is Unknown: For the reported dose, specify the vaccine brand the recipient received. If the vaccine brand is not listed, select Other type and specify in question 115. If the vaccine

			brand is unknown, leave the field blank and override the error as Unknown.
4/11/ 22	4000 Pre-CTED	Add	COVID-19 Vaccine blue box added above question 109: COVID-19 Vaccine If the recipient received a COVID-19 vaccine at any time prior to July 2021 (before the COVID-19 vaccine questions were available on the Cellular Therapy Essential Data Pre-Infusion (4000) form), select Yes for question 109 at the first opportunity this form becomes available. When reporting the vaccine date, report the actual date the recipient received the vaccine.
4/11/ 22	4000 Pre-CTED	Add	Instruction added for documenting COVID-19 infections for subsequent infusion: Do NOT report an infection: <ul style="list-style-type: none"> • A recipient has a positive antibody result. They do not have a history of positive COVID diagnostic results (PCR or antigen). • The recipient was symptomatic and treated but COVID-19 diagnostic testing was not performed and/or COVID diagnostic testing was performed and negative. DO report an infection: <ul style="list-style-type: none"> • A recipient has a positive COVID diagnostic result (PCR or antigen). No treatment was given and/or recipient was asymptomatic.
7/23/ 2021	4000: Cellular Therapy Essential Data Pre- Infusion	Modify	Version 8 of the 4000: Cellular Therapy Essential Data Pre-Infusion section of the Forms Instruction Manual released. Version 8 corresponds to revision 8 of the Form 4000.

Last modified: Apr 11, 2022

Q1-17: Recipient Data

Question 1: Ethnicity

The recipient's ethnicity is automatically populated based on the value reported in the CRID assignment tool in FormsNet3. Verify the recipient's ethnicity is correct. If an error is noted, correct the error in the CRID assignment tool and verify the recipient's ethnicity has been updated on the Pre-Cellular Therapy Essential Data (4000) form.

Question 2: Race: (check all that apply)

The recipient's race is automatically populated based on the value reported in the CRID assignment tool in FormsNet3. Verify the recipient's race is correct. If an error is noted, correct the error in the CRID assignment tool and verify the recipient's race has been updated on the Pre-Cellular Therapy Essential Data (4000) form.

Question 3: Country of primary residence

Select the recipient's country of residence. If the recipient's country of primary residence is **Brazil**, continue with question 4. If the recipient's country of primary residence is **Canada**, continue with question 5. If the recipient's country of primary residence is the **United States**, continue with question 6.

Question 4: State of residence of recipient (for residents of Brazil)

If Brazil was selected as the recipient's primary country of residence, enter the recipient's state of permanent residence at the time of infusion.

Question 5: Province or territory of residence of recipient (for residents of Canada)

If Canada was selected as the recipient's primary country of residence, enter the recipient's province or territory of permanent residence at the time of infusion.

Question 6: State of residence of recipient (for residence of USA)

If the United States was selected as the recipient's primary country of residence, enter the recipient's state of permanent residence at the time of infusion.

Question 7: Zip or postal code for place of recipient's residence (USA and Canada recipients only)

Enter the five-digit ZIP code in which the recipient resides. Only five digits are required, the last four digits are optional; however, if the ZIP+4 (nine digit) code is available, please report it in this field. The zip or postal code is required for USA residents.

The postal code is optional for Canadian residents. The question can be answered or left blank without error for Canadian residents.

Question 8: Was this infusion received within the context of a 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 or the product is “out of specification”, 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 9 to report the sponsor. If “no,” continue with question 16. If the infusion 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
- [ANZCTR](#): Australian New Zealand Clinical Trials Registry EudraCT: European Clinical Trials Database
- [EudraCT](#): European Clinical Trials Database
- [UMIN](#): University Hospital Medical Information Network Center
- Investigator initiated

* Questions 9 – 15 Reporting Participation in More Than One Study

FormsNet3SM application: Complete questions 9 – 15 for each study the recipient is participating in by adding an additional instance in the FormsNetSM application.
Paper form submission: Copy questions 9 – 15 and complete for each study the recipient is participating in.

Question 9 – 15: Study sponsor:

Select the study sponsor of the clinical trial. 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**, specify the ClinicalTrials.gov identification number in question 15. The letters “NCT” do not need to be included in the field. Investigator initiated trials include those that are initiated and managed by a non-pharmaceutical / company investigator(e.g. individual physicians or cooperative groups) and center specific trials or multi-center trials.

