Cellular Therapy Manuals

This section provides explanatory text for each question on the Pre-CTED, Pre-CTED Baseline, Cellular Therapy Product, Cellular Therapy Infusion, Post-CTED, and Post-CTED Follow-up forms.

✻ Reporting of cellular therapy infusions to CIBMTR remains voluntary. Reporting of commercially available cellular therapy product infusions (i.e. Kymriah®, Yescarta™, Tecartus™, Breyanzi™, Abecma®, Carvykti™) is strongly encouraged.

Cell therapy reporting tracks and follow up schedule
Beginning Summer 2022 and updated in Summer 2023, a reporting track is set for all cell therapy infusions reported to the CIBMTR. The track will be set by the center reporting preference and infusion details and will determine which forms come due. There are five cellular therapy reporting tracks:

- 15 years (CRF)
  - Forms: 4000, 4001, 4003, 4006, 4100, 4101, 2402 + disease forms (when applicable)
- Standard follow up TED
  - Forms: 4000, 4003, 4006, 4100, 2402
- 100 day only (TED)
  - Forms: 4000, 4003, 4006, single 4100 at 100d, 2402
- CTRM
  - Forms: 4000, 4003, 4006
- No follow up
  - Forms: 4000, 2402

See the Data Management Guide for a full description of each track and follow up schedule.

Cell therapy reporting preferences:
As part of the Summer 2022 release, every center will have a reporting preference. The options are:

- Do Not Perform

- Perform Do Not Report
- Research Level
- Regulatory Level

Please see the Data Management Guide for a full description of the different levels, including which forms will come due.

Follow up tracks as set by reporting preference
As part of the Summer 2022 release, the center reporting preference is now used in determining the cell therapy reporting track, and subsequently which forms are required.

TED (Standard & 100 day only)	CRF (15 years)	CTRM
Commercial CAR-T on study, no consent, REMS/RGL center (Standard follow up TED)	Commercial CAR-T *on* study (15 years)	_Indication = Cardiovascular disease, Musculoskeletal disorder, Neurologic disease, Ocular disease, Pulmonary disease
Commercial CAR-T not on study (Standard follow up TED)	BMT CTN (15 years)	Non-commercial genetically modified non-CAR-T products
Non-commercial CAR-T products (Standard follow up TED)	Genetically modified products (other than CAR-T) either stand alone or post-HCT (15 years)	
Stand-alone non-genetically modified cell therapy infusions without a history of HCT (Standard follow up TED)	Commercial CAR-T not on study (Standard follow up CRF)	
Post-HCT non-genetically modified cell therapy infusions (100 day only)	Registry Partners	

Commercial CAR-T = Kymriah®, Yescarta®, Tecartus™, Abecma®, Breyanzi™, Carvykti™

When to report cellular therapy infusions to the CIBMTR

Please see the Data Management Guide for a full description the guidance when determining whether to report a cellular therapy to the CIBMTR.

Donor cellular infusion (DCI)
Donor cellular infusions (DCIs) are a subtype of cellular therapy.

An infusion can be classified as a “DCI” 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 include mesenchymal cells, peripheral blood mononuclear cells, NK cells, etc.

Donor Lymphocyte Infusions (DLIs) are a subset of DCIs. DLIs meet the same criteria above but are infusions of just a lymphocyte product. DLIs are reported on the Donor Lymphocyte Infusion (2199) form. See the F2199 manual for the definition of DLI.

Date	Manual Section	Add/ Remove/ Modify	Description
5/3/ 2024	Cellular Therapy Manuals	Modify	Reformatted and added hyperlinks to the cellular therapy manuals contained in this section.
7/28/ 2023	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Version 10 of the 4000: Cellular Therapy Essential Data Pre-Infusion section of the Forms Instruction Manual released. Version 10 corresponds to revision 10 of the Form 4000.
7/28/ 2023	4001: Pre-Cellular Therapy Baseline Data	Add	Version 1 of the 4001: Pre-Cellular Therapy Baseline Data section of the Forms Instruction Manual released. Version 1 corresponds to revision 1 of the form 4001.
7/28/ 2023	4100: Cellular Therapy Essential Data Follow-Up	Add	Version 9 of the 4100: Post- Cellular Therapy Follow-Up section of the Forms Instruction Manual released. Version 9 corresponds to revision 9 of the form 4100.
7/28/ 2023	4101: Post-Cellular Therapy Follow-	Add	Version 1 of the 4101: Post- Cellular Therapy Follow-Up section of the Forms Instruction Manual released. Version 1 corresponds to revision 1 of the form 4101.

