Instructions for Pre-TED (2400) Form

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Pre-TED Form.

Pre-TED

The Pre-TED Form is now required for all transplants, including subsequent transplants on the comprehensive report form track.

All transplant centers participating in CIBMTR must submit a Pre-TED (2400) Form for each allogeneic (related or unrelated) hematopoietic cell transplant (HCT). The Pre-TED is a requirement of the SCTOD for all United States transplant centers when either the stem cell donation or the transplant occurs within the United States. For more information regarding the SCTOD, see SCTOD Requirements.

Although data regarding recipients receiving autologous HCTs are not required to be submitted as part of the C.W. Bill Young Transplant Program, CIBMTR is highly committed to collecting data on these recipients for research studies. Centers choosing to report autologous data to CIBMTR must report on all autologous transplants performed at their center. For more information regarding data reporting for autologous HCT, review HCT in the Data Management Guide.

The Pre-TED may be submitted to CIBMTR up to two weeks prior to the start of the recipient's preparative regimen (see *Helpful Hint* below).

Helpful Hint
In order to avoid having to make changes to the HCT date, complete the data for the Pre-TED, but do not submit the form until the first dose of the preparative regimen is given.

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

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(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

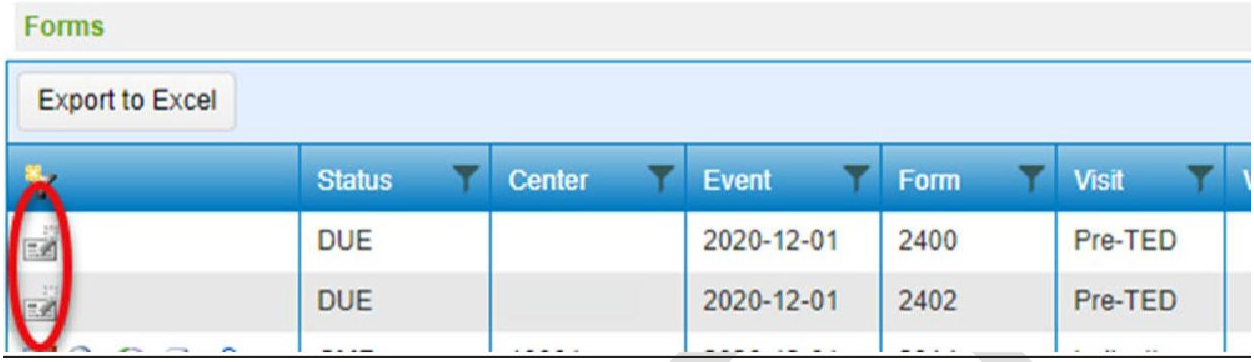
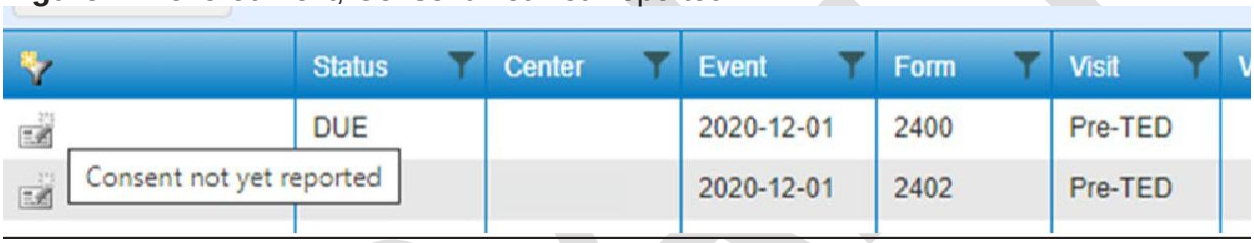


Figure 2. Hovered Text, Consent Not Yet Reported



For recipients receiving a subsequent HCT
Transplant centers must submit a Pre-TED for all subsequent HCTs; this includes recipients assigned to the TED Forms and the Comprehensive Report Forms by the form selection algorithm.

For the majority of subsequent HCTs, the recipient will remain on the original follow-up form track assigned by the form selection algorithm. For more information regarding center type and the form selection algorithm, see the Data Management Guide. A recipient may need to change tracks if enrolled on a study that requires comprehensive forms.

For recipients of multiple transplants, transplant centers are not granted access to the new Pre-TED Form in FormsNet3 until the Post-TED (Form 2450) or Post-Infusion Data Form (Form 2100) from the previous transplant has been completed.
Transplant centers can use the FormsNet3 application to determine if a Pre-TED is due by either: 1) accessing the Forms Due Report, or 2) entering the recipient's unique ID (CRID) in the Patient Forms Due field.

Links to Sections of Form:
Q1 – 29: Recipient Information
Q30 – 66: Donor Information

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Q67 – 96: Hematopoietic Cellular Transplant (HCT) and Cellular Therapy
Q97 – 104: Clinical Status of Recipient Prior to the Preparative Regimen (Conditioning)
Q105 – 142: Comorbid Conditions
Q143 – 156: Pre-HCT Preparative Regimen (Conditioning)
Q157 – 161: Additional Drugs Given in the Peri-Transplant Period
Q162 – 174: GVHD Prophylaxis
Q175 – 177: Post-HCT Disease Therapy Planned as of Day 0
Q178: Prior Exposure: Potential Study Eligibility (for consented recipients only)

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 reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
7/25/2025	Pre-TED (2400)	Add	Version 9 of the 2400: Pre-TED section of the Forms Instructions Manual released. Version 9 corresponds to revision 9 of the Form 2400.

Q1 – 21: Recipient Information

Question 1: Date of birth

The date of birth is automatically populated based on the value reported in the CRID Assignment tool in FormsNet3^{SM}. Verify that the date of birth is correct. If an error is noted, correct the CRID Assignment tool and verify that the date of birth has been updated on the Pre-TED (2400) Form.

Question 2: Sex

The recipient's sex is automatically populated based on the value reported in the CRID Assignment tool in FormsNet3^{SM}. Verify that the recipient's sex is correct. If an error is noted, correct the CRID Assignment tool and verify that the recipient's sex has been updated on the Pre-TED (2400) Form.

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Question 3: Geographic ancestry *(select one or more options that closest identifies the recipient's background)*

The recipient's geographic ancestry is automatically populated based on the value reported in the CRID Assignment tool in FormsNet3^{SM}. Verify that the recipient's geographic ancestry is correct. If an error is noted, correct the CRID Assignment tool and verify that the recipient's geographic ancestry has been updated on the Pre-TED (2400) Form.

Question 4: Geographic ancestry detail *(select one or more options that closest identifies the recipient's background)*

The recipient's geographic ancestry detail is automatically populated based on the value reported in the CRID Assignment tool in FormsNet3^{SM}. Verify that the recipient's geographic ancestry detail is correct. If an error is noted, correct the CRID Assignment tool and verify that the recipient's geographic ancestry detail has been updated on the Pre-TED (2400) Form.

Question 5: Country of primary residence

Select the recipient's primary country of residence.

Question 6: 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.

Question 7: Providence 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.

Question 8: State / territory of residence of recipient *(for residents of USA)*

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

Question 9: Is the recipient stationed on an overseas US military base?

Indicate if the recipient was stationed on an overseas US military base at the start of the preparative regimen (or infusion if no preparative regimen was given).

Question 10. NMDP Recipient ID (RID)

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The NMDP RID is automatically populated based on the value reported on the CRID Assignment (2804) Form. Verify that the NMDP RID is correct. If an error is noted, correct the CRID Assignment (2804) Form and verify that the NMDP RID has been updated on the Pre-TED (2400) Form.

Question 11: ZIP or postal code for place of recipient's residence *(USA and Canada recipients only)*

Enter the ZIP code in which the recipient resides. For USA residents, only five digits are required; however, if the ZIP+4 (nine digit) code is available, report the nine-digit code. For Canadian residents, report the six-digit code, which consists of both letters and numbers.

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

Question 12: Does the recipient require interpreter services? *(any interpreter for any level of care ex. reading / verbal)*

The intent of this question is to determine care access, regardless of the language spoken. Indicate if the recipient requires interpreter services for any aspect of care, including verbal communication, reading, or other forms of assistance.

Question 13: Is the recipient an emancipated minor?

An emancipated minor is a person under the age of 18 who has been legally granted the rights and responsibilities of an adult. Indicate if the recipient was an emancipated minor at the start of the preparative regimen (or infusion if no preparative regimen was given).

Question 14: Specify the recipient's current relationship status

Report the recipient's relationship status at the start of the preparative regimen (or infusion if no preparative regimen was given).

- **Single, never married**: If the recipient has never been married and is not currently living with a partner.
- **Married or living with a partner**: If the recipient is currently married or living with a partner, regardless of whether the partnership is legally formalized.
- **Separated / Divorced**: If the recipient was married in the past but is now separated or legally divorced.
- **Widowed**: If the recipient's spouse passed away and is no longer married.

Question 15: What is the highest degree or level of school that the recipient has completed?

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Select the option that best describes the recipient's highest degree obtained / highest level of school completed at the start of the preparative regimen (or infusion if no preparative regimen was given).

Question 16: Is the recipient covered by health insurance?

Indicate if the recipient is covered by any type of health insurance at the start of the preparative regimen (or infusion if no preparative regimen was given).

Question 17 – 21: Specify type of health insurance *(check all that apply)*

Select the recipient's health insurance coverage at the start of the preparative regimen (or infusion if no preparative regimen was given). Select all that apply.

- **Private health insurance**: Health insurance purchased by the recipient or recipient's family, through an employer / union or an insurance company. Private health insurance includes ACA / Obamacare. If selected, specify the type of private insurance.
- **National Health Insurance *(Government-sponsored, non-U.S.)***: A government-sponsored, non-U.S. health insurance system covering the cost of healthcare for a country's population. Examples include UK's National Health Service and Australia's Medicare system.
- **Medicare *(Government-sponsored, U.S., includes Medicare Advantage plans)***: A government-sponsored, U.S. health insurance program for anyone ≥ 65 years, some people < 65 years old with certain conditions / disabilities, and those with end stage renal disease. If selected, specify the type of Medicare.
- **Medigap *(Must have Medicare coverage)***: Also known as Medicare Supplement Insurance. If already covered by Medicare, additional health insurance may be purchased from a private insurance company to cover additional out-of-pocket costs.
- **Medicaid *(Government-sponsored, U.S.)***: A government-sponsored, U.S. health insurance program providing coverage for those with limited income.
- **Children's Health Insurance Program (CHIP)**: Health insurance coverage provided for children whose family does not qualify for Medicaid.
- **Military-related health care *(TRICARE (CHAMPUS) / VA health care / CHAMP-VA)***: Military-related health care provided by the Department of Defense.
- **Indian Health Service**: A federal agency within the Department of Health and Human Services providing health care to American Indians and Alaska Natives.
- **State-sponsored health plan**: Health insurance program funded by both state and federal governments.

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- **Disability insurance**: A type of insurance that replaces a portion of lost income for those who are unable to work due to illness or injury. Disability insurance may be available through an employer, the government, or private insurance.
- **Other government program**: If the recipient's health insurance coverage is a government-sponsored but not listed above, specify the type of government program health insurance.
- **Other health insurance coverage**: If the recipient's health insurance coverage is not government-sponsored and not listed above, specify the type of coverage.

Clinical Trials
As of the April 2023 release, and pre- or post-infusion key treatment clinical trials should now be reported on the Pre-TED (2400) Form, **regardless of if the sponsor uses CIBMTR forms to capture outcomes data**. Review the instructions below for additional information on key clinical treatment trials. Corporate / industry trials or investigator-initiated trials should be reported under **Other**.

Therapy Clinical Trials
Do not report clinical trials for induction / consolidation / salvage therapy (excluding clinical trials sponsored by COG or if the recipient is enrolled on the PedAL study, COG APAL2020SC), blood / tissue sample collection, or any trial the recipient is enrolled post-HCT.

Canadian Cancer Trials Group
Do not report Canadian Cancer Trials Group (CCTG) trials.

Question 22: Is the recipient participating in a clinical trial?

For the infusion being reported on this form, indicate if the recipient is a registered participant of a clinical trial **regardless of if that sponsor uses CIBMTR forms to capture outcomes data**. Only clinical trials relating to the infusion intervention and are known and consented at the time of infusion should be reported. This includes trials related to, but not limited to, the graft source, GVHD prophylaxis, or the preparative regimen. Report any clinical trial, including upfront or relapse chemotherapy, only if the sponsor is COG or if the recipient is enrolled on the PedAL study, COG APAL2020SC.