If the recipient is participating in a corporate or industry sponsored trial, indicate the study sponsor as **Corporate / Industry**, specify the name of the Corporate or Industry sponsor in question 10 and report the clinicaltrials.gov ID number in question 15. Corporate / Industry examples include, but are not limited to,

Atara Biotherapeutics, Bellicum Pharmaceuticals, BlueBird Bio, Celgene, Daiichi Sankyo, Iovance Biotherapeutics, Janssen Pharmaceuticals, Juno Therapeutics, Kite Pharma, Mesoblast, Miltenyi Biotec and Novartis. Corporate / Industry name will be reported on the Cellular Therapy Product (4003) form.

! 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 or the product is “out of specification”, report the clinical trial in this question.

If the recipient is participating in an Australian New Zealand Clinical Trials Registry trial, indicate the sponsor as **ANZCTR** and specify the ACTRN number in question 11 (not the recipient ID). The ANZCTR, established in 2005, is an online public registry of clinical trials. The ANZCTR accepts both interventional and observational studies for registration from all countries and from the full spectrum of therapeutic areas including trials of pharmaceuticals, surgical procedures, preventive measures, lifestyle, devices, treatment and rehabilitation strategies and complementary therapies. The ACTRN number is alpha-numeric, starting with “ACTRN”.

If the recipient is participating in a European Medicines Agency clinical trial, indicate the study sponsor as **EudraCT 9** and specify the study identification number in question 12 (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 May 1, 2004 or later. 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.

If the recipient is participating in a study with UMIN, indicate the study sponsor as **UMIN** and specify the alpha-numeric study identification number in question 13 (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.

If the recipient is participating in a clinical trial and the study sponsor is not listed, select **Other**, specify the sponsor name in question 14, and report the ClinicalTrials.gov identification number in 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 15, do not include the letters “NCT” that precede the digits.

Question 16-17: Is the recipient receiving this infusion outside of the context of a clinical trial?

This question is not applicable if the infusion is received within the context of a clinical trial.

Indicate **Yes** if the recipient is receiving cellular therapy outside of the context of a clinical trial and in one of the following settings:

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

✿ Select Institutional guidelines/standard of treatment if the product is commercially available (Kymriah®, Yescarta®, or Tecartus™)

- **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 18.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Jul 23, 2021

Q18-32: Cellular Therapy and HCT History

Question 18: Is this the first time the recipient is being treated using a cellular therapy (non-HCT)?

This is defined as the first application of a cellular therapy 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 this is the first application of a cellular therapy the recipient has ever received or it is not known if this is the first cellular therapy, select **Yes** or **Unknown**, respectively and continue with question 27. If this is not the first time the recipient has received a cellular therapy, select **No** and continue with question 19.

Question 19: 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 had a prior infusion, the past infusion dates can be found in the Recipient Information Grid in FormsNet3SM. Contact CIBMTR Center Support if there are questions.

If all prior cellular therapies were reported to the CIBMTR or it is not known if all cellular therapies were reported to the CIBMTR, select Yes or Unknown, respectively and continue to question 27. If all cellular therapies were not reported to the CIBMTR, report No and continue with question 20.

Question 20: 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. It is not expected to complete forms for prior unreported infusions.



Questions 21 – 26 Reporting Prior Cellular Therapies

FormsNet3SM application: Complete questions 21-26 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 21-26 and complete for each prior cellular therapy that has not yet been reported to the CIBMTR.

Question 21: Date of the prior cellular therapy:

Report the date (YYYY-MM-DD) of the prior cellular therapy for the reported 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 22: Was the cellular therapy performed at a different institution?

Indicate **Yes** or **No** if the prior cellular therapy reported in this instance was performed at another institution. If **Yes**, report the name and address of the institution in question 23.

Question 23: 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 24 – 25: Specify the primary indication for the prior cellular therapy:

Select the indication for the prior cellular therapy reported in this instance. Any indication that is followed by "(post-HCT)" or "(with HCT)" requires 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 25. If the indication for the prior cellular therapy is not documented, select **Unknown**.

Question 26: What was the cell source for the prior cellular therapy? (check all that apply)

Indicate the cell source(s) for the prior cellular therapy 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, the 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 stepparents / children.

