

4000: Cellular Therapy Essential Data Pre-Infusion

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

For recipients of hematopoietic cellular transplants, complete a form 2400 – Pre- Transplant Essential Data and form 2402 Disease Classification.

This form reflects baseline recipient data and indications for cellular therapy. All non-HCT cellular therapies are being collected on this form, including indications that reflect donor cellular infusions (DCI/DLI) done post-transplant, now referred to as “post-HCT cellular therapy”.

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

Links to Sections of Form

[Q1-14: Recipient Data](#)

[Q15-29: Cellular Therapy and HCT History](#)

[Q30-38: Planned Infusions](#)

[Q39-50: Indication for Cellular Therapy](#)

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[Q84-239: Systemic Therapy Prior to Cellular Therapy](#)

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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
11/ 15/ 17	4000: Cellular Therapy Essential Data Pre- Infusion	Modify	<p>Replaced instructions for question 35 as indicated below.</p> <p><i>Indicate whether the cellular therapy product reported in this instance contains <u>viral-specific</u> Cytotoxic T Lymphocytes (CTLs). These products are generally from allogeneic donors that have been cultured / expanded and modified to treat specific viruses such as CMV, EBV, Adenovirus, etc.</i></p> <p><i>Cytotoxic T lymphocytes (CTLs) are a type of white blood cell that can kill foreign cells, cancer cells, and cells infected with a virus. Indicate “yes” or “no” for the donor being reported in this instance and continue with question 36.</i></p>
7/ 25/ 17	4000: Cellular Therapy Essential Data Pre- Infusion	Modify	<p>Version 2 of the 4000: Cell Therapy Essential Data Pre-Infusion section of the Forms Instructions Manual released. Version 2 corresponds to revision 4 of the Form 4000.</p>

Q1-14: Recipient Data

Question 1: Ethnicity

Indicate the recipient's ethnicity. The United States Office of Management and Budget (OMB) has defined ethnicity as culturally or geographically determined. The distinction between Hispanic and non-Hispanic is for the purpose of the United States census. According to the OMB, "Hispanic" is an ethnic designation based upon where someone (his or her ancestors) was raised (e.g., "Latin America"). Hispanic people may be of any race. The CIBMTR recognizes regional differences with regard to the interpretation of ethnicity throughout the world.

If the recipient is not a resident of the USA, select "not applicable."

If the recipient declines to provide this information or the recipient's ethnicity is not documented, select "unknown."

For more information regarding ethnicity, see [Appendix I](#).

Question 2: Race: (check all that apply)

Indicate the recipient's race. If this recipient has reported that they are more than one race, you may select all the options that apply. The race groups provided are specific to the United States.

For non-U.S. centers, select "not reported" if the rules/regulations of your country prohibit the collection or reporting of race data (or due to lack of documentation).

If race is reported, it may be necessary to consult with the recipient to select the race group(s) with which they most closely identify.

If the recipient declines to provide this information, select "not reported."

If the recipient's race is not documented, select "unknown."

For more information regarding race, see [Appendix I](#).

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

- ! To be comply with Federal Regulations for human research subject protection, centers must obtain IRB-approved informed consent from recipients and donors (if applicable) to allow data submitted to the CIBMTR to be used for observational research. The NMDP/CIMBTR has written protocols and informed consent documents for the Observational Database. All centers must have local IRB approval for the Observational Database protocol. The NMDP IRB has approved these protocols and consent forms, and the documents are provided to participating sites to include with their local IRB submissions. International Centers must obtain consent of each patient participating in the Observational Database in a manner consistent with the laws and regulations of their country.

* Reporting Consent Status for DCI

If this form is being completed for a DCI reported on a Post-TED Form (Form 2450) or Post-HCT Follow-Up Data Form (Form 2100), report “not applicable” for question 3. The consent status will be reported on the Pre-TED Form (Form 2400) and should not be re-reported here. If the recipient’s consent status has changed since the Pre-TED Form was completed, update the consent status on the Pre-TED Form.

When a recipient consents to participate in the Observational Database, their data are available in the CIBMTR’s Observational Research Database and may be used for research. The database includes recipient baseline and outcome data for related and unrelated allogeneic transplants from any cell source, and for autologous transplants. The Observational Research Database now includes data on recipients of cellular therapy.