If the recipient is not participating in a clinical trial or it is unknown, select **No**.

Submit a ticket through CIBMTR Center Support when there are questions on reporting clinical trials.

Participation in Multiple Clinical Trials
If the participant is enrolled in multiple studies, even if from the same sponsor, report each study separately.

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Reporting Participation in More Than One Study
Complete the *Sponsor* through *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.

Questions 23 – 28: Sponsor

Select the study sponsor of the clinical trial the recipient is participating in from the list below.

- **ANZCTR**: Australian New Zealand Clinical Trials Registry. If selected, specify the ACTRN number.
- **BMT-CTN**: Blood and Marrow Transplant Clinical Trials Network. If selected, specify the protocol ID.
- **CIBMTR CRO Services**: Resource for Clinical Investigation in Blood and Marrow Transplant (formerly known as RCI-BMT). If selected, specify the protocol ID.
- **COG**: Children's Oncology Group. If selected, specify the protocol ID.
- **ECOG**: ECOG-ACRIN Cancer Research Group
- **PIDTC**: Primary Immune Deficiency Treatment Consortium
- **PTCTC**: Pediatric Transplantation & Cellular Therapy Consortium
- **SWOG**: SWOG Cancer Research Network
- **USIDNET:** United States Immunodeficiency Network
- **Corporate / Industry**: If selected, specify the corporate or industry sponsor name.
- **Investigator initiated**
- **Other sponsor**: If selected, specify the sponsor.

Question 29: 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.

Section Updates

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

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Q30 – 66: Donor Information

Orca Bio Products and Donor Information
Refer to the Orca Bio Reporting Guide, located on CIBMTR Portal, to determine how to report donor information for Orca Bio products.

Omidubicel Product
If the product is Omidubicel, select **No** for multiple donors.

Question 30: Multiple donors?

Indicate if cells from multiple different donors (multiple CBUs, combinations of other products from different donors) are to be used for this infusion.

For example, supplemental infusions should be included when determining if multiple donors were used for this infusion event. An infusion of supplemental cells is often given in conjunction with a preparative regimen for HCT. A supplemental infusion is defined as an infusion of cells given prior to clinical day 0 (of an HCT) for any reason other than to produce engraftment

For more information on supplemental infusions, see Appendix D: How to Distinguish Infusion Types.

If multiple donors were not used, select **No.**

Question 31: Specify number of donors

Report the number of donors used for this infusion. This value should never be "1," since it is reported **Yes**, there were multiple donors reported in the prior question.

Reporting More Than One Donor
Complete the donor specific questions to report more than one donor by adding an additional instance in the FormsNet3^{SM} application.

Question 32: Specify donor

Indicate the donor type for this product.

- **Autologous**: Cells collected from the recipient for his / her own use.
- **Allogeneic, related**: A related donor who 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.
- **Allogeneic, unrelated**: An unrelated donor who shares no known ancestry with the recipient. Include adoptive parents / children or stepparents / children.

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Omidubicel Product
If the product is Omidubicel, report the product type as **CBU**.

Multiple Products for a Single Donor
Previous CIBMTR forms required two instances to be entered in the donor section when a single donor donated multiple products. **This is no longer required**. Report all products collected from a single donor in the same instance of the donor section.

Questions 33 – 34: Specify product type (check all that apply)

Select list of product type(s) for the donor being reported in this instance.

If **Other product** is indicated, specify the product type. If there is a protocol where using "other products" is common, consistently report the same text in the specify field so that the "like" products can be grouped together. Do not report the cell type (i.e., CD3+ cells), report the product type.

Omidubicel Product
If the product is Omidubicel, report **No**, the product was not genetically modified.

Question 35: Is the product genetically modified?

Genetically modified products include any product where the cells are manipulated via either:

- Gene transfer: a process by which copies of a gene are inserted into living cells in order to induce synthesis of the gene's product; or
- Transduction: a process by which foreign DNA is introduced into a cell by a virus or viral vector

These techniques alter its gene expression through the insertion of different genes or editing of genes.

Specify if the product is genetically modified. If more than one product is being infused, indicate if any of the products are genetically modified.

Question 36: Specify the related donor type

Indicate the relationship and match between the recipient and the related donor being reported in this instance. When determining the donor's match / mismatched relationship to the recipient, only consider HLA-A, B, C, and DRB1.

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- **Syngeneic (monozygotic twin)**: 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.
- **HLA-identical sibling (may include non-monozygotic twin)**: Non-monozygotic (dizygotic, fraternal, non-identical) twins. Occurs when two eggs are fertilized by two different sperm cells at the same time. Also includes siblings who aren't twins but have identical HLA types. The recipient and donor will be allele level matched at HLA-A, B, C, and DRB1.
    - Does not include half-siblings (report as **HLA-matched other relatives** if their HLA typing is a match, or **HLA-mismatched relative** if it does not match).
- **HLA-matched other relative (does NOT include a haplo-identical donor)**: All blood-related relatives, other than siblings, who are HLA matched (i.e., parents, aunts, uncles, children, cousins, half-siblings). The recipient and donor will be allele level matched HLA-A, B, C, and DRB1.
    - Does not include adoptive parents / children or stepparents / children who are HLA matched.
- **HLA-mismatched relative (includes haplo-identical donor)**: 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) (i.e.., parents, aunts, uncles, children, cousins, half-siblings). The recipient and donor will be antigen or allele level mismatched at 1 or more loci (HLA-A, B, C, or DRB1). Select this option for haploidentical transplants.
    - Does not include adoptive parents / children or stepparents / children.

Questions 37 – 38: Specify the biological relationship of the donor to the recipient

Indicate the relationship between the recipient and the related donor being reported in this instance. If the donor is **Other biological relative**, specify the donor's relationship to the recipient.

Question 39: Degree of mismatch *(related donors only)*

If the donor being reported in this instance is an HLA-mismatched relative, indicate the degree of mismatch as either **HLA-mismatched 1 allele** or **HLA-mismatched ≥ 2 alleles (does include haploidentical donor)**.

Haploidentical means that one half of the HLA type matches the recipient. This type of HLA mismatch is common between blood-related parents and children. When determining the donor's matched/mismatched relationship to the recipient, only consider HLA-A, B, C and DRB1

Question 40: Specify unrelated donor type

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Indicate the unrelated donor type. When determining the donor's matched / mismatched relationship to the recipient, only consider HLA-A, B, C, and DRB1.

Question 41: Did NMDP facilitate the procurement, collection, or transportation of the product?

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

If the documentation is unclear if NMDP facilitated the procurement, collection, and / or transportation of the product, seek clarification from the transplant coordinator.

If the recipient received a product facilitated by NMDP select **Yes** and then either report the NMDP cord blood unit ID or the GRID. Additionally, ensure the NMDP RID is reported on the CRID Assignment (2804) Form. For products facilitated by NMDP, the Registry or UCB Bank ID question will be disabled, and the Infectious Disease Markers (2004) and HLA Typing (2005) forms will not come due.

Below is a list of donor registries who were once "non-NMDP" registries but may now be an "NMDP-facilitated" registry:

- Matchis Foundation 71 (Netherlands)
- Hadassah Medical Organization 72 (Israel)
- Knochenmarkspenderzentrale – Dusseldorf 114 (Germany)
- The Tobias Registry of Swedish Bone Marrow Donors 119 (Sweden)
- The Norwegian Bone Marrow Donor Registry 120 (Norway)
- Welsh Bone Marrow Donor Registry 131 (Wales)
- British Bone Marrow Registry 134 (United Kingdom)
- Anthony Nolan 135 (United Kingdom)
- ZKRD 136 (Germany)

Question 42: Was this donor used for any prior HCTs? *(for this recipient)*

Indicate if the current donor for this infusion was used for any prior HCTs for this recipient. If this is the recipient's first HCT or is an autologous infusion, select **No**.

GRID
The GRID has its own section on the Pre-TED (2400) form. Therefore, only the 19-character donor identifier needs to be reported. This is essential for proper donor linking and, if done incorrectly, will result in queries being placed on the form.

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GRIDs from DKMS
If receiving a GRID from the DKMS registry, the eighth character is being reported as the letter "O" however, this character should be the number "0". When entering a GRID from the DKMS ensure that the eighth character reported is the number "0".

Question 43: Global Registration Identifier for Donors (GRID)

The Global Registration Identifier for Donors (GRID) was developed by the World Marrow Donor Association (WMDA) to ensure secure, reliable and unambiguous assignment of 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 44: NMDP cord blood unit ID

Report the NMDP Donor ID (i.e., 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 45: Registry donor 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 46: 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.

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Some cord blood banks may ship their units either through NMDP or directly to the transplant center. Carefully review the accompanying documentation to determine which is appropriate for your unit. Consult with the center's transplant coordinator if it is unclear how the product was acquired.

ION and Affiliated to ION Available
If a registry or UCB bank has both an ION and an affiliated to ION, report the registry's or UCB bank's ION (not the affiliated to ION).

Determining ION or Affiliated ION
To find an ION or affiliated ION visit WMDA.

Questions 47 – 48: Registry or UCB Bank ID

Specify the registry or umbilical cord blood (UCB) bank used to obtain the adult donor or umbilical cord blood unit. If **Other Registry** is selected, specify the four-digit ION or affiliated ION. If the registry or UCB bank does not have ION or affiliated ION, report the organization's official name.

The World Marrow Donor Association (WMDA) ions have been adopted to avoid submitting the entire name and address when reporting the registry or UCB bank.

- ION: Issuing organization number allocated by International Council for Commonality in Blood Banking Automation (ICCBBA) in collaboration with the World Marrow Donor Association (WMDA)
- Affiliated ION: A registry or UCB bank may not have its own ION but is "affiliated to" a registry or UCB bank.
    - To find an affiliated ION
        - Navigate to the WMDA website
        - Use the 'Filter' to find the organization that provided the unit
        - The 'affiliated to' column will contain the affiliated ION (if one exists)

Review the diagram below when reporting the registry or UCB bank ID:

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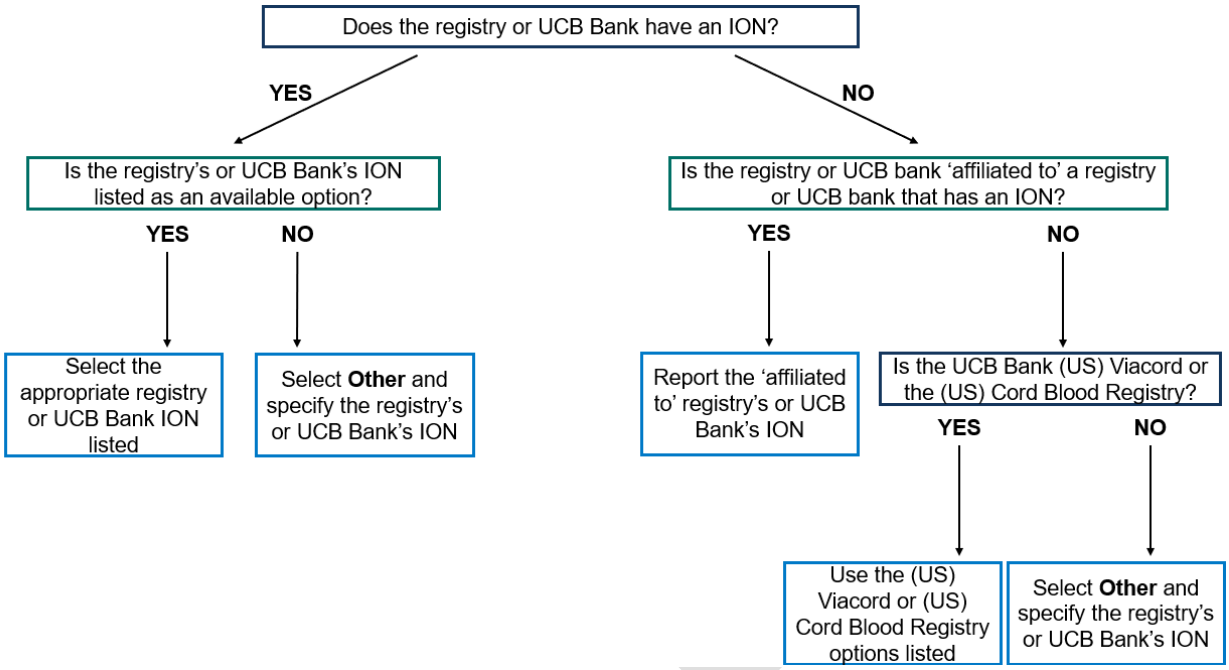

Questions 49 – 50: Donor date of birth

Report if the donor's / infant's date of birth is **Known**. If **Known**, report the date of birth (YYYY-MM-DD).