A related donor (**Allogeneic, related** or **syngeneic**) 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 27 – 32 HCT History

When both HCT and CT forms are submitted at the same time, duplicate questions will exist between the F2400 and F4000. To reduce the reporting burden, duplicated questions, including HCT history, on the Cell Therapy forms are disabled.

Question 27: 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 the recipient has had a prior HCT, select **Yes**. If the recipient has not had a prior HCT, select **No** or **Unknown**, respectively and continue with question 33.

Question 28: Were all prior HCTs reported to the CIBMTR?

This should include any / all infusions not performed at your center. If the recipient had a prior infusion, the past infusion dates can be found in the Recipient Information Grid in FormsNet3SM. Contact CIBMTR Center Support if there are questions.

If all prior HCTs were reported to the CIBMTR or it is not known if all HCTs were reported to the CIBMTR, select **Yes** or **Unknown**, respectively and continue with question 33. If all HCTs were not reported to the CIBMTR, select **No**.

Question 29: Date of the prior HCT:

Report the date (YYYY-MM-DD) of the prior HCT 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.

Questions 30 – 31: Was the HCT performed at a different institution?

Indicate **Yes** or **No** if the prior HCT reported in this instance was performed at another institution. If **Yes**, report the name, city, state, and country of the institution where the recipient's prior HCT reported in this instance was performed in question 31. 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.

If the prior HCT was not performed at a different institution, select **No** and continue with question 32.

Question 32: 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 stepparents / 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.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Jul 23, 2021

Q33-57: Product Identification

Question 33: 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 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 34-53 Reporting Donor Information

FormsNet3SM application: Complete questions 34-53 to report all donors, per protocol, by adding an additional instance in the FormsNet3SM application.
 Paper form submission: Copy questions 34-53 and complete for all donors, per protocol.

Question 34: 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.

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.

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

Question 35: Did NMDP/Be the Match facilitate the procurement, collection, or transportation of the product?

Indicate whether NMDP / Be the Match facilitated the procurement, collection, or transportation of the product. This information is included on the product label, the paperwork accompanying the product, and within the NMDP search / product documentation.

Question 36: Was the product a cord blood unit?

Indicate **Yes** if the product was a cord blood unit or was derived from a cord blood unit.

- If the product was an *autologous* cord blood unit, report the non-NMDP CBU ID in question 42.
- If the product was a *related* cord blood unit, report the non-NMDP CBU ID in question 42.
- If the product was an *NMDP unrelated* cord blood unit, report the NMDP CBU ID in question 40.
- If the product was a *non-NMDP unrelated* cord blood unit, report the non-NMDP CBU ID in question

42.

Indicate **No** if the product was not a cord blood unit.

- If the *autologous* product was not a CBU, continue with question 50.
- If the product was *related* and not a CBU, specify the related donor type in question 37 then continue with question 45 to report donor date of birth.
- If the unrelated donor was *NMDP* and not a CBU, report the GRID in question 42.
- If the unrelated donor was *non-NMDP* and not a CBU, report the non-NMDP unrelated donor ID in question 40.

Question 37: Specify the related donor type (allogenic, related only)

Indicate the relationship and match between the recipient and the related donor 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 stepparents/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 38: Was this donor used for any prior cellular therapies or HCT? (for this recipient)

Indicate if the allogeneic unrelated or related donor reported in this instance was used for prior cellular therapies or HCT for this recipient. If this is the recipient's first infusion, select **No**.

Question 39: 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 40: 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.

Question 41: Registry 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.

Question 42: Non-NMDP cord blood unit ID: (include related and autologous CBUs)

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

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

Question 43-44: Registry or UCB Bank ID:

Report the registry or UCB Bank ID used to obtain the adult donor or umbilical cord blood unit.

The Bone Marrow Donors Worldwide (BMDW) codes have been adopted to avoid submitting the entire name and address of the donor registry. Some common banks that do not list with BMDW have been added to the FormsNet3 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 question 44. Ensure the entered registry in question 44 is not already listed in the pull-down list for question 43. 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.

**Questions 45 – 49: Donor information**

Questions 45 – 49 should be answered only for related or non-NMDP donors. If the product is a cord blood unit or derived from a cord blood unit, the infant is the donor and not the mother.