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

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

- Compare outcomes of transplantation and cellular therapies between each other and to other therapies

Indicate if the recipient has signed an IRB-approved consent form to participate in the Observational Research Database. If “yes (patient consented),” continue with question 4. If “no” (patient declined), “not approached”, or “not applicable” (post-HCT scenario) continue with question 5. If the patient declines consent, any data reported will not be used in observational studies.



When to use the “Not Approached” option for the Research Database Consent

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

Question 4: Date form was signed:

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

Question 5: Is the recipient participating in a cellular therapy clinical trial?

Indicate if the recipient is a registered participant with BMT-CTN, RCI-BMT, USIDNET, COG, a Corporate / Industry trial, EudraCT, UMIN, and/or another clinical trial sponsor, **regardless if that sponsor uses CIBMTR forms to capture outcomes data**. If “yes”, continue with question 6 to report the sponsor. If “no”, continue with question 13. If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.

- [BMT-CTN: Blood and Marrow Transplant Clinical Trials Network](#)
- [RCI-BMT: Resource for Clinical Investigation in Blood and Marrow Transplant](#)
- [USIDNET: United States Immunodeficiency Network](#)
- [COG: Children’s Oncology Group](#)
- Corporate / Industry
- [EudraCT: European Clinical Trials Database](#)
- UMIN: [University Hospital Medical Information Network Center](#)
- Investigator initiated



Questions 6-12 Reporting Participation in More Than One Study

FormsNet3SM application: Complete questions 6-12 for each study the recipient is

participating in by adding an additional instance in the FormsNet application.
Paper form submission: Copy questions 6-12 and complete for each study the recipient is participating in.

Question 6: Study sponsor:

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

If the study sponsor is reported as “BMT-CTN” or “RCI-BMT,” specify the study ID number in question 7. See link listed under question 5 for more information.

If the study sponsor is reported as “USIDNET” or “COG,” specify the ClinicalTrials.gov identification number in question 12. See link listed under question 5 for more information.

If the study sponsor is reported as “Corporate/Industry”, specify the name in question 8 and the clinicaltrials.gov ID number in question 12. Corporate/Industry examples include, but are not limited to, Atara Biotherapeutics, Bellicum Pharmaceuticals, BlueBird Bio, Celgene, Juno Therapeutics, Kite Pharma, Mesoblast, and Novartis.

If the study sponsor is reported as “EudraCT”, specify the EudraCT number in question 9. The European Union Drug Regulating Authorities Clinical Trials is the European Clinical Trials Database of all clinical trials of investigational medicinal products with at least one site in the European Union commencing 1 May 2004 or later. See link listed under question 5 for more information.

If the study sponsor is reported as “UMIN”, specify the UMIN in question 10. 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. . See link listed under question 5 for more information.

If the study sponsor is reported as “Investigator initiated”, specify the clinicaltrials.gov ID number in question 12. These include trials that are initiated and managed by a non-pharmaceutical/company researcher (e.g. individual physicians or cooperative groups) and center specific trials or multi-center trials.

If “other sponsor” is reported, specify the study sponsor in question 11 and the clinicaltrials.gov ID number in question 12.

Question 7: Study ID Number:

If the recipient is participating in a BMT-CTN or RCI-BMT clinical trial, specify the identification number and continue with question 13.

Question 8: Specify corporate / industry sponsor name:

If the recipient is participating in corporate / industry sponsored trial, report the name of the Corporate or Industry sponsor and continue with question 12. Corporate/Industry examples include, but are not limited to, Atara Biotherapeutics, Bellicum Pharmaceuticals, BlueBird Bio, Celgene, Juno Therapeutics, Kite Pharma, Mesoblast, and Novartis.

Question 9: Specify the EudraCT number:

If the recipient is participating in a European Medicines Agency clinical trial, specify the identification number and continue with question 13. 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.

Question 10: Specify the UMIN number:

If the recipient is participating in a UMIN clinical trial, specify the alpha-numeric identification number and continue with question 13.

Question 11: Specify other sponsor:

If the recipient is participating in a clinical trial and the study sponsor is not listed, specify the sponsor and continue with question 12.

Question 12: 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 number here. It is not necessary to include the letters “NCT” that precede the digits. Continue with question 13.