Questions 51 – 52: Donor age

Report if the donor's / infant's age is **Known**. If **Known**, report the donor's / infant's age at the time of product collection. Report the age in months if the donor is less than one year old, otherwise report the age in years.

Question 53: Donor sex

Indicate the donor's sex. Sex shall refer to an individual's immutable biological classification as either male or female. Sex is not a synonym for and does not include the concept of gender identity. For cord blood units, report the infant's sex.

Question 54: Specify blood type *(donor) (non-NMDP allogeneic donors only)*

Indicate the donors' blood type as **A**, **B**, **AB**, or **O**. Blood type is an important characteristic in allogeneic transplant because products may require manipulation to minimize the risk of immune reaction due to incompatibility.

Question 55: Specify Rh factor *(donor) (non-NMDP allogeneic donors only)*

The Rh factor is an important characteristic in allogeneic transplant because products may require manipulation to minimize the risk of immune reaction due to incompatibility.

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Report the donor's Rh (rhesus) factor.

Question 56: Donor CMV-antibodies (IgG or Total) *(Allogeneic HCTs only)*

CMV is a common virus that infects 50-80% of adults worldwide and is transmitted from person to person through bodily fluids. The virus that causes CMV is part of the herpes virus family and, like other herpes viruses, CMV may be dormant for a period of time before the virus is activated in the host. CMV infections are usually harmless in a healthy immune system and typically cause only mild symptoms, if any. However, if a person's immune system is seriously weakened (as in an immunosuppressed stem cell recipient) the virus can have serious consequences such as pneumonia, liver failure, and even death.

Most laboratory reports indicate a positive result as *reactive*, and a negative result as *non-reactive*. Occasionally, laboratory reports show a specific antibody titer. In this case, compare the laboratory result to the reported standards to determine if the result was reactive or non-reactive.

Report the test result as documented on the laboratory report.

If the laboratory reports the results as "inconclusive" or "equivocal," select **Indeterminant**.

If the laboratory reports a CMV IgM antibody only, not total IgG/IgM or CMV IgG antibody; report the result as **Not done**.

If the laboratory reports CMV testing by PCR (DNA detection), report the result as **Not done**. CMV testing by PCR is used to detect the presence of the CMV virus and does not test for prior exposure.

Question 57: Has the donor signed an IRB / ethics committee (or similar body) approved consent form to donate research blood samples to NMDP / CIBMTR? *(Related donors only)*

Indicate if the related donor signed an IRB-approved consent form to donate research blood samples to NMDP / CIBMTR.

Question 58: Date form signed

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

Questions 59 – 60: Did the donor submit a research sample to the NMDP / CIBMTR repository? *(Related donors only)*

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There are a select number of transplant centers participating in the Related Sample Repository. If the center is one of the participating centers, and the donor provided a research sample, select **Yes** and provide the donor's sample ID. The ID number is located on the bar code that is attached to the sample tube.

Omidubicel Product
If the product is Omidubicel, report the number of products from the donor as **two**.

Question 61: Specify number of products infused from this donor

Report the number of products infused from the donor being reported for this HCT.

Single vs Multiple Products

- Single Product: CIBMTR defines a single product (i.e., cellular product) as *cells collected from a single donor using the same mobilization cycle and collection method regardless of the number of collection days.*
    - Example 1 (multiple bags): A G-CSF stimulated donor had two PBSC collections on subsequent days. The products collected over the two days were divided into four bags. Although the product is contained in multiple bags, this collection is considered a single product, as there was no change in mobilization technique or collection method.
    - Example 2 (change in mobilization): A G-CSF stimulated donor had a PBSC collection, but the cell count was poor. Plerixafor (Mozobil) was added as part of the mobilization and the donor was re-collected the following day. As the change in mobilization occurred during the same mobilization cycle, these collections are considered a single product.
- Multiple Products: For the purposes of this manual, CIBMTR defines multiple products as cells collected using more than one mobilization technique and / or collection method.
    - Example 3 (multiple collection methods): A G-CSF-stimulated donor had a PBSC collection, and the product was cryopreserved. One month later the donor had a marrow collection; both products were infused at the time of transplant. Each collection is considered a separate product because different collection methods were used. The number of products infused from this donor is two.
    - Example 4 (re-mobilization): A G-CSF-stimulated donor had a PBSC collection, but the cell count was poor. No further collections were attempted and a week later the donor was re-mobilized with G-CSF and a second PBSC collection was performed. Each collection is considered a separate product due to the re-mobilization of the donor.
    - Example 5 (two different product types): A cord blood unit is infused at the same time as marrow. Each product type is considered a separate product. The number of products infused is two.

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Omidubicel Product
If the product is Omidubicel, report the number of products intended to achieve hematopoietic engraftment as **two** and complete two HCT Product and Infusion (2006) forms.

Question 62: Specify the number of these products intended to achieve hematopoietic engraftment

If infusions of additional cells (not intended to product engraftment) were given as a supplemental infusion either prior to the HCT being reported (i.e., prior to clinical Day 0) or shortly after the HCT being reported, the cells must be reported as a product on the Pre-TED Form (2400) form and on a separate Cellular Therapy Product (4003) form.

If additional cells were infused post-HCT, for any reason other than a subsequent HCT or a supplemental infusion as part of the HCT, they should be reported as cellular therapy on the appropriate follow-up form. Reporting the additional cells (given pre-HCT and not intended to produce engraftment) on the Cellular Therapy Product (4003) form is the only mechanism CIBMTR has in place to collect this data and ensure that the quality assurance data is reported to the cord blood banks, if applicable.

Report the number of products administered to achieve hematopoietic engraftment.

Questions 63 – 64: What agents were used to mobilize the autologous recipient for this HCT? *(check all that apply)*

Report the agents used in the mobilization event(s).

- **G-CSF:** TBO-filgrastim, filgrastim, Granix, Neupogen® and biosimilars
- **GM-CSF:** sargramostim, Leukine
- **Pegylated G-CSF:** pegfilgrastim, Neulasta®
- **Motixafortide:** Aphexda
- **Perlixafor:** Mozobil® and biosimilars
- **Combined with chemotherapy:** Systemic therapies used to enhance the stem cell product may include cyclophosphamide or ICE chemotherapy (Ifosfamide, carboplatin, and etoposide) with or without rituximab.
- **Anti-CD20:** rituximab, Rituxan®
- **Other agent**: If an agent was used but not listed above, select **Other agent** and specify.

If completing this form for a subsequent infusion and the same mobilizing agents used for the previous were used for the current infusion, re-report the mobilizing agents used for the current infusion.

Questions 65 – 66: Name of product *(gene therapy recipients)*

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Report the name of the product. If the name is not listed, select **Other name** and specify the gene therapy product name.

Section Updates

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

Q67 – 96: Hematopoietic Cellular Transplant (HCT) and Cellular Therapy

Question 67: Is a subsequent HCT planned as part of the overall treatment protocol? *(not as a reaction to post-HCT disease assessment) (For autologous HCTs only)*

If, at the time of the current HCT, a second (tandem transplant) or subsequent HCT is planned according to the protocol, check **Yes** even if the recipient does not receive the planned subsequent HCT. The word “planned” should not be interpreted as: if the recipient relapses, then the “plan” is to perform a subsequent HCT.

Question 68: Specify subsequent HCT planned

Report the planned type subsequent HCT.

Subsequent Infusions for Poor Graft Response
If the allogeneic recipient receives an infusion due to poor graft response, count the infusion as a subsequent HCT. The exception to this is “autologous rescue.” Autologous rescues should not be counted as a separate HCT and the data collection forms will not start over (i.e., the forms will continue from the previous HCT).

Question 69: Has the recipient ever had a prior HCT?

Specify if the recipient ever had a prior HCT. Include all HCTs in the recipient’s history, even if the transplants were performed at different centers. The intent is to capture the full picture of the recipient’s treatment / transplant history.

Question 70: Specify the number of prior HCTs

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Enter the number of prior HCTs for the recipient. An HCT event is defined as an infusion of mobilized peripheral blood stem cells (PBSC), bone marrow, or cord blood. For more information on how to distinguish infusion types [example: HCT versus donor cellular infusion (DCI)], see Appendix D: How to Distinguish Infusion Types.

Reporting Scenarios
For recipients who have received a previous HCT (prior to the HCT for which this form is being completed), the following are examples of how to calculate the number of prior HCTs.

- Example 1: A recipient was previously transplanted under a protocol that included an infusion of cells over multiple days: day 0, day +1 and day +2. This series of infusions is considered one HCT event (as opposed to three HCT events) and should be counted as *HCT Event #1*.
- Example 2: A recipient previously received an allogeneic HCT (*HCT Event #1*). Then, due to delayed neutrophil recovery, the recipient received additional cryopreserved allogeneic mobilized PBSC from the original donor, without a preparative regimen (i.e., "boost" – *HCT Event #2*). One prior HCT should be reported.
- Example 3: A recipient previously received an autologous HCT (*HCT Event #1*). Then due to delayed neutrophil recovery, the recipient received additional cryopreserved autologous cells without a preparative regimen (i.e., "boost" which is not counted as an HCT event because the intent of the autologous infusion is to treat the graft failure). The boost is successful, but a few years later the recipient develops a new malignancy. The recipient is scheduled to receive a subsequent autologous HCT with preparative regimen (*HCT Event #2*). One prior HCT should be reported.

Prior HCTs reported to CIBMTR
If **Unknown** is selected for *Were all prior HCTs reported to CIBMTR, Date of prior HCT, Was the prior HCT performed at a different institution, Specify the institution that performed the last HCT, and What was 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 71: Were all prior HCTs reported to CIBMTR?

Specify if *all* prior HCTs were reported to CIBMTR. This should include any / all HCTs not performed at this center. If the recipient is a transfer recipient, reported past HCT dates can be found in the Recipient Information Grid in FormsNet3^{SM}. Contact CIBMTR Customer Support if there are questions.

Reporting Prior HCTs
Complete the *Date of prior HCT, Was the prior HCT performed at a different institution, Specify the institution that performed the last HCT*, and *What was the HPC source for*

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the prior HCT questions to report all prior HCTs that have not yet been reported to CIBMTR by adding an additional instance in the FormsNet3SM application.

Question 72: Date of prior HCT

Report the date (YYYY-MM-DD) of the prior HCT 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 73: Was the prior HCT performed at a different institution?

Indicate if the prior HCT being reported in this instance was performed at another institution.

Questions 74 – 75: Was the prior HCT performed at a CIBMTR Affiliated Network Center?

Specify if the prior HCT was performed at a CIBMTR Affiliated Network Center. If **Yes**, select the CIBMTR Center Number (CCN).

Question 76: Specify Non-CIBMTR Affiliated Network Center

Report the name, city, state, and country of the non-CIBMTR Affiliated Network Center where the recipient's prior HCT 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 77: What was the donor source(s) for the prior HCT? *(check all that apply)*

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

- **Autologous** Cells collected from the recipient for his / her own use.
- **Allogeneic, unrelated**: An unrelated donor who shares no known ancestry with the recipients. Include adoptive parents / children or stepparents / children.
- **Allogeneic, related**: A related donor who is a blood-related relative. This includes monozygotic (identical twins), non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-sibling, etc.

Questions 78 – 79: Specify product type *(check all that apply)*

Specify the product type infused for the prior HCT.

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If **Other product type** is selected, specify the other product infused.

Questions 80 – 84: Reason for current HCT

Indicate the reason for the current HCT (check only one). If this was a subsequent transplant, verify that this answer is consistent with the reason for the subsequent transplant reported on the previous series of report forms.