Question 45-46: Donor date of birth:

Report if the donor's date of birth is **Known** or **Unknown**. If the donor's date of birth is known, report the date of birth (YYYY-MM-DD) in question 46 and continue with question 49.

Question 47-48: Donor age:

If the donor's DOB is unknown, report if the donor's age is **Known** or **Unknown**. If the donor's age is known, report the donor's age at the time of product collection in question 48. Report the age in months if the recipient is less than 1 year old, otherwise report the age in years.

Question 49: Donor sex:

Indicate the donor's biological sex as **Male** or **Female**. For cord blood units, report the infant donor's sex.

Question 50: Specify the total number of products: (per protocol, as part of this course of cellular therapy)

For infusions of Breyanzi™ (both commercially available and non-conforming products),

which has both CD4+ and CD8+ components, report both components as a single product, requiring a single Product Form 4003.

Report the total number of products 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 Cellular Therapy Product Forms (Form 4003).

Example 4. A single collection from the donor is separated into two portions. One portion is the cells for a DLI that are infused the same day. The second portion is selected and expanded for NK cells and then infused the next day. This is considered two products, each requiring a Cellular Therapy Product Forms (Form 4003).

Question 51: 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 allogeneic donor as the HCT
- Indication is suboptimal donor chimerism, immune reconstitution, GVHD treatment, prevent or treat disease relapse
- Composition of cells is lymphocytes

Infusions that are given with the intent to engraft should be reported as an HCT and complete the Pre-TED (2400) and Disease Classification (2402) forms.

Question 52-53: Name of product:

This question is limited to commercially available or pre-commercial products and is used for study enrollment and validation. If the name of the product is not an option, select **Other product** and specify the name in question 53. If the product has no name, such as clinical trial or study product select **No product name** from the list.

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 54: 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 55: 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. It is not intended to capture an HCT given prior to this cellular therapy infusion. 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 a subsequent HCT is not planned as part of the overall treatment protocol, select **No** and continue with question 58.

Question 56: Specify the HCT type:

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

- **Autologous product** has cells collected from the recipient for his / her own use.
- **Allogeneic product** is from a donor who is not the recipient, either related or unrelated to the recipient.

Question 57: 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**.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Feb 22, 2022

Q58-77: Indication for Cellular Therapy

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

From the list provided, select the primary 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 per CIBMTR. Please confirm with your local IRB:

- GVHD prophylaxis (with HCT)
- GVHD treatment (post-HCT)
- Immune reconstitution (post-HCT)
- Infection prophylaxis
- Prevent disease relapse (post-HCT)
- Suboptimal donor chimerism (post-HCT)

The Disease Classification (2402) Form 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 Disease Classification (2402) form for the disease that has relapsed / persisted / progressed. This will capture / confirm the diagnosis and reporting the disease status prior to the DCI/DLI.

* If the indication for cellular therapy is **cardiovascular disease**, **musculoskeletal disorder**, **neurologic disease**, **ocular disease** or **pulmonary disease**, follow up on the Cellular Therapy Essential Data Follow-Up (4100) form is not required.

* 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, visit the WHO website and consult a transplant physician, as needed. If any questions remain after review with the transplant physician, visit the WHO website or Contact CIBMTR Center Support if there are questions.

* Malignant vs. Non-Malignant

Malignant disease involves 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:

If the primary indication for the cellular therapy is **cardiovascular disease**, **musculoskeletal disease**, **neurologic disease**, **ocular disease**, **pulmonary disease**, **infection treatment** or **other indication**, report the diagnosis date of the primary indication. The diagnosis date for **malignant hematologic disorder**, **non-malignant disorder** or **solid tumor** will be captured on the Disease Classification (2402) form.

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. If **Other cardiovascular disease** is selected, specify the other **cardiovascular disease** in question 61. If **Other peripheral vascular disease** is selected, specify the other peripheral vascular disease in question 62.

Report “induced cardiomyopathy” as **Heart failure (non-ischemic etiology)** (703).

Question 63-64: Specify musculoskeletal disorder:

If musculoskeletal disorder is the indication for cellular therapy, indicate the specific disorder. If **Other musculoskeletal disorder** is selected, specify the other musculoskeletal disorder in question 64.

Question 65-66: Specify neurologic disease:

If neurologic disease is the indication for cellular therapy, indicate the specific disease. If the specific disease is not explicitly listed, select the broad category for the primary indication for infusion.