	Up		
2/8/23	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Updated the text in the blue box below question 121: Serologic tests should be completed during the pre-HCT work-up phase, or approximately one month prior to the start of the preparative regimen. ~~If a recipient tests positive for Hepatitis B core antibody (Anti HBc), Hepatitis B surface antigen (HBsAg), Hepatitis B NAAT, Hepatitis C antibody (Anti HCV), and/or Hepatitis C NAAT serologic tests, also complete the HEP Form (Form 2047).~~ If a recipient tests positive for HIV antibody or HIV NAT serologic tests, also complete the HIV Form (Form 2048).
9/23/2022	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Version 9 of the Cellular Therapy Manuals section of the Forms Instruction Manual released.

Last modified: May 03, 2024

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. CAR-T cells, tumor-infiltrating lymphocytes, and cytotoxic T cells are common cellular therapies that should be reported using this form. Regenerative medicine indications can be reported using this form with the exception of genetic modified hematopoietic stem cells to treat malignant 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.

Donor Lymphocyte Infusions (DLI) are no longer captured on the Pre-CTED (4000) form.
An infusion can be classified as a DLI when:

- It's an infusion of a lymphocyte-only product
- The infusion must be post-Allogeneic HCT and will most likely be from the same HCT donor
- The product cannot be genetically modified

Donor Lymphocyte Infusion (2199) form should be completed.

This form reflects pre-infusion essential data for a course of cellular therapy. All cellular therapies (non-HCT) are collected on this form, including indications that reflect donor cellular infusions (DCI) 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)).

✻ 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

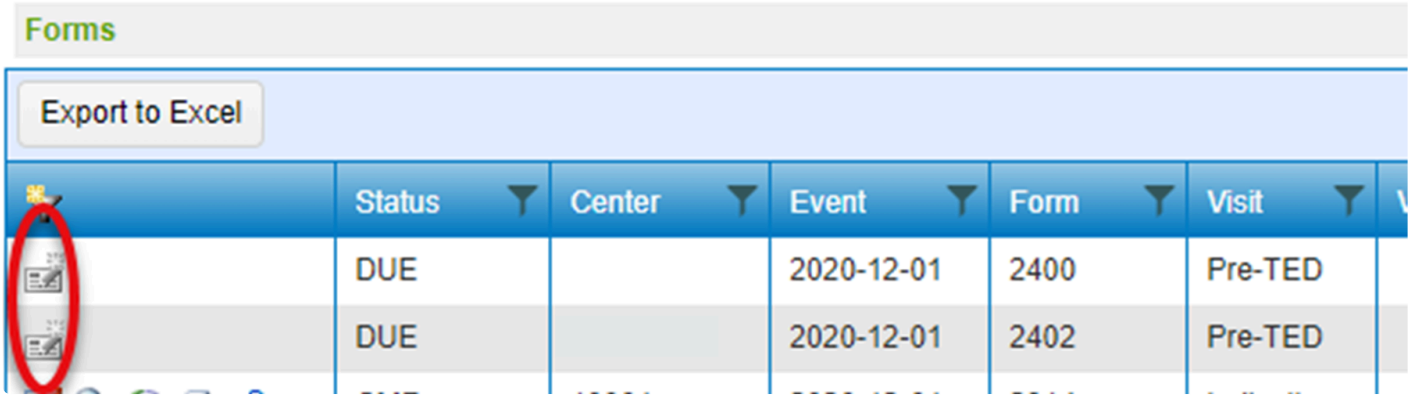
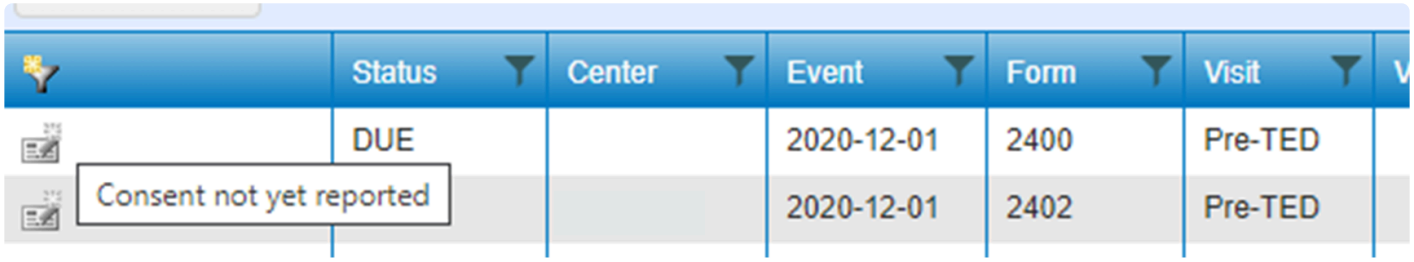