- **Graft failure**: Additional stem cells are required because the ANC did not recover following HCT (primary graft failure), or hematopoietic recovery indefinitely declined after the initial hematopoietic recovery or hematopoietic recovery (secondary graft failure). If selected, report the date of graft failure / rejection.
    - Autologous infusion: If autologous cells are infused for this reason, this is considered an autologous rescue; in this case, reporting will continue under the prior HCT date, and a new Pre-TED form is not required.
    - Allogeneic infusion: If allogeneic cells are infused, this would be considered a subsequent HCT, and a new Pre-TED is required, and a new set of follow-up forms will come due, as applicable.
- **Poor graft function / insufficient donor chimerism**: Additional stem cells are required because hematopoietic recovery was deemed insufficient or too slow for survival following previous high-dose therapy and HCT.
    - If autologous cells are infused for this reason, this is considered an autologous rescue; in this case, reporting will continue under the prior HCT date, and a new Pre-TED form is not required. If allogeneic cells are infused, this would be considered a subsequent HCT, and a new Pre-TED is required, and a new set of follow-up forms will come due, as applicable.
    - In the case of a stable, mixed donor chimerism, the infusion of additional cells (usually lymphocytes and not mobilized stem cells) is typically classified as a DCI. Verify with the transplant physician that the cells given should be reported as a subsequent transplant and that stable, mixed chimerism is the reason for the transplant. However, in the case of declining chimerism – when the percentage of donor cells is sequentially decreasing on several studies, indicating possible impending graft failure – additional stem cells are required. Usually, the donor chimerism has fallen below 30-50%.
- **Persistent primary disease**: Additional stem cells are required because of the persistent presence of disease pre- and post-infusion (i.e., clinical / hematologic complete remission was never achieved following the previous infusion, clinical / hematologic complete remission was achieved but disease persisted by other methods of assessments (molecular, flow cytometry, cytogenetics)).
- **Recurrent primary disease**: Additional stem cells are required because of relapse of the primary disease by any method of assessment (i.e., clinical / hematologic complete remission was achieved pre- or post-infusion, but the

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disease relapsed following the previous infusion, clinical / hematologic and molecular complete remission was achieved pre- or post-infusion, but the disease relapsed by molecular assessments following the previous infusion). If selected, report the relapse date. If multiple relapses have occurred since the previous infusion, report the date of the most recent relapse.

- **Planned subsequent HCT, per protocol**: Additional stem cells are given as defined by the protocol for a subsequent transplant / infusion. This infusion is not based upon recovery, disease status, or any other assessment.
- **New malignancy *(including PTLD and EBV lymphoma)***: Additional stem cells are required because the recipient developed a new malignancy. This does not include a transformation or progression of the original malignancy for which the recipient was transplanted (i.e., MDS progressed to AML). If selected, report the diagnosis date of the new malignancy.
- **Other**: If additional stem cells are given for a reason other than the options listed, select **Other** and specify.

Question 85: Has the recipient ever had a prior cellular therapy? *(do not include DLIs)*

Specify if the recipient ever had a prior cellular therapy, excluding DLIs. Include all cellular therapy infusions, except DLIs, in the recipient's history, even if the infusions were not performed at the same center. The intent is to capture the full picture of the recipient's treatment history.

Prior cellular therapy reported to CIBMTR
If **Unknown** is selected for *Were all prior cellular therapies reported to CIBMTR, 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 86: Were all prior cellular therapies reported to CIBMTR?

Indicate if all prior cellular therapies were reported to CIBMTR. This should include all cellular therapy infusions (except for DLIs) not performed at your center. If the recipient is a transfer recipient, reported past infusion dates can be found in the Recipient Information Grid in FormsNet3^{SM}.

Contact CIBMTR Customer Support if there are any questions.

Reporting Multiple Prior Cellular Therapies
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

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cellular therapies that have not yet been reported to CIBMTR by adding an additional instance in the FormsNet3SM application.

Question 87: Date of the prior cellular therapy

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

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

Question 88: 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.

Questions 89 – 90: Was the prior cellular therapy performed at a CIBMTR Affiliated Network Center?

Specify if the prior cellular therapy was performed at a CIBMTR Affiliated Network Center. If **Yes**, select the CIBMTR Center Number (CCN).

Question 91: Specify Non-CIBMTR Affiliated Network Center

Report the name, city, state, and country of the non-CIBMTR Affiliated Network Center where the recipient's prior cellular therapy 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 92: Specify the donor source(s) for the prior cellular therapy? *(check all that apply)*

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

- **Autologous** Cells collected from the recipient for his / her own use.
- **Allogeneic, unrelated**: An unrelated donor who shares no known ancestry with the recipients. Include adoptive parents / children or stepparents / children.
- **Allogeneic, related**: A related donor who is a blood-related relative. This includes monozygotic (identical twins), non-monozygotic (dizygotic, fraternal, non-identical) twins, siblings, parents, aunts, uncles, children, cousins, half-sibling, etc.

Question 93: Has the recipient signed an IRB / ethics committee (or similar body) – approved consent form to donate research blood samples to NMDP / CIBMTR? *(for allogeneic HCTs only)*

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The Research Sample Repository contains blood samples from unrelated recipients and/or their adult volunteer donors or cord blood units. Related allogeneic recipients and/or donors will participate at selected transplant centers.

The primary objective of the Research Repository is to make blood samples available for research studies related to histocompatibility and hematopoietic cellular transplantation.

Studies in which these data may be used include

- Improving the understanding of tissue matching hematopoietic cellular donors and recipients.
- Determining and evaluating the factors that affect transplant outcomes.
- Studying the distribution of HLA tissue types in different populations (e.g., study tissue typing differences between different racial and ethnic populations to help develop methods to improve tissue matching between donors and recipients, including testing of rare HLA types).

Indicate if the recipient signed an IRB-approved consent form to donate research blood samples to NMDP / CIBMTR.

For subsequent infusions, this question is disabled, and blood samples are not submitted.

Question 94: Date form was signed

Report the date the research sample consent form was signed by the recipient. Do not report the date that the witness or health care professional signed the consent form.

Questions 95 – 96: Did the recipient submit a research sample to the NMDP / CIBMTR repository? *(Related donors only)*

There are a select number of transplant centers participating in the Related Specimen Repository. If this center is one of the participating centers, and the recipient provided a research sample, select **Yes** and provide the recipient's sample ID in *Research sample recipient ID*. The ID number is located on the bar code that is attached to the sample tube.

Section Updates

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

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Q97 – 104: Clinical Status of Recipient Prior to the Preparative Regiment (Conditioning)

Question 97: What scale was used to determine the recipient's functional status?

CIBMTR uses the Karnofsky / Lansky scale to determine the functional status of the recipient immediately prior to the start of the preparative regimen. 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.

If the recipient is less than one year old, leave the *Performance score* questions blank.

Questions 98 – 99: Performance score prior to the start of the preparative regimen

Recipient performance status is a critical data field that has been determined to be essential for all outcome-based studies. CIBMTR uses the Karnofsky / Lansky scale to determine the functional status of the recipient immediately prior to the start of the preparative regimen. For the purposes of this manual, the term "immediately prior" represents the **pre-HCT work-up phase**, or **approximately one month** prior to the start of the preparative regimen. In cases where the pre-transplant work-up occurs in months prior to transplant (i.e., the pre-transplant workup occurs more than one month prior to transplant), a documented performance score may be submitted *if* the recipient does not have a score closer to the start of the preparative regimen, the recipient receives no additional treatment after the date of assessment, and the recipient's status does not clearly decline.

Select the appropriate performance scale, based on the recipient's age. Using this scale, select the score (10 – 100) as documented by the clinician 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: Karnofsky / Lansky Performance Status.

If a Karnofsky / Lansky score is not documented in the source documentation (i.e., 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.

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For scenarios where only an ECOG performance score is documented, convert the ECOG to Karnofsky / Lansky using the conversion worksheet provided in Appendix L. For more information regarding EGOG scores and converting an ECOG score to a Karnofsky / Lansky score, see Appendix L: Karnofsky / Lansky Performance Status.

Question 100: Specify blood type *(of recipient) (For allogeneic HCTs only)*

Blood type is an important characteristic in allogeneic transplant because products may require manipulation to minimize the risk of immune reaction due to incompatibility.

Indicate the recipient's blood type at the start of the preparative regimen / infusion. If the recipient received a prior transplant and the blood type is now 'mixed,' select **Mixed**.

Question 101: Specify Rh factor *(of recipient) (For allogeneic HCTs only)*

The Rh factor is an important characteristic in allogeneic transplant because products may require manipulation to minimize the risk of immune reaction due to incompatibility. Indicate the recipient's Rh (rhesus) factor.

Question 102: Recipient CMV-antibodies (IgG or Total)

Report the cytomegalovirus (CMV) status of the recipient immediately prior to the start of the preparative regimen. For the purposes of this manual, the term "immediately prior" represents the **pre-HCT work-up phase**, or **approximately one month** prior to the start of the preparative regimen. An exception to this definition would apply to a recipient with a documented history of a "reactive" CMV test result. In this case, the CMV test may not be repeated during the pre-HCT work-up phase. Therefore, a timeframe of greater than one month prior to the start of the preparative regimen is acceptable. In cases where the pre-transplant work-up occurs in months prior to transplant (i.e., the pre-transplant workup occurs more than one month prior to transplant), a CMV assessment may be submitted if the recipient does not have an assessment closer to the start of the preparative regimen.

CMV is a common virus that infects 50-80% of adults worldwide and is transmitted from person to person through bodily fluids. The virus that causes CMV is part of the herpes virus family and, like other herpes viruses, CMV may be dormant for a period of time before the virus is activated in the host. CMV infections are usually harmless in a healthy immune system and typically cause only mild symptoms, if any. However, if a person's immune system is seriously weakened (as in an immunosuppressed stem cell recipient) the virus can have serious consequences such as pneumonia, liver failure, and even death.

Most laboratory reports indicate a positive result as *reactive*, and a negative result as *non-reactive*. Occasionally, laboratory reports show a specific antibody titer. In this

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case, compare the laboratory result to the reported standards to determine if the result was reactive or non-reactive.

Report the test result as documented on the laboratory report.

If the laboratory reports a CMV IgM antibody only, not total IgG/IgM or CMV IgG antibody, report the result as **Not done**.

If the laboratory reports the results as 'inconclusive' or 'equivocal,' select **Indeterminant**.

Additional Considerations:

- **Recipients < 6 months:** If the recipient is less than 6 months old, report any positive CMV antibody results as "not done" due to the presence of maternal antibodies. However, in infants greater than 6 months old, positive CMV PCR results indicate a CMV infection, and the results may be reported as "reactive."
- **Exposure to IVIG:** Exposure to IVIG may result in a false positive CMV antibody result. If the recipient has been exposed to IVIG leading up to HCT (within 3-6 months), indicate the CMV antibody results using the following guidelines:
    - If the recipient had a non-reactive CMV antibody result prior to IVIG therapy and then routine CMV PCR results showed no copies of CMV, the CMV antibody may be reported as "non-reactive," even if the CMV antibody became reactive during IVIG treatment.
    - If CMV PCR results quantified copies of CMV DNA (i.e., was positive) during IVIG treatment, the results may be reported as "reactive."
    - If the recipient did not have a CMV antibody test prior to the initiation of IVIG but had a positive antibody test during the IVIG therapy, report "not done."
    - "Not done" should be reported if no CMV antibody tests were done prior to the initiation of IVIG therapy, even if CMV PCR testing was negative during IVIG treatment (because CMV PCR only detects active infection, not prior exposure).
- **Documented history of "reactive" CMV:** In cases where a recipient has a documented history of a "reactive" CMV test and does not have a history of IVIG or blood transfusions from a CMV positive donor, "reactive" should be reported for the CMV status even if the CMV test is repeated during the pre-HCT work-up phase and is "non-reactive".
- **CMV testing by PCR:** If the laboratory reports CMV testing by PCR (DNA detection) but no CMV antibody testing is done during the pre-transplant work-up or within one month prior to transplant, report the result as "not done." CMV testing by PCR is used to detect the presence of the CMV virus and does not test for prior exposure.

Question 103: Height at start of preparative regimen

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Report the recipient's height just prior to the start of the preparative regimen. The intent of this question is to capture the recipient's most recent height prior to the start of the preparative regimen (or infusion if a preparative regimen was not given). Report the height using the admission records and / or vitals. If the height was assessed multiple times prior to the start of the preparative regimen (or infusion), report the most recent weight.

Question 104: Actual weight at start of the preparative regimen

Report the recipient's actual body weight just prior to the start of the preparative regimen. The intent of this question is to capture the recipient's most recent (actual) weight prior to the start of the preparative regimen (or infusion if a preparative regimen was not given). Report the weight using the admission records and / or vitals. If the weight was assessed multiple times prior to the start of the preparative regimen (or infusion), report the most recent weight.

Report weight to the nearest tenth of a kilogram or pound. Do not report adjusted body weight, lean body weight, or ideal body weight.

Section Updates

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

Q105 – 142: Comorbidities

Question 105: Is there a history of mechanical ventilation?

A history of mechanical ventilation may impact the recipient's pulmonary function post-HCT. Mechanical ventilation is any assisted ventilation on behalf of the recipient. Mechanical ventilation can occur as both an endotracheal tube and ventilator, or as a BIPAP machine with a tight fitting mask in continuous use. The one exception to BIPAP is CPAP used for sleep apnea, which generally involves overnight use only for patients with documented sleep apnea. Therefore, **do not** report a CPAP used for sleep apnea, as it does not have the same implications as other forms of mechanical ventilation.