If **Other neurologic disease** is selected, specify the other neurologic disease in question 66.

Question 67: Specify ocular disease:

If ocular disease is the indication for the cellular therapy, specify the ocular disease. Examples include treatment of glaucoma or photoreceptor degeneration

Question 68-69: Specify pulmonary disease:

If pulmonary disease is the indication for the cellular therapy, specify the pulmonary disease. If **Other pulmonary disease** is selected, specify the other pulmonary disease in question 69.

Question 70-76: Specify the organism for which the cellular therapy is being given to treat:

If infection treatment is the indication for the cellular therapy, indicate the organism(s) being treated in questions 70-76.

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

210 Aspergillus, NOS	503 Suspected fungal infection	309 Human Immunodeficiency Virus 1 or 2
211 Aspergillus flavus	304 Adenovirus	343 Human metapneumovirus
212 Aspergillus fumigatus	341 BK Virus	322 Human Papillomavirus (HPV)
213 Aspergillus niger	344 Coronavirus (excluding COVID-19 (SARS-CoV-2))	349 Human T-lymphotropic Virus 1 or 2

215 Aspergillus terreus	350 COVID-19 (SARS-CoV-2)	310 Influenza, NOS
214 Aspergillus ustus	303 Cytomegalovirus (CMV)	323 Influenza A Virus
270 Blastomyces (dermatitidis)	347 Chikungunya virus	324 Influenza B Virus
201 Candida albicans	346 Dengue Virus	342 JC Virus (Progressive Multifocal Leukoencephalopathy (PML))
208 Candida non-albicans	325 Enterovirus (ECHO, Coxsackie)	311 Measles Virus (Rubeola)
271 Coccidioides (all species)	327 Enterovirus D68 (EV-D68)	312 Mumps Virus
222 Cryptococcus gattii	326 Enterovirus (polio)	345 Norovirus
221 Cryptococcus neoformans	328 Enterovirus NOS	316 Human Parainfluenza Virus (all species)
230 Fusarium (all species)	318 Epstein-Barr Virus (EBV)	314 Respiratory Syncytial Virus (RSV)
261 Histoplasma (capsulatum)	306 Hepatitis A Virus	321 Rhinovirus (all species)
241 Mucorales (all species)	307 Hepatitis B Virus	320 Rotavirus (all species)
260 Pneumocystis (PCP / PJP)	308 Hepatitis C Virus	315 Rubella Virus
242 Rhizopus (all species)	340 Hepatitis E	302 Varicella Virus
272 Scedosporium (all species)	301 Herpes Simplex Virus (HSV)	348 West Nile Virus (WNV)
240 Zygomycetes, NOS	317 Human herpesvirus 6 (HHV-6)	504 Suspected viral infection
		777 Other organism

Question 77: Specify other indication

If the indication for the cellular therapy does not fit into a category listed, specify the **other indication**. This option should be used sparingly. Contact CIBMTR Center Support with any questions prior to using this field.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Jul 23, 2021

Q78-84: Lymphodepleting Therapy Prior to Cellular Therapy

Question 78: 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 (e.g. T cells). Indicate **Yes** or **No** if the lymphodepleting therapy was given prior to the infusion. Do not include therapy given to treat disease – this therapy should be reported on the disease specific form, if applicable.

* Bridging therapy is a new terminology and is defined as any treatment that is given after the leukapheresis, during the period of cell manufacturing, with the goal of controlling the disease until the cellular product is ready to be infused. 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 as a line of therapy, if applicable.

Question 79: Weight at start of lymphodepleting therapy:

Report the recipient's actual body weight just prior to the start of the lymphodepleting therapy. The intent of this question is to report the actual weight at the time the lymphodepleting therapy starts (which may be different than the weight used to determine lymphodepleting therapy doses). This weight is usually documented on the infusion orders or admitting orders. Report weight to the nearest tenth of a kilogram or pound. Do not report adjusted body weight, lean body weight, or ideal body weight.

Question 80: Height at start of lymphodepleting therapy:

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

Questions 81 – 82: Specify lymphodepleting drugs

The form lists each drug by the generic name.

For each lymphodepleting drug administered, check the box to indicate the drug was given as part of the lymphodepleting therapy used prior to the cellular therapy infusion.