Figure 2. Hovered Text, Consent Not Yet Reported



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	
3/13/2024	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Updated instructions in Q9 to clarify RCI-BMT is now known as CIBMTR CRO Services: If the study sponsor is reported as **BMT-CTN**, **CIBMTR CRO Services** (formerly RCI-BMT), **USIDNET**, **COG**, **PedAL**, or **Investigator initiated**, specify the ClinicalTrials.gov identification number. The letters “NCT” do not need to be included in the field. I
3/13/2024	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Updated hyperlink in Q8 for CIBMTR CRO Services: https://cibmtr.org/CIBMTR/Studies/Research-Programs/Clinical-Trials-Support/CRO-Services
3/13/2024	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Updated instructions in Q8 to clarify RCI-BMT is now known as CIBMTR CRO Services: For the infusion being reported on this form, indicate if the recipient is a registered participant with BMT-CTN, CIBMTR CRO Services (formerly 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.
1/12/24	4000: Cellular Therapy Essential Data Pre-Infusion	Remove	Removed the red warning box regarding clinical trials from question 9: ~~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.~~
1/12/24	4000: Cellular Therapy Essential Data Pre-Infusion	Remove	Removed the red warning box regarding clinical trials from question 8: ~~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.~~
8/28/2023	Q81-91: Comorbid Conditions	Remove	Condensed instructions for reporting comorbidities in Q92 and Q93
8/22/2023	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Clarified the intention of the question: Indicate if the recipient received pre-exposure drugs for COVID-19 in this reporting period.

7/28/2023	4000: Cellular Therapy Essential Data Pre-Infusion	Modify	Version 10 of the 4000: Cellular Therapy Essential Data Pre-Infusion section of the Forms Instruction Manual released. Version 10 corresponds to revision 10 of the Form 4000.

Last modified: Mar 13, 2024

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^{SM}. 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^{SM}. 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 State of residence of recipient (for residents of Brazil).
• If the recipient's country of primary residence is Canada, continue with Providence or territory of residence of recipient (for residents of Canada).
• If the recipient's country of primary residence is the United States, continue with State of residence of recipient (for residents of USA).
• If the recipient's country of primary residence is not Brazil, Canada, or the United States, continue with Was this infusion received within the context of a clinical trial.

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 providence 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; 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?

For the infusion being reported on this form, indicate if the recipient is a registered participant with BMT-CTN, CIBMTR CRO Services (formerly 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
- CIBMTR CRO Services: CIBMTR Clinical Research Organization Services
- USIDNET: United States Immunodeficiency Network
- COG: Children’s Oncology Group
  PedAL: Pediatric Acute Leukemia Master Clinical Trial
- 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

Reporting Participation in More Than One Study

FormsNet3^{SM} application: Complete the Study Sponsor, applicable Number, and Specify the ClinicalTrials.gov identification number questions for each study the recipient is participating in by adding an additional instance in the FormsNet3^{SM} application.
Paper form submission: Copy the Study Sponsor, applicable Number, and Specify the ClinicalTrials.gov identification number questions and complete for each study in which the recipient is participating.
If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.

Question 9 – 14: 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**, **CIBMTR CRO Services** (formerly RCI-BMT), **USIDNET**, **COG**, **PedAL**, or **Investigator initiated**, specify the ClinicalTrials.gov identification number. 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 and report the clinicaltrials.gov ID number. 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.

If the recipient is participating in an Australian New Zealand Clinical Trials Registry trial, indicate the sponsor as **ANZCTR** and specify the ACTRN number (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** and specify the study identification number (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 (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’s name, and report the ClinicalTrials.gov identification number.

Question 15: Specify the 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 identification number – do not include the letters “NCT,” preceding the digits.

Question 16-17: Was this infusion received outside 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®, Tecartus™, Breyanzi™, Abecma®, Carvykti™))

- **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**.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
9	3/13/ 2024	Modify	Updated instructions in Q9 to clarify RCI-BMT is now known as CIBMTR CRO Services: If the study sponsor is reported as **BMT-CTN**, **CIBMTR CRO Services** (formerly RCI-BMT), **USIDNET**, **COG**, **PedAL**, or **Investigator initiated**, specify the ClinicalTrials.gov identification number. The letters “NCT” do not need to be included in the field. I	RCI-BMT is now known as CIBMTR CRO Services
8	3/13/ 2024	Modify	Updated hyperlink in Q8 for CIBMTR CRO Services: https://cibmtr.org/CIBMTR/Studies/Research-Programs/Clinical-Trials-Support/CRO-Services	RCI-BMT is now known as CIBMTR CRO Services
8	3/13/ 2024	Modify	Updated instructions in Q8 to clarify RCI-BMT is now known as CIBMTR CRO Services: For the infusion being reported on this form, indicate if the recipient is a registered participant with BMT-CTN, CIBMTR CRO Services (formerly 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.	RCI-BMT is now known as CIBMTR CRO Services

9	1/12/24	Remove	Removed the red warning box regarding clinical trials: ~~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.~~	No longer applicable and confusing.
8	1/12/24	Remove	Removed the red warning box regarding clinical trials: ~~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.~~	No longer applicable and confusing.