Indications for mechanical ventilation include, but are not limited to:

- Apnea with respiratory arrest (excludes sleep apnea)

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- Acute lung injury
- Vital capacity < 15 mL/kg
- Chronic obstructive pulmonary disease (COPD)
- Clinical deterioration
- Respiratory muscle fatigue
- Obtundation or coma
- Hypotension
- Tachypnea or bradypnea

Specify if the recipient was placed on mechanical ventilation at any time prior to this HCT event (excluding mechanical ventilation during surgery).

Question 106: Is there a history of invasive fungal infection?

Fungal infections play a major role in the clinical outcome of transplant recipients. If the recipient has a history of proven, suspected, or documented invasive fungal infection at any time prior to this HCT, check **Yes**. If the recipient has not had a history of a proven, suspected, or documented invasive fungal infection, check **No**. For a subsequent HCT, report any documented significant fungal infections in the recipient's medical history, starting with the preparative regimen of the previous HCT to the time prior to the preparative regimen for the current HCT.

Examples of invasive fungal infections include, but are not limited to invasive aspergillosis, zygomycosis and other molds, invasive candidiasis, cryptococcosis, endemic mycosis, other yeasts, and pneumocystosis.

Non-invasive fungal infections such as thrush and nail fungus should not be reported.

For assistance with reporting fungal infections, consult a transplant physician.

Question 107: Does the recipient have a known complex congenital heart disease? *(corrected or uncorrected) (excluding simple ASD, VSD, or PDA repair)*

The intent of this question is to determine the recipient's history of any known complex congenital heart disease (corrected or uncorrected). Exceptions for reporting would be any simple ASD, VSD, or PDA repair. Specify if the recipient has known complex congenital heart disease.

Question 108: Did the recipient have a prior malignancy?

Specify if the recipient has any history of a prior malignancy (treated or untreated) preceding this infusion.

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Prior Malignancies

Report all prior malignancies diagnosed prior to the infusion, regardless of if therapy was administered.

Questions 109 – 112: Specify prior malignancy *(check all that apply)*

Specify the recipient's prior malignancy(ies) and indicate if the prior malignancy was treated. Select all that apply.

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

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

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: Reporting Comorbidities.

Question 113: Were there any co-existing diseases or organ impairment present according to the HCT comorbidity index (HCT-CI)?

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

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

Report 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 infusion. See examples below.

- A recipient with sickle cell had a stroke prior to HCT, 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** and **Heart valve disease**.

The intent of this question is to identify serious pre-existing conditions that may influence 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 (i.e., appendectomy), and/or that would not pose a concern during or after the infusion should not be reported.

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

Question 114: Specify co-existing disease or organ impairments *(check all that apply)*

Select each clinically significant co-existing disease or organ impairment for this recipient. 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.

The physician performing the recipient's pre-infusion evaluation may use the HCT Co-Morbidity Index (HCT-CI) to document co-morbid conditions. For detailed information on what should and shouldn't be reported for each category see Appendix J: Reporting Comorbidities.

Question 115: Was the recipient on dialysis immediately prior to start of preparative regimen?

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

Laboratory Values Prior to Start of Preparative Regimen
Report the most recent laboratory values prior to the start of the preparative regimen, regardless of when the assessment was completed. If the assessment was performed multiple times, report the closest value to the start of the preparative regimen. The following are considered biomarkers according to the augmented HCT comorbidity index

ATG / Campath
If ATG / Campath was given prior to the preparative regimen, use the following guidelines to determine which lab values to report:
- If there are more than two days between when ATG / Campath ended and the drugs listed in the preparative regimen began, report the most recent lab values prior to the drugs listed in the preparative regimen.
- If there are two days or less between when ATG / Campath ended and the drugs listed in the preparative regimen began, report the most recent lab values prior to starting ATG / Campath.

Plasma vs Serum Samples
It is acceptable to report chemistry laboratory results based on plasma sample analysis in instances where serum sample analysis is not conducted or if it is not a standard practice at your center, even if the question text states 'serum.'

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Questions 116 – 136: Provide the most recent laboratory values prior to the start of the preparative regimen

These questions are intended to determine the clinical status of the recipient prior to the start of the preparative regimen for stem cell transplantation. For each assessment below, indicate if the result was **Known** prior to the start of the preparative regimen, regardless of when the assessment was completed. If **Known**, specify the value, the sample collection date, and the upper limit of normal, if applicable. If testing was performed multiple times prior to the start of the preparative regimen, report the most recent laboratory value obtained for each specific test.

- **Serum ferritin:** Ferritin is a protein that stores, transports, and releases iron. Iron is toxic to cells, so it is stored within the ferritin protein for use. Ferritin that is too low might be indicative of iron deficiency related anemia. Ferritin that is too high might be indicative of iron overload. It is tracked for some diseases, such as hemaophagocytic lymphohistiocytosis.
- **C-reactive protein (CRP):** C-reactive protein (CRP) is a protein made by the liver. The level of CRP increases when there is inflammation in the body. CRP tests are often used to diagnose or monitor for causes of inflammation, such as infections or certain autoimmune conditions.
- **Cystatin-C:** Cystatin-C is a protein produced by all nucleated cells in the body. It plays a key role in regulating the activity of proteases, which are enzymes that break down proteins. Cystatin-C is a biomarker that is primarily used to assess kidney function.
- **Glomerular filtration rate (GFR):** GFR is a key measure of kidney function and represents the rate at which the kidneys filter blood to remove waste and excess fluids. GFR may be measured directly through a specialized test or estimated. If the GFR is an estimated value, select **GFR estimated**.
    - Use the Cockcroft-Gault equation to report the calculated value, or for pediatric recipients, use the 'Bedside Schwartz' or Cystatin C-based equation if the actual GFR value cannot be reported.
- **Serum albumin:** Serum albumin is a protein found in the blood. Levels are most often reported on a chemistry panel but may occasionally be found in a separate liver function test report.
- **Platelets:** Platelet are formed elements within the blood that help with coagulation. A low platelet count, call thrombocytopenia, may lead to easy bleed or bruising. Thrombocytopenia may require platelet transfusions. Additionally. indicate if the recipient received a platelet transfusion within 7 days prior to testing.

Use the following guidelines when reporting the sample collection date and upper limit of normal:

- Date Sample Collected: Report the date the sample was collected. This date should be before the date of the start of the preparative regimen; however,

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laboratory values obtained on the first day of the preparative regimen may be reported as long as the blood was drawn before any radiation or systemic therapy was administered. If testing was performed multiple times prior to the start of the preparative regimen, report the value and date of the most recent test.

- Upper Limit of Normal for your Institution: Report the upper limit of normal as documented on the lab report. Normal values may vary by laboratory, so it is important to report the upper limit of normal for each assessment.

Reporting More Than One Prior Solid Organ Transplant
Complete *Specify organ and Year of prior solid organ transplant questions* for each solid organ transplant by adding an additional instance in the FormsNet3^{SM} application.

Question 137: Weight loss over the preceding 12 months *(optional)*

Indicate the percentage of weight loss the recipient experienced during the 12 months leading to infusion.

Question 138: Montreal Cognitive Assessment (MoCA) Score *(optional for ages 55 – 85 only)*

The Montreal cognitive Assessment (MoCA) is a screening tool used to detect mild cognitive impairment and provides an overall score. The MoCA score ranges from 0 to 30. The higher the score, the better cognitive performance.

Report the recipient's MoCA score prior to the start of the preparative regimen. If the assessment was performed multiple times, report the most score.

Questions 139 – 142: Did the recipient have a prior solid organ transplant?

Indicate if the recipient had a prior solid organ transplant. If **Yes**, specify the organ transplant, and the year of the solid organ transplant.

If **Other organ** is reported, specify the organ.

If the recipient did not receive a prior solid organ transplant or it is not known, report **No**.

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

Section Updates

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

Q143 – 156: Pre-HCT Preparative Regimen (Conditioning)

MIBG Therapy
MIBG therapy given for recipients with neuroblastoma is no longer considered preparative regimen and should not be reported.

Question 143: Dosing weight used for preparative regimen orders

Report the dosing (adjusted) weight used for determining the preparative regimen orders. The intent of this question is to report the weight used to calculate the preparative regimen drug doses. Report the dosing weight as listed on the preparative regimen / chemotherapy orders If weight is adjusted between chemo orders and administration, report the new weight. Report weight to the nearest tenth of a kilogram or pound.

This weight may be the same weight reported above in *Actual weight at start of the preparative regimen* and / or could also be the same weight reported on the Recipient Baseline (2000) Form, if applicable.

Question 144: Was a pre-HCT preparative regimen prescribed?

Recipients are generally transplanted under a specific protocol that defines the radiation and/or systemic therapy the recipient is intended to receive as a preparative regimen. This protocol, which may be either a research protocol or standard of care protocol, should be referred to when completing this section.

However, there are instances when a preparative regimen is not given. Examples may include, but are not limited to:

- Primary diagnosis of an immune deficiency.
- Subsequent allogeneic HCT due to loss of, or poor, neutrophil engraftment.

Specify if a preparative regimen is prescribed

For more information regarding the recipient's preparative regimen, consult a transplant physician or contact CIBMTR Center Support.

Question 123: Classify the recipient's prescribed preparative regimen *(Allogeneic HCTs only)*

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Myeloablative pre-transplant conditioning destroys bone marrow cells using high-dose radiation and/or systemic therapy. It is used to eliminate the recipient's immune system and to leave space in the bone marrow niche for the donated cells. A myeloablative regimen is sometimes used for recipients with non-malignant diseases who require HCT for marrow reconstitution (i.e., immunodeficiencies) or to produce a complete donor chimerism.

Non-myeloablative stem cell transplant (**NMA** or **NST**) and reduced-intensity conditioning (**RIC**) preparative regimens generally use lower doses of radiation and/or systemic therapy to prevent graft rejection and to suppress the recipient's hematopoietic immune system, but not eliminate it completely. Non-myeloablative protocols rely on the immune cells of the donor to destroy the disease (called graft versus tumor or GVT effect), and typically produces mixed chimerism. NST is a common treatment option for recipients who are older or who have other health problems, as the lower radiation and/or systemic therapy doses are easier for the recipient to tolerate.

In general, RIC includes any regimen that does not meet the criteria for either myeloablative or non-myeloablative regimens.

The determination of the intent of the regimen should be based on the center's protocol or the opinion of the physician overseeing the care of the recipient. However, if the intent is not specified, the regimen intensity may be reported based on CIBMTR operational guidelines below.

Table 1. Examples of Myeloablative, Reduced Intensity, and Non-Myeloablative Regimens

Myeloablative Regimens	**Reduced Intensity Regimens**	**Non-Myeloablative Regimens**
• TBI > 500 cGy (single) or > 800 cGy (fractionated) • Cyclophosphamide + TBI (> 500 cGy (single) or > 800 cGy (fractionated)) • Cyclophosphamide + Etoposide + TBI (> 500 cGy (single) or > 800 cGy (fractionated)) • Busulfan > 7.2 mg/kg IV or >9.0mg/kg orally • Busulfan >300 mg/m2 IV or >375 mg/m^2 orally • Busulfan (> 7.2 mg/kg IV	• TBI ≤ 500 cGy (single) or ≤ 800 cGy (fractionated) • BEAM (Carmustine [BCNU], Etoposide, Cytarabine [Ara-C], Melphalan) • Busulfan ≤ 7.2 mg/kg IV or ≤ 9.0mg/kg orally • Busulfan ≤ 300 mg/m^2 IV or ≤ 375 mg/m^2 orally • Melphalan ≤ 150 mg/m^2 • Fludarabine + TBI > 200 and ≤ 500 cGy (single) or ≤ 800 cGy (fractionated)	• TBI ≤ 200 cGy (single) • ATG + Cyclophosphamide • Fludarabine + Cytarabine • Fludarabine + Cyclophosphamide • Fludarabine + TBI ≤ 200 cGy (single)

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or >9.0mg/kg orally) + Cyclophosphamide • Busulfan (>7.2 mg/kg IV or >9.0 mg/kg orally) + Melphalan >150 mg/m^2 • Melphalan >150 mg/m^2 • Thiotepa ≥ 10 mg/kg • Treosulfan > 30,000 mg/m^2 or > 30 g/m^2	• Thiotepa < 10 mg/kg • Treosulfan ≤ 30,000 mg/m^2 or ≤ 30 g/m^2 • Etoposide + Cyclophosphamide	

Preparative Regimen – Intensity
These values represent the total prescribed doses. For example, if a recipient is scheduled to receive Melphalan 100 mg/m^2 for two days (200 mg/m^2), the regimen would be myeloablative because the total prescribed dose is > 150 mg/m^2.