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

Indicate “yes” if the recipient is receiving cellular therapy in the setting of “institutional guidelines/standard of care”, “hospital exemption”, or “compassionate use” and continue with question 14 (see below for definitions). If “no”, continue with question 15.

Question 14: Specify the reason for not being on a clinical trial: (check all that apply)

Institutional guidelines/standard of treatment: internal protocols at the center

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

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

Q15-29: Cellular Therapy and HCT History

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

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

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

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

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

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

Question 17: Specify the number of prior cellular therapies:

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

Questions 18-23 Reporting Prior Cellular Therapies

FormsNet3SM application: Complete questions 18-23 to report all prior cellular therapies that have not yet been reported to the CIBMTR by adding an additional instance in the FormsNet application.

Paper form submission: Copy questions 18-23 and complete for each prior cellular therapy that has not yet been reported to the CIBMTR.

Question 18: Date of the prior cellular therapy:

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

For more information regarding reporting partial or unknown dates, see [General Instructions, General Guidelines for Completing Forms.](#)

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

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

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

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

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

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

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

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

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

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

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

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



Questions 24-29 HCT History

For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2100 and F4000. To reduce the reporting burden, duplicated questions on the Cell Therapy forms are disabled. This includes HCT History reported in Q24-29.

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

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

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

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

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

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

Question 26: Date of the prior HCT:

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

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

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

Indicate if the last HCT was performed at another institution. If "yes" continue with question 28. If "no" continue with question 29.

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

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

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

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

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

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

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

Q30-38: Planned Infusions

Question 30: Specify the number of planned infusions: (per protocol) (as part of this course of cellular therapy)

Report the number of infusions to be infused per protocol. This question is used to make the correct number of Cellular Therapy Infusion forms (Form 4006) come due. Each infusion must be part of the protocol and will be given regardless of disease response.

Example 1. The protocol specifies three infusions are to be given as part of the course of cellular therapy. Report the total number of planned infusions as “3”.

Example 2. The protocol specifies three infusions are to be given as part of the course of cellular therapy. The patient will be assessed to see if additional infusions will be tolerated and two more infusions may be given. Report the total number of planned infusions as “5”. If the last two infusions do not occur, contact your CIBMTR CRC.

Question 31: Is the product 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).

Questions 32-35 Reporting donor information

FormsNet3SM application: Complete questions 32-35 to report all donors, per protocol, used for the infusions reported in question 31 by adding an additional instance in the FormsNet application.

Paper form submission: Copy questions 32-35 and complete for all donors, per protocol, used for the infusions reported in question 31.

Question 32: Specify the cell source:

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

An autologous product has cells collected from the recipient for his/her own use. Continue with question 35.

An unrelated donor (allogeneic, unrelated) is a donor who shares no known ancestry with the recipient. Include adoptive parents/children or step-parents/children. Continue with question 34.

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. Continue with question 33.

Question 33: Specify the related donor type:

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

Syngeneic:

Includes: Monozygotic (identical) twins. Occurs when a single egg is fertilized to form one zygote, which then divides into two separate embryos.

Does not include: Other types of twins or HLA-identical siblings (see below).

HLA-identical sibling:

Includes: Non-monozygotic (dizygotic, fraternal, non-identical) twins. Occurs when two eggs are fertilized by two different sperm cells at the same time. This category also includes siblings who aren't twins, but have identical HLA types.

Does not include: Half-siblings should be reported as "HLA matched other relatives" if their HLA typing is a match, or "mismatched relative" if it does not match.

HLA-matched other relative:

Includes: All blood-related relatives, other than siblings, who are HLA matched (e.g., parents, aunts, uncles, children, cousins, half-siblings).

Does not include: Adoptive parents/children or step-parents/children who are HLA matched.

HLA-mismatched relative:

Includes: Siblings who are not HLA-identical and all other blood-related 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).

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

Question 34: Was this donor used for any prior cellular therapies?

Indicate if the allogeneic unrelated or related donor being reported in this instance was used for prior cellular therapies or HCT for this recipient. Do not answer this question for autologous donors.

Question 35: Does this product contain cytotoxic T lymphocytes (CTLs)?