Last modified: Mar 13, 2024

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.

Prior cellular therapy reported to the CIBMTR
If **Unknown** is selected for *Were all prior cellular therapies reported to the CIBMTR*, then *Date of the prior cellular therapy*, *Was the cellular therapy performed at a different institution*, *Specify the institution that performed the cellular therapy*, and *Specify the source(s) for the prior cellular therapy* questions can be answered to report information regarding prior cellular therapies; however, these questions are not required to be completed.

Question 19: Were all prior cellular therapies (non-HCT) reported to the CIBMTR?

This should include all cellular therapy infusions (except for DLIs) 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 FormsNet3^{SM}. Contact the CIBMTR Customer Support if there are questions.

If **Yes**, all prior cellular therapies were reported to the CIBMTR or **Unknown**, continue with the Donor Information section.

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.

Reporting Prior Cellular Therapies
FormsNet3^{SM} application: Complete the *Date of the prior cellular therapy*, *Was the cellular therapy performed at a different institution*, *Specify the institution that performed the cellular therapy*, and *Specify the source(s) for the prior cellular therapy* questions to report all prior cellular therapies that have not yet been reported to the CIBMTR by adding an additional instance in the FormsNet3^{SM} application.
Paper form submission: Copy the *Date of the prior cellular therapy*, *Was the cellular therapy performed at a different institution*, *Specify the institution that performed the cellular therapy*, and *Specify the source(s) for the prior cellular therapy* questions and complete for 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 if the prior cellular therapy being reported in this instance was performed at another institution. If the prior cellular therapy was not performed at a different institution, select **No**.

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. 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.

HCT History
When both HCT and CT forms are submitted, duplicate questions will exist between the

Pre-TED (2400) form and Pre-CTE (4000) form. 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 never had a prior HCT, report **No**.

Prior HCTs reported to the CIBMTR
If **Unknown** is selected for *Were all prior HCTs reported to the CIBMTR*, *Date of prior HCT*, *Was the prior HCT performed at a different institution*, *Specify the institution that performed the last HCT*, and *Specify the HPC source for the prior HCT* questions can still be answered to report information regarding prior HCTs; however, these questions are not required to be completed.

Question 28: 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 HCT dates in the Recipient Information Grid in FormsNet3^{SM}. Contact CIBMTR Customer Support if there are questions.

If **Yes** or **Unknown**, continue with Are any of the products, associated with this course of cellular therapy, genetically modified.
p(banner tip). **Reporting Prior HCTs**

FormsNet3^{SM} application: Complete the *Date of prior HCT*, *Was the prior HCT performed at a different institution*, *Specify the institution that performed the last HCT*, and *Specify the HPC source for the prior HCT* questions to report all prior HCTs that have not yet been reported to the CIBMTR by adding an additional instance in the FormsNet3^{SM}SM application.
Paper form submission: Copy the *Date of prior HCT*, *Was the prior HCT performed at a different institution*, *Specify the institution that performed the last HCT*, and *Specify the HPC source for the prior HCT* questions and complete for the prior HCT that has not yet been reported to the CIBMTR.

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: Was the HCT performed at a different institution?

Indicate if the prior HCT being reported in this instance was performed at another institution. If the prior HCT was not performed at a different institution, select **No**.

Questions 31: Specify the institution that performed the 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 other institution where the previous infusion was administered

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)
.	.	.	.	.

Last modified: Mar 06, 2024

Q33-52: 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.

Reporting Donor Information
FormsNet3^{SM} application: Complete all donor related questions, *Specify the total number of products*, and_ Name of cellular therapy produc_t to report all donors, per protocol, by adding an additional instance in the FormsNet3^{SM} application.
Paper form submission: Copy all donor related questions, *Specify the total number of products*, and *Name of cellular therapy product* to report 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.
- If the product was a *related* cord blood unit, report the non-NMDP CBU ID.

- If the product was an *NMDP unrelated* cord blood unit, report the NMDP CBU ID.
- If the product was a *non-NMDP unrelated* cord blood unit, 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 to *Specify the total number of products*.
- If the product was *related* and not a CBU, specify the related donor type, continue to *Donor date of birth*.
- If the unrelated donor was *NMDP* and not a CBU, continue to *Global Registration Identifier for Donors (GRID)*.
- If the unrelated donor was *non-NMDP* and not a CBU, continue to *Registry donor ID*.