Indicate whether the intent of the preparative regimen was **Myeloablative** (to produce marrow ablation or pancytopenia), **Non-myeloablative**, or **Reduced intensity**.

Question 146: Was irradiation planned as part of the pre-HCT preparative regimen?

Specify if irradiation is planned as part of the preparative regimen.

Irradiation performed as previous treatment should not be reported in this section. Report irradiation performed as previous treatment on the appropriate Disease Specific Form. Additionally, “radiation boosts,” often given to smaller sites that may have residual malignant cells or to areas that were shielded (i.e., chest wall or lung), should not be reported in this section. Report irradiation boosts administered on the applicable Recipient Baseline Data (2000) Form.

Question 147: What was the prescribed radiation field?

Indicate if the planned irradiation was to **Total body**, **Total body by intensity-modulated radiation therapy (IMRT)**, **Total lymphoid or nodal regions**, or **Thoracoabdominal region**.

Question 148: Total prescribed dose (dose per fraction x total number of fractions)

Enter the total dose of radiation prescribed. If radiation was prescribed as a single dose, the amount of radiation delivered in the single dose constitutes the total dose. If the radiation was prescribed in fractionated doses, multiply the dose per fraction by the total number of fractions to determine the total dose. Enter the total dose of radiation in either grays (Gy) or centigrays (cGy).

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- Example 1: Radiation Order: TBI, 200 cGy/day for three days (3 doses)
  - Total dose: 200 cGy x 3 doses = 600 cGy
  - Report “Total Dose” as: 600 cGy

Question 149: Date started

Enter the date the single dose or first fraction of radiation was administered.

Question 150: Was the radiation fractionated?

Radiation is either delivered as a single dose or in several treatments (fractions). Radiation is fractionated to increase the loss of diseased cells, as they do not recover as quickly as disease-free cells.

Indicate if the radiation was fractionated. If the radiation was not fractionated, check **No**.

Question 151: Total number of fractions

Enter the total number of fractions (treatments) of radiation that were administered. The recipient may receive more than one fraction per day (hyperfractionation).

The total number of fractions multiplied by the dose per fraction must be equal to the total dose reported above.

Reporting Multiple Drugs for Preparative Regimen
Complete the drug-specific preparative regimen questions for each drug given as part of the preparative regimen by adding an additional instance in the FormsNet3^{SM} application.

Preparative Regimen – Drugs
The following questions report the **prescribed** drug therapy that was part of the preparative regimen. Do not report the dose that was actually given. If the recipient has comprehensive report forms due, the actual dose given will be reported on the Recipient Baseline Form (Form 2000). **Do not include drugs that are intended to offset the side effects of the chemotherapy** (e.g., corticosteroids for nausea, MESNA for hemorrhagic cystitis, etc.).

Drugs After Transplant
Occasionally, protocols list drugs that may be given before and after transplant. If the drugs are planned to be given before and after transplant, only the doses given before transplant should be quantified in the preparative regimen section. The doses given after transplant should be reported in the **Post-HCT Disease Therapy Planned as of Day 0** or **GVHD Prophylaxis** section. For example, if bortezomib or rituximab is planned to be given on Days -2, +1, +4, and +7, report the Day -2 dose in the

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preparative regimen section, and the post-transplant doses as planned post-HCT therapy.

Drugs during the Peri-Transplant Period
ATG, alemtuzumab (Campath), defibrotide, KGF, and ursodiol may be given during the peri-transplant period. Previously, if these drugs were administered prior to Day 0, they were reported in the preparative regimen section of the Pre-TED (2400) Form. However, the Pre-TED (2400) Form has been updated – if these drugs were administered prior to Day 0, report them in the Additional Drugs Given in the Peri-Transplant Period section, not in the Pre-HCT Preparative Regimen (Conditioning) section

Questions 152 – 153: Drug

Specify the preparative regimen drug. The form lists each drug by the generic name. The following website provides the trade names under which generic drugs are manufactured: http://www.rxlist.com/script/main/hp.asp.

The **Other drug** category should be used only if the drug is not one of the listed options. If an "other" drug is prescribed, list the name of the drug.

Additional Information:

- Intrathecal drugs: Include any intrathecal drugs the recipient received for prophylaxis or treatment of CNS disease within 21 days prior to the start of the preparative regimen.
- Additional sites of radiation: Do not report additional sites of radiation (e.g., cranial boost) in the "other" drug category.
    - If the recipient is assigned to the Comprehensive Report Forms, additional sites of radiation will be reported on the Recipient Baseline (2000) Form. If the recipient is assigned to TED Forms, additional sites of radiation will not be reported.
- GVHD prophylaxis: Do not report GVHD prophylaxis such as Methotrexate.
- Pre-infusion treatment: Do not report pre-infusion treatment such as Venetoxlax in the "other" drug category.
    - If the Pre-TED (2400) Form is being completed for a subsequent infusion, do not report therapy that was given to treat the recipient's disease (between the previous and current planned infusions) in the preparative regimen section.
- Change in preparative regimen: If there is a change to the chemotherapy preparative regimen (i.e., from busulfan + fludarabine to melphalan + fludarabine) after the Pre-TED (2400) form has been submitted, return to the form and make this correction directly in FormsNet3^{SM} to ensure that the chemotherapy reported reflects the actual chemotherapy regimen given.

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Calculating Total Drug Doses
Drug doses are calculated either by recipient weight in kilograms (kg) or recipient body surface area (BSA) in m^2. The HCT protocol will specify "x mg/kg" or "x mg/m^2" and the total number of doses to be administered.
For example, if the protocol requires cyclophosphamide at 60 mg/kg x 2 days (i.e., 2 doses), the "total prescribed dose" should be reported as "120 mg/kg."

Units of Measurement: Milligrams
The **Milligram** units of measurement is only enabled if the preparative regimen drug is **Carboplatin**.

Question 154: Total prescribed dose

Report the ***total* dose** of each drug as **prescribed** in the preparative regimen section of the HCT protocol and specify the units of measurement. **Do not report the prescribed *daily* dose**. Report the drug doses to the nearest tenth. The pharmacy record or Medication Administration Record (MAR) should be used for determining the date the drug started.

If the total prescribed dose is reported in a unit other than those listed, convert the dose to the appropriate unit. If drug doses cannot be converted to the unit listed, leave the unit field blank, override the error (using "unable to answer"), and attach a copy of the source document to the Pre-TED (2400) Form using the attachment feature in FormsNet3^{SM}.

Pharmacokinetics
Pharmacokinetic testing can be used to determine whether the drug concentration in the bloodstream is appropriate to the dose given. This reflects the speed of absorption and elimination of the drug. These tests are usually performed using the first dose of systemic therapy, or a test dose, where multiple samples are drawn at specific time points following the first dose. The samples are sent to a laboratory that performs the testing to determine the drug concentration. If carboplatin was prescribed, indicate if pharmacokinetic testing was performed to determine the preparative regimen dosing. If it is not known whether or not this testing was performed, consult a transplant physician.

A common example of this situation occurs in the use of busulfan. When pharmacokinetic (pK) testing is performed, the ordered busulfan dose can be calculated from either the *AUC dose* or *daily AUC*. If an *AUC dose* is documented, this can be multiplied by the number of ordered doses in order to calculate the ordered busulfan dose. When a *daily AUC* is documented, this can be multiplied by the number of days in order to calculate the ordered busulfan dose. See the example below for more information.

- Example 2 – Calculating the ordered dose of Busulfan using *AUC dose*: The AUC dose in the example below is 2842 uMol x Min, which

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was prescribed for a total of 5 doses. The total ordered dose of Busulfan in this scenario should be reported as 14,210 uMol x Min.

Description	Result	Units
Area Under the Curve(AUC)	2842 for Dose #1	uMol x Min
AUC Target	Cumulative 21924	uMol x Min
AUC Estimated Average Exposure	[See comments]	uMol x Min
Clearance Rate	5.45	ml/min/kg
Recommended Dosing Type	Q24	
Dose recommended starts at dose #	2	
Dose recommended ends at dose #	5 [See comments]	

Pharmacokinetics and Test Dose

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 CIBMTR forms depends upon this distinction. This helps distinguish whether the dose is part of the therapeutic regimen, or not.

- Example 3: A test dose was given **> 24 hours** prior to the intended therapeutic dosing.
    - A recipient with AML underwent allogeneic HCT from a sibling; busulfan and cyclophosphamide were used as the preparative regimen. The recipient presented to clinic 9 days before the HCT, 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 HCT 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 following should be reported:
        - On the Pre-TED (2400) form, the total prescribed dose per protocol would NOT include the test dose.

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    - On the Baseline (2000) form, 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.
- Example 4: The first dose of therapeutic dosing is used for monitoring.
    - A recipient with MDS received an allogeneic HCT from an unrelated donor; busulfan and fludarabine were used as the preparative regimen. She was admitted to the hospital 7 days before her HCT 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. The total prescribed dose per protocol should be reported as “13 mg/kg.” (0.8 mg/kg x 16 doses = 12.8 mg/kg rounded to 13 mg/kg).
      If the first dose of the preparative regimen was used to determine pharmacokinetics, the following should be reported:
        - On the Pre-TED (2400) form, the total prescribed dose per protocol would include the dose used for monitoring.
        - On the Baseline (2000) form, 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 by the 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.

Question 155: Date started

Enter the date when the first dose of the preparative regimen drug was administered. The pharmacy record or Medication Administration Record (MAR) should be used for determining the date the drug started.

Question 156: Specify administration *(busulfan only)*

Report the busulfan administration route as either **Oral**, **IV**, or **Both**.

Section Updates

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

Q157 – 161: Additional Drugs Given in the Peri-Transplant Period

Drugs may be given during the peri-transplant (before and after infusion) period to prevent transplant-related complications, such as liver injuries or to facilitate engraftment.

Questions 157 – 161: Drugs

For each agent listed, indicate whether the drug was administered during the peri-transplant period to prevent transplant-related complications or facilitate engraftment, and any additional question(s) for each drug administered.

- **ALG (Anti-Lymphocyte Globulin), ALS (Anti-Lymphocyte Serum), ATG (Anti-Thymocyte Globulin, ATS (Anti-Thymocyte Serum)**: Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes. Report the total dose *prescribed* pre- and post-infusion and the animal source. If **Other** is selected, specify the source.
- **Alemtuzumab (Campath)**: Antibody preparations that are infused in the recipient. Report the total dose *prescribed* pre- and post-infusion to the nearest tenth and specify the units of measurement.
- **Defibrotide**: Antithrombotic agent used to prevent veno-occlusive disease.
- **Ursodiol**: A naturally occurring bile acid used to dissolve small gall stones and to increase bile flow in patients with primary biliary cirrhosis.

If the recipient did not receive any of the drugs listed above, select **None**.

Section Updates

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

Q162 – 174: GVHD Prophylaxis

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ATG and Campath
If ATG or Campath were ordered for GVHD prophylaxis prior to or after Day 0, report these drugs in the Additional Drugs Given in the Peri-Transplant Period section of the Pre-TED (2400) Form. Do not report these drugs in the GVHD Prophylaxis section.

Questions 162 – 172: Specify drugs *(check all that apply)*

After allogeneic HCT, specific immunosuppressive therapy may be administered to prevent GVHD or to immunosuppress the host marrow, thereby promoting engraftment of the donor stem cells. Most transplant centers have specific GVHD prophylaxis protocols and graft rejection protocols. *Planned* agents a recipient receives as a result of these protocols should be included in this section. This answer does not have to match what is reported on the Post-Infusion Follow-Up (2100) Form.

Specify the planned GVHD prophylaxis. Select all that apply.

If the planned GVHD prophylaxis is **Abatacept**, **Cyclophosphamide**, or **Methotrexate**, report the planned start date, the total number of planned doses, and the total planned prescribed dose, along with the unit of measurement.

The prophylactic drug options listed on the form are intended to be administered in a *systemic or oral form*. If the recipient received one of the listed drugs in a topical form, select the **Other agent** option and specify the drug and route of administration.

Do not report product manipulations for GVHD prophylaxis. Manipulations / interventions for GVHD prophylaxis are captured below.

If the recipient did not receive GVHD prophylaxis, select **None**.

If GVHD prophylaxis is used for a syngeneic (monozygotic or identical twin) or autologous HCT, attach a copy of the source document using the attachment feature in FormsNet3^{SM}.