Select **Other drug** and specify the drug name in question 82 only if the lymphodepleting drug is not listed as an option. If more than one "other" drug is prescribed, each "other" drug should be reported in a separate instance. List the generic name of the drug in the space provided and attach a copy of the source document using the attachment feature in FormsNet3SM.

Question 83: Total prescribed dose:

Report the **total prescribed dose** of each drug in mg/m² as stated in the protocol. **Do not report the prescribed daily dose.** Report the drug doses to the nearest tenth.

Question 84: Date started:

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



Copy and complete questions 81-84 to report all drugs given as lymphodepleting therapy.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Jul 23, 2021

Q85-88: Toxicity Prophylaxis

Question 85-86: Therapy given for the prevention of CRS: (prophylactic therapy)

Presently, CRS prophylaxis is not routinely performed. However, practices related to CRS are evolving rapidly and some programs have considered using drugs like tocilizumab preemptively in patients with high risk to develop serious CRS. If therapy was given for the prevention of CRS check all that apply from the list of the drugs given. If **Other therapy** is selected, specify the therapy in question 86.

If more than one “other” drug is prescribed, report each “other” drug in the specify field. List the generic name of the drug in the space provided and attach a copy of the source document using the attachment feature in FormsNet3SM.

Question 87-88: Therapy given for the prevention of neurotoxicity (ICANS: (prophylactic therapy))

For ICANS, anti-epileptic drugs are often prescribed to prevent seizures. The intent of this question to separate the use of these drugs from prevention to treatment of seizure, which is captured in F4100. Additionally and similar to CRS, practices are evolving rapidly and other drugs might be used to prevent ICANS among patients with high risk for serious manifestations of this complication. If therapy was given for the prevention of neurotoxicity (ICANS), check all that apply from the list of the drugs given. If **Other therapy** is selected, specify the therapy in question 88.

If more than one “other” drug is prescribed, report each “other” drug in the specify field. List the generic name of the drug in the space provided and attach a copy of the source document using the attachment feature in FormsNet3SM.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Jan 22, 2021

Q89-102: Hematologic Findings Prior to Lymphodepleting Therapy

Question 89: Date complete blood count (CBC) sample drawn:

These questions are intended to determine the clinical status of the recipient prior to the start of lymphodepleting therapy for cellular therapy. Testing may be performed multiple times within the pre-infusion work-up time period; report the most recent CBC obtained. Laboratory values obtained on the first day of the lymphodepleting therapy may be reported as long as the blood was drawn before any lymphodepleting therapy was administered.

If no lymphodepleting therapy is given, report most recent CBC result prior to the cellular infusion.

Questions 90-97: Complete blood count results available: (check all that apply)

For each cell type listed, checking the box will indicate a result is available. Provide the most recent laboratory values from the CBC on the date reported in the prior question.

WBC: The white blood cell count is a value that represents all of the white blood cells in the blood. If the count is too high or too low, the ability to fight infection may be impaired.

Neutrophils: Neutrophils are a subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage or an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. Neutrophils are also known as polymorphonuclear leukocytes (PMNs).

Lymphocytes: Lymphocytes are another subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage of an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage.

Hemoglobin: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered “anemia” and blood transfusions, or growth factors may be required to increase the hemoglobin level.

Hematocrit: The hematocrit is the percentage (sometimes displayed as a proportion) of red blood cells relative to the total blood volume. A low hematocrit may require red blood cell transfusions or growth factors. Indicate if the recipient received a red blood cell transfusion within 30 days prior to obtaining the blood sample.

If a hematocrit value is reported, also indicate if the recipient received a red blood cell transfusion within 30 days prior to the date of the CBC reported in question 89.

Platelets: Platelets are formed elements within the blood that help with coagulation. A low platelet count, called thrombocytopenia, may lead to easy bleeding or bruising. Thrombocytopenia may require platelet transfusions. Indicate if the recipient received a platelet transfusion within 7 days prior to testing.

If a platelet value is reported, also indicate if the recipient received a platelet transfusion within 7 days prior to the date of the CBC reported in question 89.

Question 99: Did the recipient receive any growth factors <7 days before the start of systemic therapy?

Indicate if the recipient received any growth factor (e.g. GCS-F) within 7 days prior to the start of systemic therapy (i.e. lymphodepleting therapy). If no systemic therapy was given, indicate if the recipient received any growth factor (e.g. GCS-F) within 7 days prior to the infusion. In the event of a long acting growth factor (e.g. pegfilgrastim (Neulasta®), please answer this question as **yes** if the recipient received it within 14 days prior.