Question 37: Specify the related donor type (allogeneic, 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.

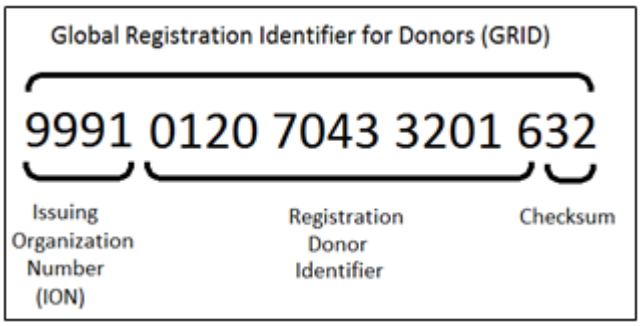
HLA-mismatched relative:
Includes: Siblings who are not HLA-identical and all other blood- relatives who have at least one HLA mismatch (mismatch can be at the antigen or allele level) (e.g., parents, aunts, uncles, children, cousins, half-siblings). The patient and donor will be allele-level mismatched 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 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.

Question 41: Registry ID: (not applicable for related donors)

Report the non-NMDP unrelated donor ID. Examples of non-NMDP donor registries include Australia Bone Marrow Donor Registry and REDOME. This ID may be located on the product label, the paperwork accompanying the product, and registry-specific search / product documentation.

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 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.

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.

Donor information
Donor date of birth/age and *Donor sex* 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).

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. 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**, or **Unknown**. For cord blood units, report the infant donor's sex. **Unknown** should be used if the cell therapy product was "off the shelf" and/or the donor sex is not provided.

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 Cellular Therapy Product (4003) Form.

Report the total number of products infused per protocol. This question is used to make the correct number of Cellular Therapy Product (4003) Forms 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 (4003) Forms.

Donor lymphocyte infusions (DLIs) should be reported on the Donor Lymphocyte Infusion (2199) form.

Question 51-52: 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. 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).

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Jul 29, 2023

Q53-72: Indication for Cellular Therapy

Question 53: 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) 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.

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 54: 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 55-57: 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**. If **Other peripheral vascular disease** is selected, specify the other peripheral vascular disease.

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

Question 58-59: 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.

Question 60-61: 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.

Question 62: 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 63-64: 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.

Question 65-71: 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.

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	350 COVID-19 (SARS-CoV-2)	310 Influenza, NOS

terreus		
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 72: 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 29, 2023

Q73: Lymphodepleting Therapy Prior to Cellular Therapy

Lymphodepleting therapy data collection has been split between TED and CRF level reporting. TED level reporting will capture just **Yes** or **No** if lymphodepleting therapy was given. All details will be capture on the Pre-Cellular Therapy Baseline Data (4001) form if the infusion is selected for CRF level reporting.

Question 73: 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.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
.	.	.	.	.

Last modified: Jul 29, 2023

Q74-76: Hematologic Findings Prior to Lymphodepleting Therapy

Current hematologic findings data collection has been split between TED and CRF level reporting. TED level reporting will capture only LDH values. All other lab values will be captured on the Pre-Cellular Therapy Baseline Data (4001) form if the infusion is selected for CRF level reporting.

Question 74-76: LDH

Testing may be performed multiple times within the pre- infusion work-up time period; report the most recent LDH value obtained within 30 days of the start of lymphodepleting therapy. 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.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
.	.	.	.	.

Last modified: Jul 29, 2023

Q77-80: 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 77: What scale was used to determine the recipient's functional status prior to the cellular therapy? (check all that apply)

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. If a performance score is not documented in the source documentation (e.g., inpatient progress note, physician's clinic note), data management professionals should not assign a performance score based on analysis of available documents. Rather, a physician should provide documentation of the performance score. Documentation from an RN who has been trained and authorized to determine performance scores may also be used.

The ECOG Performance Status Scale and the Karnofsky Performance Status Scale are two widely used methods to assess the functional status of a patient. 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, Karnofsky / Lansky questions should be left blank.

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

Question 78-79: 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.

Question 80: ECOG score:

Recipient performance status is a critical data field that has been determined to be essential for all outcome-

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

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
.	.	.	.	.

Last modified: Jul 29, 2023

Q81-91: Comorbid Conditions

> **!** COIVD-19 Infections
> The COVID-19 infection questions are disabled as of April 2024.

Prior viral exposure/infection and *Were there any co-existing diseases or organ impairment present according to the HCT comorbidity index (HCT-CI)?* to be completed for **malignant hematologic disorders** and **solid tumor indications** ONLY.