Product Manipulation for GVHD Prophylaxis
Product manipulation is not captured anywhere else on the Pre-TED (2400) Form and any manipulation done for GVHD Prophylaxis should be reported below. An example of product manipulation for GVHD prophylaxis is T-cell depletion.

Questions 173 – 174: Specify intervention *(check all that apply)*

Specify and product manipulations or interventions performed for GVHD prophylaxis. If **Other intervention** is selected, specify the intervention.

If interventions for GVHD prophylaxis were not completed, select **None**.

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Section Updates

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

Q175 – 177: Post-Infusion Disease Therapy Planned as of Day 0

Question 175: Is additional post-HCT therapy planned?

Specify if additional post-HCT therapy is planned according to the protocol or standard of care (even if the recipient does not receive the planned therapy). The word "planned" should not be interpreted as: *if the recipient relapses, then the "plan" is to treat with additional therapy*.

If additional post-HCT therapy is not planned per protocol or it is unknown, check **No**.

Planned Post-HCT Therapy
The following post-HCT planned therapy questions are optional for non-U.S. centers.

Questions 176 – 177: Specify post-HCT therapy planned *(check all that apply)*

Indicate if the options listed on the form are intended to be part of the post-HCT planned therapy according to the protocol or standard of care. Select **Other therapy** for other planned therapies and specify the other therapy.

Examples of when the **Unknown** option would be used include inclusion in a treatment protocol where a trial drug is used and randomized, or if post-HCT therapy is planned, but the specific therapy intended for use is not known pre-HCT.

Section Updates

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

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Q178: Prior Exposure: Potential Study Eligibility (for consented recipients only)

Question 178: Specify if the recipient received the following (at any time prior to HCT / infusion)

Indicate if the following agent was administered to the patient prior to HCT / infusion:

- **Mogamulizumab**: A monoclonal antibody used to treat mycosis fungoides or Sezary syndrome (types of cutaneous T-cell lymphoma). It is also being studied in the treatment of other types of cancer

If the recipient did not receive the agent listed above select **None of the above**.

Section Updates

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

DRAFT

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Instructions for Disease Classification (2402) Form

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Disease Classification Form.

Disease Classification

The Disease Classification Form is required for all transplants, including subsequent transplants on the comprehensive report form track and cellular therapy infusions when the indication is malignant hematologic disorder, non-malignant disorder or solid tumor.

All transplant centers participating in the CIBMTR must submit a Disease Classification (2402) form for each allogeneic (related or unrelated) hematopoietic cell transplant (HCT). The Disease Classification (2402) form is a requirement of the SCTOD for all United States transplant centers when either the stem cell donation or the transplant occurs within the United States. For more information regarding the SCTOD, see General Instructions, Stem Cell Therapeutics Outcomes Database.

Although data regarding recipients receiving autologous HCT are not required to be submitted as part of the C.W. Bill Young Transplant Program, the CIBMTR is highly committed to collecting data on these recipients for research studies. Centers choosing to report autologous data to CIBMTR must report on all autologous transplants performed at their center. For more information regarding data reporting for autologous HCT, see General Instructions, Autologous Hematopoietic Stem Cell Transplant.

The Disease Classification (2402) form may be submitted to CIBMTR up to two weeks prior to the start of the recipient's preparative regimen. This form is designed to capture important details regarding the recipient's primary disease for which the reported infusion is being given. Key reporting areas differ depending on the disease

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reported, but may include disease type, subtype, transformations, cytogenetic and molecular markers, disease-specific laboratory results, staging, and disease status.

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

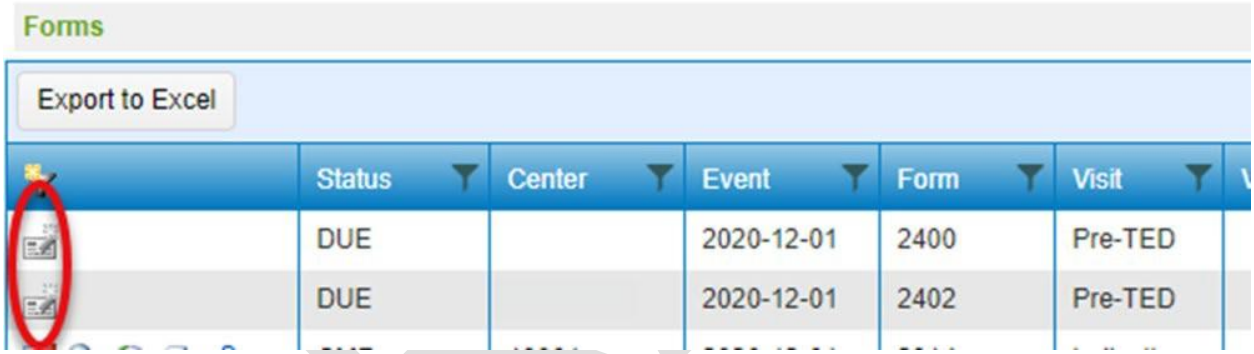
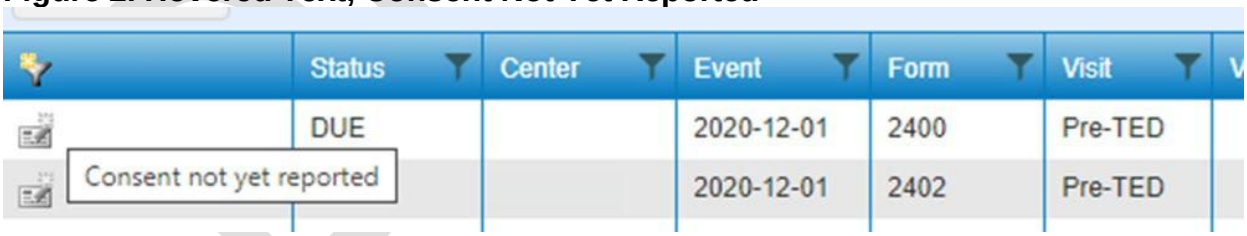


Figure 2. Hovered Text, Consent Not Yet Reported



For recipients receiving a subsequent infusion
Transplant centers must submit a Disease Classification (2402) form for all subsequent infusion; this includes recipients assigned to the TED Forms and the Comprehensive Report Forms by the form selection algorithm.

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For the majority of subsequent infusions, the recipient will remain on the original follow-up form track (TED or CRF) assigned by the form selection algorithm. For more information regarding center type and the form selection algorithm, see General Instructions, Center Type and Data Collection Forms. A recipient may need to change tracks if enrolled in a study that requires comprehensive forms.

For recipients of multiple infusions, transplant centers are not granted access to a subsequent Disease Classification (2402) form in FormsNet3^{SM} until the Post-TED (2450) or Post-Infusion Follow-Up (2100) form from the previous infusion has been completed.

Links to Sections of Form:

Q1 – 2: Primary Disease for infusion
Q3 – 127: Acute Myelogenous Leukemia
Q128 – 194: Acute Lymphoblastic Leukemia
Q195 – 301: Acute Leukemias of Mixed or Ambiguous Lineage
Q302 – 308: Chronic Myelogenous Leukemia
Q309 – 378: Myelodysplastic Diseases
Q379 – 479: Myeloproliferative Diseases
Q480 – 483: Other Leukemia
Q484 – 500: Hodgkin and Non-Hodgkin Lymphoma
Q501 – 558: Multiple Myeloma / Plasma Cell Disorder
Q559 – 561: Solid Tumors
Q562 – 564: Severe Aplastic Anemia
Q565: Inherited Bone Marrow Failure Syndromes
Q566 – 599: Hemoglobinopathies
Q600: Paroxysmal Nocturnal Hemoglobinuria (PNH)
Q601 – 608: Inborn Errors of Immunity (IEI)
Q609 – 610: Inherited Abnormalities of Platelets
Q611 – 613: Inherited Disorders of Metabolism
Q614 – 619: Histiocytic Disorders
Q620 – 623: Autoimmune Diseases
Q624 – 625 Tolerance Induction Associated with Solid Organ Transplant
Q626: Other Disease

Manual Updates

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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.

To review the historical Manual Change History for this form, reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
7/25/2025	2402: Disease Classification	Modify	Version 10 of the 2402: Disease Classification section of the Forms Instructions Manual released. Version 10 corresponds to revision 10 of the Form 2402.

Q1 – 2: Primary Disease for Infusion

Disease Classification Questions
The current versions of the CIBMTR forms use the World Health Organization (WHO) disease classifications. The Disease Classification questions contain all the established WHO disease types and subtypes. The **Other disease** 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 physician, contact the CIBMTR Customer Service Center, or visit the WHO website at: http://www.who.int/classifications/icd/en/.
Several of the Disease Classification questions ask for "Status at Infusion." Although there are many interpretations of disease response criteria, **when reporting data to the CIBMTR, use the guidelines in this manual to determine disease status**. A majority of the disease response criteria are established by an international working group. Citations of resources used to define disease responses are included where applicable. If the recipient's status is unclear, consult with the physician for further information or contact the CIBMTR Customer Service Center.

Subsequent HCT / Cellular Therapy
For many diseases, the CIBMTR data collection forms capture disease assessments at

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multiple time points pre- and post-infusion. If the recipient is receiving a subsequent infusion for the same disease and they have had a previous infusion that was reported to the CIBMTR, only disease assessments performed after the previous infusion until the current infusion are required to be reported. If relapse / progression occurred following the previous infusion but prior to the Last Evaluation timepoint for the current infusion, report the relapse / progression assessments at the In Between timepoint. Some pre-infusion forms on the Case Report Form (CRF) track have different reporting rules, depending on if a pre-infusion CRF had been previously complete for the recipient. Carefully review the Disease-Specific CRF manuals for additional information.

Malignant vs. Non-Malignant

Malignant diseases 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 diseases involve cell overgrowth but lack the malignant properties of cancer.

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.

If the indication for infusion is due to a combination of diseases or a transformation of one disease to another, it may be necessary to report multiple disease classifications. The tables below list how common examples of disease combinations and transformations should be reported using the Disease Classification questions.

Table 1. Common Disease Combinations

Disease Combinations	Report Primary Disease as:	Report disease diagnosis date of:	Complete multiple disease sections of the Disease Classification Form?
FAN or SAA and AML	AML	AML	No
FAN or SAA and MDS	MDS	MDS	No

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MYE and AMY	MYE	MYE	No

Table 2. Common Disease Transformations

Disease Transformation	Report primary disease as:	Report disease diagnosis date of:	Complete multiple disease sections of the Disease Classification Form?
MDS or MPN to AML	AML	AML	Yes – AML and MDS or MPN
JMML to AML	AML	AML	Yes – AML and MDS (select questions only)
NHL to another NHL	Second NHL diagnosis	Second NHL diagnosis	No
HL to NHL*	NHL	NHL	No
CLL to NHL (i.e., Richter's Syndrome)	NHL	NHL	No

AML=Acute Myelogenous Leukemia; AMY=Amyloidosis; CLL=Chronic Lymphocytic Leukemia; FAN=Fanconi Anemia; MDS=Myelodysplastic Syndrome; MPS=Myeloproliferative Disease; MYE=Multiple Myeloma; NHL=Non-Hodgkin Lymphoma; SAA=Severe Aplastic Anemia.

***Ensure that the disease process is a transformation from Hodgkin lymphoma to Non-Hodgkin lymphoma (typically diffuse large B-cell lymphoma), rather than the distinct entity "B-cell lymphoma, unclassifiable, with features indeterminate between DLBCL and classical Hodgkin Lymphoma."**

Question 1: Date of diagnosis for primary disease for infusion

The date of diagnosis is important because the interval between diagnosis and infusion is often a significant indicator for the recipient's prognosis post-HCT. Refer to the disease-specific section of the Disease Classification (2402) manual for guidelines when reporting the diagnosis date for each disease.

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If the recipient was diagnosed prenatally (*in utero*) or was diagnosed with a **congenital** immunodeficiency, report the date of birth as the date of diagnosis.

If this is a subsequent infusion for the same disease, report the date of diagnosis as the first date when the primary disease for infusion was diagnosed.

If this is a subsequent infusion for a new malignancy (or other new indication), report the date of diagnosis of the new malignancy.

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

Question 2: What was the primary disease for which the infusion was performed?

Select the primary disease for which the recipient is receiving the infusion and continue with the appropriate disease classification questions. If documentation is unclear, seek clinician clarification.