Question 100-102: LDH

Testing may be performed multiple times within the pre- infusion work-up time period; report the most recent LDH value obtained. Laboratory values obtained on the first day of the lymphodepleting therapy may be reported as long as the blood was drawn before any lymphodepleting therapy was administered. If no lymphodepleting therapy is given, report most recent LDH result prior to the cellular infusion.

Indicate whether the LDH result was **Known** or **Unknown** prior to the start of lymphodepleting therapy. If **Known**, report the result, the unit of measure, and specify the upper limit of normal in question 102.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Jul 23, 2021

Q103-105: Functional Status

* Specify the functional status of the recipient immediately prior to the start of lymphodepleting therapy or the cellular therapy if no lymphodepleting therapy was given.

Question 103: 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 103 – 105 should be left blank.

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

Question 104-105: 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](#).

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Jul 23, 2021

Q106-123: Comorbid Conditions

✿ **Diagnosis of COVID-19 after the start of the lymphodepleting therapy:** Questions 106 – 108 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 (Cellular Therapy Essential Data Follow-Up (4100) form, Post-HSCT Data (2100) or Post-Transplant Essential Data (2450)).

Questions 106-115 will be answered for all recipients.

Question 106: 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 lymphodepleting therapy or infusion (if no lymphodepleting therapy was given).

If the recipient has had a documented COVID-19 (SARS-CoV-2) infection, report **Yes**.

If the recipient has not had a documented COVID-19 (SARS-CoV-2) infection, report **No** and continue with question 109.

If this is a subsequent infusion and the documented COVID-19 (SARS-CoV-2) infection was already reported on previous forms, report **No** and continue with question 109.

Do NOT report an infection:

- A recipient has a positive antibody result. They do not have a history of positive COVID diagnostic results (PCR or antigen).
- The recipient was symptomatic and treated but COVID-19 diagnostic testing was not performed and/or COVID diagnostic testing was performed and negative.

DO report an infection:

- A recipient has a positive COVID diagnostic result (PCR or antigen). No treatment was given and/or recipient was asymptomatic.

Question 107: 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 106.

Question 108: Was mechanical ventilation used 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** or **No** if the recipient was placed on mechanical ventilation for COVID-19.

**COVID-19 Vaccine**

If the recipient received a COVID-19 vaccine at any time prior to July 2021 (before the COVID-19 vaccine questions were available on the Cellular Therapy Essential Data Pre-Infusion (4000) form), select **Yes** for question 109 at the first opportunity this form becomes available. When reporting the vaccine date, report the actual date the recipient received the vaccine.

Question 109: Was a vaccine for COVID-19 (SARS-CoV-2) received at anytime prior to the start of systemic therapy?

Indicate if the recipient received a vaccine for COVID-19 (one dose without a planned second dose, first dose with planned second dose, second dose, third dose and / or booster) at any time prior to the start of the systemic therapy (e.g. lymphodepleting therapy) / infusion.

If the recipient did not receive a vaccine for COVID-19 or it is not known if the recipient received a vaccine, select **No** *or* **Unknown**, respectively, and continue with question 116.

If this is a subsequent infusion and all vaccine doses have already been reported on previous forms, select **No** and continue with question 116.

If this is a subsequent infusion and some, but not all vaccine doses have already been reported on previous forms, select **Yes** and only report the vaccine doses not previously reported.

Question 110-113: Select dose(s) received (check all that apply)

Select the vaccine dose(s) the recipient received prior to the start of the systemic therapy (e.g. lymphodepleting therapy) / infusion (check all that apply) and report the date when the vaccine was received. If the exact date is not known, use the process described in the General Instructions, Guidelines for Completing Forms and select **Date estimated**.

Question 114-115: Specify vaccine type:

Specify the type of vaccine the recipient received. If the vaccine type is not listed, select **Other type** and specify in question 115. If the vaccine brand is unknown, leave the field blank and override the error as **Unknown**.

Question 116: Is the recipient HIV positive?

Indicate if the recipient has confirmed to be HIV positive and/or is receiving treatment for HIV. Of note, recipients who received a prior CAR T cell product might have a false positive HIV test. Thus this question does not apply in this situation. Only patients proven to be infected by HIV should be reported under this question.