Question 81-82: Pre-exposure drugs given for COVID-19 (SARS-CoV-2)?

Indicate if the recipient received pre-exposure drugs for COVID-19 in this reporting period. Specify if **Other** is selected.

Question 83: Has the patient been infected with COVID-19 (SARS-CoV-2) based on a positive test result at any time prior to the start systemic therapy?

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 systemic therapy (e.g., lymphodepleting therapy) or infusion (if no systemic 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**.

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

Possible Reporting Scenarios:

An infection **should not** be reported if:

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

An infection **should** be reported if:

*A recipient has a positive COVID-19 diagnostic result (PCR or antigen). No treatment was given and / or recipient was symptomatic.

Question 84: 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**.

Question 85: 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. Indicate **Yes** or **No** if the recipient was placed on mechanical ventilation for COVID-19.

COVID-19 Vaccine
The COVID-19 vaccine questions are disabled as of April 2024.

Question 86: 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.

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

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.

Reporting multiple COVID-19 Vaccine
FormsNet3^{SM} application: Complete Specify vaccine type and Select dose(s) received questions to report all COVID-19 vaccine doses received prior to the start of systemic therapy (e.g., lymphodepleting therapy) / infusion by adding an additional instance in the FormsNet3SM application. A separate instance should be added for each dose.
Paper form submission: Copy the Specify vaccine type and Select dose(s) received questions and complete report all COVID-19 vaccine doses received prior to systemic therapy (e.g., lymphodepleting therapy) / infusion. A separate instance should be completed for each dose

Question 87-88: Specify vaccine brand:

For the vaccine dose being reported, specify the brand of vaccine the recipient received. If the vaccine brand is not listed, select **Other type** and specify.

If the vaccine brand is unknown, leave the data field blank and override the error as 'unknown.'

> **Third dose versus Booster dose**
> To determine between a third dose and a booster dose, seek clinician clarification, as needed, using the guidelines listed below:
> *Third dose*: An additional primary dose required for recipients who did not build enough protection from their primary vaccine series, typically for immunocompromised individuals
> *Booster dose*: Administered to recipients who have enough protection after completing their primary vaccine series but then protection decreases over time
> Primary vaccine series:

- Two doses of Pfizer-BioNTech or Moderna
- One dose of Johnson & Johnson's Janssen

Question 89-90: Select dose received:

For the reported dose, specify the vaccine dose the recipient received prior to the start of the preparative regimen / infusion and report the date when the dose was received.

Select **One dose (without planned second dose)** if the recipient received a single dose, without the plans of receiving the second dose and report the date of administration.

Select **First dose (with planned second dose)** if the recipient received their first dose, with plans for receiving the second dose and report the date of administration.

Select **Second dose** if this is the recipient's planned second dose of the vaccine and report the date of administration.

Refer to the blue instructional box above for additional information regarding third and booster doses.

If the exact date is not known, use the process described in the General Instructions, Guidelines for Completing Forms and select **Date estimated**.

> Question 91 applies only for malignant hematologic disorder or solid tumor indications.

Question 91: Prior viral exposure/infection: (check all that apply)

Indicate if the recipient was positive for any of the viral exposure or infections listed below. Do not select the viral exposure or infection if the test was performed and the results were negative.

If testing for evidence of prior viral exposure / infection was not performed, select **Not done**.

Select **Not applicable** if testing for evidence of prior viral exposure / infection was performed and all of the results were negative.

Serologic Tests
Serologic tests should be completed during the pre-infusion work-up phase, or approximately one month prior to the start of systemic therapy (e.g., lymphodepleting therapy

If a recipient tests positive for HIV antibody or HIV NAT serologic tests, also complete the HIV Form (Form 2048).

HTLV1 antibody: Human T-Lymphotropic virus I/II (HTLV I/II) is a retrovirus in the same class as HIV. HTLV I/II is associated with certain leukemias and lymphomas, as well as demyelinating diseases such as multiple sclerosis.

Anti-EBV (Epstein-Barr virus antibody): Epstein-Barr Virus (EBV) is a common virus of the herpes family. It can cause infectious mononucleosis, but in most cases is asymptomatic. EBV establishes a lifelong dormant infection in some cells of the body's immune system. Serious post-transplant complications related to EBV include EBV viremia (reactivation) and post-transplant lymphoproliferative disease (PTLD).

Hepatitis B surface antibody:
Hepatitis B is caused by the hepatitis B virus (HBV). Infection with this virus can cause scarring of the liver, liver failure, liver cancer, and even death. Hepatitis B is spread through infected blood and other body fluids. Acute hepatitis B infection does not usually require treatment because most adults clear the infection. Treatment of chronic infection may be necessary to reduce the risk of cirrhosis and liver cancer.