Indicate whether the cellular therapy product reported in this instance contains viral-specific Cytotoxic T Lymphocytes (CTLs). These products are generally from allogeneic donors that have been cultured / expanded and modified to treat specific viruses such as CMV, EBV, Adenovirus, etc.

Question 36: 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 a HCT, either planned or dependent upon the response to the cellular therapy. If a subsequent HCT is part of the overall treatment plan, indicate “yes”, continue with question 37. If “no”, continue with question 39.

Question 37: Specify the HCT type:

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

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

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

Question 38: 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”.

Q39-50: Indication for Cellular Therapy

Question 39: What was the indication for performing treatment with cellular therapy?

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

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

- Suboptimal donor chimerism (post-HCT)
- Immune reconstitution (post-HCT)
- GVHD prophylaxis (with HCT)
- GVHD treatment (post-HCT)
- Prevent disease relapse (post-HCT)
- Relapsed, persistent or progressive disease (post-HCT)

If the indication for cellular therapy is relapsed, persistent or progressive disease (post-HCT), there must be a documented relapse on the appropriate post-HCT follow up form. If the recipient has never had an HCT and is getting a cellular therapy for relapsed disease, the indication should be the primary disease for which the cellular therapy is being given.

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

Disease Classification Questions

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

Malignant vs. Non-Malignant

Malignant diseases involve cells dividing without control that can spread to other parts of

the body through blood and lymph systems. These diseases are usually characterized by unlimited, aggressive growth, invasion of surrounding tissues, and metastasis. Non-malignant 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 40: Date of diagnosis:

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, Guidelines for Completing Forms](#).

Question 41- 43: Specify cardiovascular disease:

If cardiovascular disease is the indication for cellular therapy, indicate the specific disease in question 41. If “other cardiovascular disease” is selected, specify in question 42. If “other peripheral vascular disease” is selected, specify in question 43. Continue with question 84.

Question 44 & 45: Specify musculoskeletal disorder:

If musculoskeletal disorder is the indication for cellular therapy, indicate the specific disorder in question 44. If “other musculoskeletal disorder”, specify in question 45. Continue with question 84.

Question 46 & 47: Specify neurologic disease:

If neurologic disease is the indication for cellular therapy, indicate the specific disease in question 46. If “other neurologic disease”, specify in question 47. Continue with question 84.

Question 48: Specify ocular disease

If ocular disease is the indication for which the recipient is receiving the cellular therapy, specify in Q48. Examples include treatment of glaucoma or photoreceptor degeneration.

Question 49: Specify pulmonary disease

If pulmonary disease is the indication for which the recipient is receiving the cellular therapy, specify in Q49. Examples include Chronic Obstructive Pulmonary Disease (COPD) or pulmonary fibrosis.

Question 50: Specify other indication

If the indication for which the recipient is receiving the cellular therapy is “other indication” because it does not fit into a category listed above, specify the indication in Q50. An example is treatment of autism by cellular therapy.

Q51-57: Infection

Question 51-57: Organism:

Indicate the fungal or viral organism for which the patient is receiving the cellular therapy. Only one instance is required, the other instances may be skipped.

Organism:

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

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

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

Table 1: Codes for Commonly Reported Organisms

201 <i>Candida albicans</i>	301 Herpes Simplex Virus (HSV)	323 Influenza A Virus
208 <i>Candida non-albicans</i>	302 Varicella Virus	324 Influenza B Virus
210 <i>Aspergillus</i> , NOS	303 <i>Cytomegalovirus</i> (CMV)	325 Enterovirus (ECHO, Coxsackie)
211 <i>Aspergillus flavus</i>	304 <i>Adenovirus</i>	326 Enterovirus (polio)
212 <i>Aspergillus fumigatus</i>	306 Hepatitis A Virus	327 Enterovirus D68 (EV-D68)
213 <i>Aspergillus niger</i>	307 Hepatitis B Virus	328 Enterovirus NOS
214 <i>Aspergillus ustus</i>	308 Hepatitis C Virus	340 Hepatitis E
215 <i>Aspergillus terreus</i>	309 Human Immunodeficiency Virus 1 or 2	341 BK Virus
221 <i>Cryptococcus neoformans</i>	310 Influenza, NOS	342 JC Virus (Progressive Multifocal Leukoencephalopathy (PML))