Patients with HIV have a higher risk to develop lymphoid malignancies which can be treated with CAR T cells. The rationale of this question is to inquire additional information on the status and treatment of HIV before and after the cellular therapy for malignancy.

Question 117: Were there clinically significant co-existing disease or organ impairment at the time of patient assessment prior to preparative regimen?

* This section does not apply if your center considers this infusion to be donor lymphocyte infusion (DLI)

* Please report co-morbidities that were detected within six months of the cellular therapy, which is different than HCT reporting. The 6 month rule applies to assessments that need to be performed in order to determine if a comorbidity is present (i.e., PFT for pulmonary, liver values for hepatic, creatinine for renal, BMI for obesity, etc.). If the co-morbidity is denoted as "ANY history", the 6 month rule does not apply.

* **Hepatic and Renal Comorbidities¹**

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/lymphodepleting therapy. If no 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/lymphodepleting therapy. 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 if the recipient has a documented history and/or current diagnosis of any of the following:

Documented Medical History
Arrhythmia
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

²Ejection fraction (EF) \leq 50% should be reported only if present on most recent test

³Excluding asymptomatic mitral valve prolapse

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

⁵Including any history of hepatitis B or hepatitis C infection

⁶Including 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 systemic therapy. 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 118: 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 [Sorrer, M. L. \(2013\). How I assess comorbidities before hematopoietic cell transplantation. Blood, 121\(15\), 2854-2863.](#)⁷

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 requiring treatment.

Cardiac: Any history of coronary artery disease (one or more vessel coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, and / or ejection fraction $\leq 50\%$ (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 107.

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 117.

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.

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. Do not report a psychiatric comorbidity if therapy was given "as needed" for any mood, anxiety, or other psychiatric disorder.

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: $DLCOc = \{uncorrected\ DLCO\} / [0.06965 \times \{hemoglobin\ g/dL\}]$

Pulmonary (severe): Corrected diffusion capacity of carbon monoxide (e.g., DLCOc, DLCOcorr, DLCO)

and/or FEV1 \leq 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 μ mol/L, or on any form of dialysis at transplant, or prior renal transplantation. See note in question 117.

If renal (moderate / severe) comorbidity is selected, complete question 119.

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 110.

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 119: 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 120-123: 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 121. If **Other hematologic malignancy** is selected, specify the prior hematologic malignancy in question 122. If **Other solid tumor** is selected, specify the prior solid tumor in question 123.

⁷Sorrow, M. L. (2013). How I assess comorbidities before hematopoietic cell transplantation. *Blood*, 121(15), 2854-2863.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
114-115	4/11/22	Add	Clarification added on what to report if vaccine brand is Unknown: For the reported dose, specify the vaccine brand the recipient received. If the vaccine brand is not listed, select Other type and specify in question 115. If the vaccine brand is unknown, leave the field blank and override the error as Unknown.	Added for clarification
109	4/11/22	Add	COVID-19 Vaccine blue box added above question 109: COVID-19 Vaccine If the recipient received a COVID-19 vaccine at any time prior to July 2021 (before the COVID-19 vaccine questions were available on the Cellular Therapy Essential Data Pre-Infusion (4000) form), select Yes for question 109 at the first opportunity this form becomes available. When reporting the vaccine date, report the actual date the recipient received the vaccine.	Added for clarification
106	4/11/22	Add	Instruction added for documenting COVID-19 infections for subsequent infusion: Do NOT report an infection: <ul style="list-style-type: none"> A recipient has a positive antibody result. They do not have a history of positive COVID diagnostic results (PCR or antigen). The recipient was symptomatic and treated but COVID-19 diagnostic testing was not performed and/or COVID diagnostic testing was performed and negative. DO report an infection: <ul style="list-style-type: none"> A recipient has a positive COVID diagnostic result (PCR or antigen). No treatment was given and/or recipient was asymptomatic. 	Added for clarification
109	4/1/2022	Modify	Replaced “preparative regimen” with “systemic therapy”	Systemic therapy is the cellular therapy equivalent to preparative regimen. Lymphodepleting therapy is a type of systemic therapy.
110	4/1/	Modify	Replaced “preparative regimen” with “systemic therapy”	Systemic therapy

	2022			is the cellular therapy equivalent to preparative regimen. Lymphodepleting therapy is a type of systemic therapy.
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