The hepatitis B surface antibody test reveals the presence of hepatitis B antibodies, indicating previous exposure to HBV (or successful vaccination), but the virus is no longer present, and the person cannot pass on the virus.

Anti-HBc (hepatitis B core antibody): The enzyme-linked immunosorbent assay (ELISA) technique tests for the antibody directed against the hepatitis B virus core proteins. The hepatitis B core antibody test can indicate previous HBV infection. Currently there is no licensed confirmatory test for Anti-HBc. If the screening test is reactive, a second Anti-HBc test is performed using a different manufacturer's test kit.

HBsAg (hepatitis B surface antigen): The ELISA or enzyme immunoassay (EIA) techniques test for the presence of proteins produced by the hepatitis B virus. Confirmatory testing is done using a neutralization test. The first marker appears approximately three weeks following infection, and disappears

approximately six months later.

Hepatitis B – NAAT: The HBV NAAT test is more sensitive than regular serologic tests and is often used in conjunction with those tests to monitor patients with chronic HBV infections. If Hepatitis B – NAAT testing was done, report the results in this section.

Anti-HCV (hepatitis C antibody): Hepatitis C is a serious infection caused by the hepatitis C virus (HCV), which attacks the liver and may cause life-long infection. HCV is considered the most serious hepatitis infection because of its significant long-term health consequences. The infection is often asymptomatic, but once established, chronic infection can cause inflammation of the liver. This condition can progress to fibrosis and cirrhosis. In some cases, those with cirrhosis will go on to develop liver failure or liver cancer. Presence of the antibody in the blood represents exposure to HCV, which is most often spread by blood-to-blood contact. No vaccine against HCV is available.

The ELISA technique tests for antibodies to the HCV. Confirmatory testing is done using the recombinant immunoblot assay (RIBA) test. These tests can determine past exposure to HCV, but not current viral load.

Hepatitis C – NAAT: Nucleic acid testing (NAAT) is a combination PCR test that detects the presence of viral genes (HCV RNA) rather than antigens or antibodies. This test allows earlier detection and provides more sensitivity than previously used tests.

HIV antibody: HIV infection is caused by exposure to one of two viruses: HIV-1 or HIV-2. HIV-2 is less virulent and has a longer incubation period than HIV-1. Both types of HIV progressively destroy lymphocytes, which are an important part of the body's immune defense. HIV can lead to acquired immunodeficiency syndrome (AIDS), a condition in which the immune system begins to fail, leading to life-threatening opportunistic infections. Infection with HIV occurs by the transfer of bodily fluids and is present as both free virus particles and virus within infected immune cells.

HIV antibody testing is done using combination ELISA which detects antibodies to the HIV-1 and HIV-2 viruses. HIV-1 is confirmed by Western Blot, which detects specific proteins using gel electrophoresis. There is currently no licensed confirmatory test for HIV-2. If the screening test is reactive, HIV-2 is confirmed by specific ELISA.

The results of HIV assessments are often kept in confidence and may not be reportable to anyone other than the patient and their physician. If HIV testing was done, but the results are not available, do not select this option.

If the result is "positive," an HIV insert (Form 2048) is also required.

HIV – NAAT: Nucleic acid testing (NAAT) is a PCR test that detects the presence of viral genes rather than antigens or antibodies. This test allows earlier detection and provides more sensitivity than previously used tests.

The results of HIV assessments are often kept in confidence and may not be reportable to anyone other

than the patient and their physician. If HIV testing was done, but the results are not available, do not select this option.

If the result is "positive," an HIV insert (Form 2048) is also required.

Toxoplasmosis antibody: Toxoplasmosis is caused by the parasitic protozoan Toxoplasma gondii, or T. gondii. Toxoplasmosis is spread through ingestion of contaminated food or water or contact with infected cat feces. T. gondii infection is usually subclinical in healthy individuals, but infection can cause serious symptoms in pregnant women and immunocompromised individuals. Chronic, dormant T. gondii infection may follow initial exposure, and can then reoccur. Severe toxoplasmosis can affect the brain, eyes, and other organs and can cause permanent organ damage.

Testing for antibodies to T. gondii is generally done by enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). These immunoassays can be used to detect IgM and / or IgG antibodies to T. gondii. The presence of IgM antibodies indicates a recent or current infection, usually within the past four to six months. The presence of IgG antibodies indicates a previous infection and confers a long-term immune response to the virus. Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative. Confirmatory testing is available to verify a positive serological result; this is done by Toxoplasma Serological Profile (TSP), which is a panel of multiple antibody ELISAs and agglutination testing.