222 <i>Cryptococcus gattii</i>	311 Measles Virus (Rubeola)	343 Human metapneumovirus
230 <i>Fusarium</i> (all species)	312 Mumps Virus	344 <i>Coronavirus</i>
240 <i>Zygomycetes</i> , NOS	314 Respiratory Syncytial Virus (RSV)	345 <i>Norovirus</i>
241 <i>Mucorales</i> (all species)	315 Rubella Virus	346 Dengue Virus
242 <i>Rhizopus</i> (all species)	316 Human Parainfluenza Virus (all species)	347 Chikungunya virus
260 <i>Pneumocystis</i> (PCP / PJP)	317 Human herpesvirus 6 (HHV-6)	348 West Nile Virus (WNV)
261 <i>Histoplasma</i> (capsulatum)	318 Epstein-Barr Virus (EBV)	349 Human T-lymphotropic Virus 1 or 2
270 <i>Blastomyces</i> (dermatitidis)	320 <i>Rotavirus</i> (all species)	503 Suspected fungal infection
271 <i>Coccidioides</i> (all species)	321 <i>Rhinovirus</i> (all species)	777 Other organism
272 <i>Scedosporium</i> (all species)	322 <i>Human Papillomavirus</i> (HPV)	

Q58-83: Disease Assessment at Last Evaluation Prior to Cellular Therapy

- ! These questions are for malignant disease indications with relapsed, persistent or progressive disease only. This section should not be completed if the indication for cellular therapy is “Suboptimal donor chimerism” (post-HCT), “Immune reconstitution” (post-HCT), “GVHD prophylaxis (with HCT)”, “GVHD treatment (post-HCT)”, “Prevent disease relapse (post-HCT)”, “Infection treatment” or “Infection prophylaxis”.

Question 58: Was the disease assessed prior to the cellular therapy?

Indicate if the disease status was assessed prior to the cellular therapy. If “yes”, continue with question 59. If “no”, continue with question 84.

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

Question 59: Was the disease status assessed by molecular testing (e.g. PCR)?

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

Select “yes” if a molecular method was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 60. If a molecular method was not used to determine disease status, check “no” and continue with question 63.

If a molecular method was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 63.

Question 60: Date sample collected:

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by molecular method. The sample collection date should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 85).

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

Question 61: Was disease detected?

If molecular markers for disease were found, check “yes” and continue with question 62.

If molecular markers for disease were not found, check “no” and continue with question 63.

Question 62: Was the status considered a disease relapse or progression?

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

Question 63: Was the disease status assessed via flow cytometry (immunophenotyping)?

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material.

Select “yes” if flow cytometry was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 64. If flow cytometry was not performed or could not be used to determine disease status, check “no” and continue with question 67.

If flow cytometry was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 67.

Question 64: Date sample collected:

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by flow cytometry. The sample collection date should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 85).

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

Question 65: Was disease detected?

If flow cytometry detected disease, check “yes” and continue with question 66.

If flow cytometry did not detect disease, check “no” and continue with question 67.

Question 66: Was the status considered a disease relapse or progression?

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

Question 67: Was the disease status assessed by cytogenetic testing (karyotyping or FISH)?

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

Select “yes” if cytogenetic testing was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 68. If cytogenetic testing was not performed or was not used to determine disease status, check “no” and continue with question 76.

If cytogenetic testing was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 76.

Question 68: Was the disease status assessed by karyotyping?

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

Select “yes” if karyotyping was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 69. If karyotyping was not performed or used to determine disease status, check “no” and continue with question 72.

If karyotyping was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 72.

Question 69: Date sample collected:

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by karyotyping. The sample collection date should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 85).

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

Question 70: Was disease detected?

If disease was detected by karyotyping, check “yes” and continue with question 71.

If disease was not detected by karyotyping, check “no” and continue with question 72.

Question 71: Was the status considered a disease relapse or progression?

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

Question 72: Was the disease status assessed by FISH?

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

Select “yes” if FISH was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 73. If FISH was not performed or used to determine disease status, check “no” and continue with question 76.

If FISH was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 76.

Question 73: Date sample collected:

Indicate the date (YYYY-MM-DD) the sample was collected for disease assessment by FISH. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy (date reported in question 85).

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

Question 74: Was disease detected?

If FISH markers for disease were found, check “yes” and continue with question 75.

If FISH markers for disease were not found, check “no” and continue with question 76.

Question 75: Was the status considered a disease relapse or progression?

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

Question 76: Was the disease status assessed by radiological assessment? (e.g., PET, MRI, CT)

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

Select “yes” if a radiologic assessment was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 77. If a radiologic assessment was not performed or used to determine disease status, check “no” and continue with question 79.

If radiological assessment was used to evaluate the disease status, but has never been positive, check “not applicable” and continue with question 79.

Question 77: Date assessed:

Indicate the date (YYYY-MM-DD) the disease was assessed by radiological assessment. The sample collection date should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 85).

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

Question 78: Was disease detected?

If radiologic evidence of disease was found, check “yes”.

If radiologic evidence of disease was not found, check “no”.

Question 79: Was the disease status assessed by clinical / hematologic assessment?

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

Select “yes” if a clinical/hematologic assessment was used to determine disease status at the last evaluation prior to cellular therapy and continue with question 80. If a clinical/hematologic assessment was not performed or used to determine disease status, check “no” and continue with question 82.

Question 80: Date assessed:

Indicate the date (YYYY-MM-DD) the disease was assessed by clinical/hematologic assessment. The sample collection date should be prior to the start of any systemic therapy given immediately prior to the cellular therapy (date reported in question 85).

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

Question 81: Was disease detected?

If clinical/hematologic evidence of disease was found, check “yes”.

If clinical/hematologic evidence of disease was not found, check “no”.

Question 82: What was the recipient’s disease status immediately prior to the cellular therapy?

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

Question 83: Date assessed:

Indicate the date (YYYY-MM-DD) of the disease status reported in question 82. The date assessed should be prior to the start of any systemic therapy given immediately prior the cellular therapy (date reported in question 85).

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

Q84-239: Systemic Therapy Prior to Cellular Therapy

Question 84: Was systemic therapy given immediately prior to cellular therapy as part of the cellular therapy protocol?

Indicate “yes” if the recipient received systemic therapy prior to the cellular therapy infusion or “no” if the recipient did not. Systemic therapy may include intravenous or oral chemotherapy with the intent to deplete circulating lymphocytes, reduce tumor burden or other. . If “yes”, continue with question 85. If “no”, continue with question 240.

Question 85: Date started:

Indicate the date (YYYY-MM-DD) the systemic therapy started. This should be the earliest start date of the first drug given.

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

Question 86 & 87: Specify the reason for which the systemic therapy was given per protocol:

If systemic therapy was given as “Lympho-depleting therapy” or for “Reduction of tumor burden”, continue with question 88. If systemic therapy was given for another reason, select “other reason” and specify in question 87.

Question 88-239: Specify preparative regimen drugs:

- * The form lists each drug by the generic name. The form also lists some drugs by broad categories, with specific drugs listed individually. For example, anthracycline is listed as the broad drug category, followed by the specific drugs of daunorubicin, doxorubicin, and idarubicin.

For each drug listed, indicate whether or not it was given as part of the preparative regimen. Report the total dose of each drug that was actually given. Do not report the prescribed dose or the daily dose. The pharmacy record or Medication Administration Record (MAR) should be used for determining the exact total dose given.

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

A common example of this situation occurs in the use of busulfan. In some cases, a "test dose" of the drug is given before the actual preparative regimen is started, and this dose is used for acquiring drug levels that are used to adjust the dose that will be used in the preparative regimen. In other situations, the first dose of the drug is given in the usual fashion as part of the preparative regimen. After this first dose, serum drug levels are drawn and sent to a reference lab. The drug is continued at the starting dose until the lab results are reported and adjustment is made to later doses.

When a drug is used for the preparative regimen where pharmacokinetics will be tested, it is important to distinguish whether the testing will be done with a "test dose" before beginning the preparative regimen or using the first dose of the preparative regimen. The reporting of the dosing for the CIBMTR forms depends upon this distinction. This helps distinguish whether the dose is part of the therapeutic regimen, or not.

A test dose was given > 24 hours prior to the intended therapeutic dosing.