Comorbidities
Prior to answering Were there any co-existing diseases or organ impairment present according to the HCT comorbidity index (HCT-CI) question, review the list of co-existing disease(s) and/or organ impairments listed in Appendix J.

Question 92: Were there any co-existing diseases or organ impairment present according to the HCT comorbidity index (HCT-CI)?

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.

The criteria for reporting comorbidities is based on Sorror, M. L. (2013). How I assess comorbidities before hematopoietic cell transplantation. Blood, 121(15), 2854-2863.

Report **Yes** if the recipient has a documented history and / or current diagnosis of any of the conditions listed in Appendix J: Reporting Comorbidities

Report all comorbidities including those that are considered complications of the primary disease for

transplant. See examples below.

- 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 infusion. 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 prior to the start of the preparative regimen. If the recipient does not have a documented history of clinically significant disease(s) or organ impairment(s), check **No**.

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

Question 93: Co-existing diseases or organ impairments

Indicate if the recipient had any of the co-existing diseases or organ impairments listed in Appendix J. The definitions for each of the categories are taken from Sorror, M. L. (2013). How I assess comorbidities before hematopoietic cell transplantation. Blood, 121(15), 2854-2863. [7]

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 94: 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 95-97: Specify prior malignancy (check all that apply)

Specify the recipient’s prior solid tumor(s) and / or hematologic malignancy(ies).

If **Other prior hematologic malignancy** is selected, specify the hematologic malignancy.

If **Other prior solid tumor** is selected, specify the solid tumor.

[7]Sorror, 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)
Q81	4/19/ 2024	Modify	The Diagnosis of COVID-19 After the Start of the Preparative Regimen blue box removed and the COVID-19 Infection red box added to clarify these questions are now disabled.	Due to disabling of questions with the Spring 2024 release
Q86	4/19/ 2024	Modify	The COVID-19 Vaccine red box updated to clarify these questions are now disabled.	Due to disabling of questions with the Spring 2024 release
81-82	8/22/ 2023	Modify	Clarified the intention of the question: Indicate if the recipient received pre-exposure drugs for COVID-19 in this reporting period.	This question applies to each reporting period.
Q91	8/28/ 2023	Remove	Remove the Hepatic and Renal Comorbidities blue box: ~~*Hepatic and Renal Comorbidities 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. When determining the severity of the hepatic comorbidity, the value closest to the start of the systemic therapy regimen/ lymphodepleting therapy should be used. If the liver function test values closest to the start of the preparative regimen do not meet the criteria specified above, a hepatic comorbidity should not be reported.*~~ ~~*Renal (Moderate/Severe) Comorbidity: Serum creatinine > 2*~~	All comorbidity information has been consolidated to Appendix J

			~~*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. If the serum creatinine value closest to the start of the systemic therapy regimen/lymphodepleting therapy did not meet the criteria specified above, a renal (moderate/severe) comorbidity should not be reported.*~~	
Q91	8/28/ 2023	Remove	Remove the 'documented medical history' instructions:~~*Documented Medical History*~~ ~~*-Arrhythmia that has required specific antiarrhythmic treatment*~~ ~~*-Cardiac*~~ ~~*-Cerebrovascular disease*~~ ~~*-Inflammatory bowel disease*~~ ~~*-Peptic ulcer*~~ ~~*-Rheumatologic*~~ ~~*-Prior malignancy, requiring treatment*~~ ~~*Current Diagnosis at the Time of Pre-Infusion Evaluation*~~ ~~*-Diabetes*~~ ~~*-Heart valve disease*~~ ~~*-Hepatic, mild*~~ ~~*-Hepatic, moderate/severe*~~ ~~*-Infection*~~ ~~*-Obesity*~~ ~~*-Psychiatric disturbance*~~ ~~*-Pulmonary, moderate*~~ ~~*-Pulmonary, severe*~~ ~~*-Renal, moderate/severe*~~ ~~*2Ejection fraction (EF) ≤ 50% should be reported only if present on most recent test*~~ ~~*3Excluding asymptomatic mitral valve prolapse*~~ ~~*4Including any history of hepatitis B or hepatitis C infection*~~ ~~*5If the PFT lists both a "control" FEV1 and a "post-dilator" FEV1, the "control" FEV1 should be used to determine if a pulmonary comorbidity is present.*~~ ~~*6Including renal transplantation at any time in the patient's history*~~	All comorbidity information has been consolidated to Appendix J
Q93	8/28/ 2023	Remove	Remove each comorbidity and it's criteria from instructions	All comorbidity information

				has been consolidated to Appendix J

Last modified: Apr 26, 2024