Example: A patient with AML underwent a cellular therapy; busulfan and cyclophosphamide were used as the preparative regimen. The patient presented to clinic 9 days before the cellular therapy infusion, where a dose of busulfan at 0.5 mg/kg was given intravenously. Blood samples were drawn for the next 6 hours, after which the patient left the clinic. His samples were sent to a lab, results were returned the next day, and an adjusted dose of busulfan was calculated. He returned to the hospital 6 days before the cellular therapy infusion, and began to receive busulfan at the adjusted dose intravenously for 4 days, followed by cyclophosphamide, and proceeded to receive his cells. Since he received 0.5 mg/kg as a "test dose," this would not be reported in his total preparative regimen dose.

If a test dose was given, where the dose was distinct from the therapeutic dosing preparative regimen (often 1-2 or more days prior to the initiation of regular dosing), the start date of the chemotherapy agent should be reported as the date the first therapeutic dose was administered. The actual dose received would NOT include the test dose.

The first dose of therapeutic dosing is used for monitoring.

Example: A patient with ALL underwent a cellular therapy infusion; busulfan and fludarabine were used as the preparative regimen. She was admitted to the hospital 7 days before her cellular therapy infusion, and received a dose of busulfan at 0.8 mg/kg IV at 6:00 AM. Serum samples were drawn every 30 minutes until the next dose of Busulfan at 0.8 mg/kg IV was given at 12:00 noon. Her blood was sent to a reference lab, and she continued to receive busulfan every 6 hours. On day -6, the lab called with her drug levels, and it was determined that the current dose was correct. No adjustment was made, and she completed all 16 doses of busulfan. Since the dose of busulfan (0.8 mg/kg) that was used for drug

testing was ALSO her first dose of the preparative regimen, it should be included in the amount of drug that was given for preparative regimen.

If the first dose of the preparative regimen was used to determine pharmacokinetics, the start date of the chemotherapy agent should be reported as the date the first dose was administered. The actual dose received would include the dose used for monitoring.

Test doses must be reported consistently at your center. Since most centers follow a consistent approach to pharmacokinetic testing, it should be straightforward for the center to adopt a consistent approach to the reporting of test doses.

For each drug indicated as “yes”:

- Drug doses must be reported in whole numbers. If the total dose includes a decimal, round to the nearest whole number (round up if 0.5 or greater). For paper submission, do not modify the number of boxes or include decimal values.
- Report the date (YYYY-MM-DD) the drug was administered. If the exact date is unknown, please view [General Instructions, General Guidelines for Completing Forms](#) for more information on reporting partial and unknown dates.

If monoclonal antibody (mAb) is indicated as “yes”, examples of “other mAb” include Inotuzumab, Daratumomab, and Immune Checkpoint Inhibitors (Pembrolizumab, Nivolumab, Durvalinomab).

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

Q240-242: Functional Status

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

* These questions are for malignant disease indications or relapsed, persistent or progressive disease only.

Question 240: 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 240-242 should be left blank.

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

Question 241 & 242: 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 cellular therapy. For the purposes of this manual, the term "**immediately prior**" represents approximately one month prior to the cellular therapy infusion.

Using the appropriate scale as selected in question 240, select the score (10-100) that best represents the recipient's activity status immediately prior to the start of the preparative regimen. For an example of the Karnofsky/Lansky scale, see [Appendix L](#).

If a Karnofsky/Lansky score is not documented in the source documentation (e.g., inpatient progress note, physician's clinic note), data management professionals should not assign a performance score based on analysis of available documents. Rather, a physician should provide documentation of the performance score.

! The CIBMTR recognizes that some transplant centers prefer to collect and use the ECOG performance score as opposed to the Karnofsky/Lansky score. Although the ECOG and Karnofsky/Lansky performance score systems are based on similar principles, the scales are not the same. For example, the Karnofsky/Lansky scale is described in 11 categories, whereas the ECOG performance status is reported in six categories. Due to the overlap between the two systems, an ECOG score of “one” can represent either “80” or “90” on the Karnofsky/Lansky scale. For centers that collect only an ECOG performance score, CIBMTR will make the following accommodations when auditing the source data: Centers collecting ECOG scores should do so using standard practices to ensure accuracy. For the purposes of CIBMTR reporting, conversion of ECOG to Karnofsky/Lansky should follow a standard and consistent practice. This practice should be clear and reproducible. For more information regarding converting an EGOG score to a Karnofsky/Lansky score, see [Appendix L](#).