Section Updates

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

Q3 – 127: Acute Myelogenous Leukemia

Acute Myelogenous Leukemia (AML) is a cancer of the white blood cells. It is characterized by the rapid proliferation of abnormal, immature myelocytes, known as myeloblasts, in the bone marrow. This accumulation of blasts in the marrow prevents the formation of healthy red blood cells, white blood cells, and/or platelets. Normal myeloblasts develop into neutrophils, basophils, and eosinophils, which are all white blood cells that fight infection. In AML, the leukemic myeloblasts do not fully develop and are unable to fight infection. The symptoms of AML result from a drop in red blood

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cell, platelet, and normal white blood cell counts caused by the replacement of normal bone marrow with leukemic cells.

Certain prognostic indicators are associated with poorer outcomes. These include advanced age (50+ years of age), AML arising from MDS or secondary / therapy-related AML, and certain genetic mutations that are described in greater detail later in this manual.

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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 AML transformed from MPS or MPN, report the diagnosis date of the AML.
The MPS or MPN diagnosis date will be captured in the MDS or MPN sections below.

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

Question 3: Specify the AML classification

CIBMTR captures the classification of AML based on the World Health Organization (WHO) 2022, but also recognizes International Consensus Classification (ICC) 2022 and those classifications are also included, when applicable. Additionally, the European LeukemiaNet (ELN) 2022 is also included from a risk stratification standpoint. Indicate the disease classification at diagnosis.

Report the most specific entity that applies to the recipient. For example, if the disease classification is defined by both genetic abnormalities and differentiation, the defining genetic abnormality classification should be reported for classification purposes.
In some cases, disease specific cytogenetic and / or molecular abnormalities are not identified at the initial diagnosis but identified at some point prior to the infusion, report the most disease specific entity. Review the example below for further clarification:

- Example 1: A recipient diagnosed with AML had only a bone marrow biopsy and FISH testing for BCR-ABL performed at diagnosis. The bone marrow

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identified AML with maturation and FISH was negative for BCR-ABL. Induction began and additional molecular testing completed after starting treatment which identified NPM1. The disease classification should be reported as **AML with NPM1 mutation**.

For some AML classifications, the requirement of ≥ 20% blasts in blood or bone marrow is no longer applicable. The guidelines below provide an overview of which AML classifications require ≥ 20% blasts in the blood or bone marrow.

- If the disease is a 'AML with defining genetic abnormalities,' ≥ 20% blasts in blood or bone marrow is no longer required, except for **AML with BCR::ABL1 fusion**, **AML with CEBPA mutation**, and **AML with myelodysplasia – related**.
    - For **AML with BCR::ABL1 fusion** and **AML with CEBPA mutation**, ≥ 20% blasts in blood or bone marrow is required
    - For **AML with myelodysplasia – related**, the following is required:
        - ≥ 20% blasts in blood or bone marrow are required, and *one* of the following:
            - History of MDS / MPN; or
            - At least one defining cytogenetic abnormality present; or
                - Complex karyotype (i.e., ≥ 3 abnormalities)
                - Deletion or loss 5q
                - Monosomy 7, deletion, or loss 7q
                - Deletion 11q
                - Deletion or loss 12p
                - Monosomy 13 or deletion 13q
                - Deletion or loss 17p
                - Isochromosome 17q
                - Idic(X)(q13)
            - At least one defining somatic mutation present
                - ASXL1
                - BCOR
                - EZH2
                - SF3B1
                - SRSF2
                - STAG2
                - U2AF1
                - ZRSR2

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  - If the disease is **AML with other defined genetic alterations**, ≥ 20% blasts in blood or bone marrow is not required; however, seek physician clarification if it is unclear if the disease should be reported as AML.
- If the disease is a 'AML, defined by differentiation,' ≥ 20% blasts in blood or bone marrow are required.

Subsequent Infusion and Transformation, Therapy Related, and Predisposing Conditions
If this is a subsequent infusion for the same disease, the *Did AML transform form MDS or MPN*, *Is the disease therapy related*, and *Did the recipient have predisposing condition* questions are disabled.

Question 4: Did AML transform from MDS or MPN?

AML often evolves from MDS or MPN. This transformation is typically distinguished by the percentage of blasts in the bone marrow

AML that transforms from MDS or MPN has a lower survival prognosis because of the association with unfavorable cytogenetic abnormalities.

AML can also evolve from Juvenile Myelomonocytic Leukemia (JMML). JMML is a rare form of chronic leukemia that affects young children, usually before the age of five. JMML results from DNA mutations in cells called monocytes. Normal monocytes attack invading microorganisms and assist lymphocytes in carrying out immune functions. Abnormal monocytes in JMML accumulate in the bone marrow and interfere with the production of normal white blood cells, red blood cells, and platelets.

Specify if AML transformed from MDS or MPN (including JMML). If **Yes**, complete both the *AML and MDS / MPN* disease classification sections of this form. If AML did not transform from MDS or MPN or it is not known, check **No**.

If MDS / MPN is suspected, but not confirmed by documented laboratory or pathologic findings, or if there is documentation of MDS / MPN *concurrent* with AML, check **No**.

Question 5: Is the disease (AML) therapy related?

Agents such as radiation or systemic therapy used to treat other diseases (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, or breast cancer) can damage the marrow

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and lead to a secondary malignancy such as AML. Indicate if the diagnosis of AML is therapy-related.

If AML was preceded by therapy-related MDS, report **No**.

If the recipient developed AML after an environmental exposure (e.g., exposure to benzene), report **No**.

If it is unknown whether the diagnosis of AML was therapy-related, check **Unknown**.

If documentation is unclear, seek clinician clarification.

Concurrent AML and MDS or MPN Diagnosis
If there is a concurrent diagnosis of AML and MDS or MPN, do not report there was a transformation above. Instead, report **Yes** there was predisposing condition / antecedent hematologic disorder and specify the MDS or MPN classification.

Question 6: Did the recipient have a predisposing condition or antecedent hematologic disorder?

Certain predisposing conditions and antecedent hematologic disorders contribute to the susceptibility of developing leukemia. Therefore, diagnosis of specific conditions / disorders increases the likelihood that the recipient will develop leukemia.

Indicate if the recipient has a documented history of a predisposing condition or antecedent hematologic disorder. If there is no history of predisposing condition / antecedent hematologic disorder or it is not known, indicate **No** or **Unknown**, respectively.

Questions 7 – 8: Specify condition

Specify the recipient's predisposing condition / antecedent hematologic disorder prior to the diagnosis of leukemia. If the recipient has a documented history of a predisposing condition / antecedent hematologic disorder but it is not listed as an option, select **Other condition** and specify the condition.

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Subsequent Infusion and At Diagnosis Time Point
If this is a subsequent infusion for the same disease, the *At Diagnosis* time point is disabled

At Diagnosis Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes, use the following definition when reporting for the *at diagnosis* time point: Any testing performed closest to (before or after) the date of diagnosis (question 1) and prior to the start of any treatment for AML.

Question 9: Were cytogenetics tested (karyotyping or FISH)? *(at diagnosis)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at diagnosis. If cytogenetic studies were obtained, select **Yes**. If no cytogenetic studies were obtained, or it is unknown if chromosome studies were performed, select **No** or **Unknown**, respectively.

Table 1. Examples of AML Cytogenetic Findings Categorized by Prognosis

Favorable	Intermediate	Poor
t(15;17) t(8;21) inv(16) or t(16;16)	Normal +8 t(9;11) *All other abnormalities*	≥ 3 abnormalities 5- or 5q- 7- or 7q- t(9;22)

Question 10: Were cytogenetics tested via FISH? *(at diagnosis)*

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Specify if FISH studies were performed at diagnosis. If FISH studies were not performed at diagnosis or FISH samples were inadequate, report **No**. If it is not known if it was performed, report **Unknown**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 11: Results of tests

Specify if FISH abnormalities were identified at diagnosis.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 12 – 15: Specify FISH abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at diagnosis and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report “see attachment” and attach the final report(s) for any other abnormalities detected.

Question 16: Were cytogenetics tested via karyotyping? *(at diagnosis)*

Specify if karyotyping studies were performed at diagnosis. Report **Yes** even if there were no evaluable metaphase cells / failed (these results will be specified below).

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If karyotyping studies were not performed at diagnosis or it is unknown if performed, report **No** or **Unknown**, respectively.

Question 17: Results of tests

Specify if abnormalities were detected by karyotype at diagnosis.

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 18 – 21: Specify karyotype abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at diagnosis and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Questions 22 – 41: Specify molecular marker results *(at diagnosis)*

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often

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performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

The molecular markers listed below are ELN AML markers and prognostic of AML. Due to the importance of these markers, it is necessary to know if the marker was positive, negative, or not assessed.

- ASXL1
- BCOR
- BCR::ABL1
- CEBPA
- DDX41
- EZH2
- FLT3-ITD
- GATA2
- NPM1
- RUNX1
- SF3B1
- SRSF2
- STAG2
- TP53
- U2AF1
- ZRSR2

For each molecular marker, specify if the marker was **Positive** or **Negative** at diagnosis and answer and additional questions. If the molecular marker was not assessed at diagnosis, select **Not done**.

If CEBPA was **Positive**, specify the CEBPA variant mutation and allelic expression. If the variant mutation is not documented, report the mutation as **Unknown**. If the allelic expression is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

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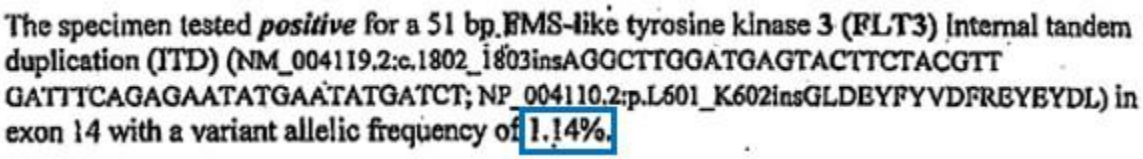
If FLT3-ITD was **Positive**, specify the allelic ratio, if known. If the allelic ratio is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

The allelic ratio data field is intended to capture the ratio of the FLT3-ITD mutation. This data field does not collect the allelic frequency, the allelic frequency is used to calculate the allelic ratio. The FLT-3 ITD allelic ratio (or signal ratio) compares the number of ITD-mutated alleles to the number of wild-type (normal) alleles. If the allele frequency was assessed, the ITD-mutated allele frequency will be documented on the molecular report; however, the wild-type allele frequency will need to be calculated. To determine the wild-type allele frequency, subtract the ITD-mutated allele frequency from 1 (or 100.0%). After determining the wild-type allele frequency, the allelic ratio can be assessed. To calculate the allelic ratio, divide the mutant allele frequency by the wild-type (normal) allele frequency. Review example 2 below for more information:

- Example 2:


The specimen tested ***positive*** for a 51 bp FMS-like tyrosine kinase 3 (FLT3) internal tandem duplication (ITD) (NM_004119.2:c.1802_1803insAGGCTTGGATGAGTACTTCTACGTT GATTTCAGAGAATATGAATATGATCT; NP_004110.2:p.L601_K602insGLDEYFYVDFREYEYDL) in exon 14 with a variant allelic frequency of 1.14%.

  - ITD variant allele frequency: 1.14% (0.0114)
    - As documented in the molecular report
  - Wild-type allele frequency: 98.86% (0.9886)
    - Determined by subtraction 1.14% from 100.0%
  - FLT3-ITD allelic ratio: 0.0114 / 0.9886 = 0.0115

    Report the FLT3-ITD allelic ratio as 0.0115

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 42 – 43: Specify any other positive molecular marker(s) identified *(check all that apply)*

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Indicate if any other *positive* molecular markers (excluding the ELN AML molecular markers listed above), including variance of unknown significant markers, were detected at diagnosis.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality, along with the amino acid change, if known.

If molecular markers were not detected at diagnosis, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

In Between Diagnosis and Last Evaluation Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes, use the following definition when reporting for the *in between* time point: Any pre-infusion testing which cannot be reported as part of *at diagnosis* or *last evaluation*. For subsequent infusions, any testing performed after the prior infusion until the last evaluation for the current infusion should be reported here. For example, if relapse / progression occurred after the previous infusion but prior to Last Evaluation of the current infusion, report the relapse / progression abnormalities at the In Between timepoint.

Question 44: Were cytogenetics tested (karyotyping or FISH)? *(between diagnosis and last evaluation)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were performed between diagnosis and the last evaluation. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate **No**.

Question 45: Were cytogenetics tested via FISH? *(between diagnosis and last evaluation)*

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Specify if FISH studies were performed between diagnosis and the last evaluation. If FISH studies were not performed at this time point, FISH sample was inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 46: Results of tests

Specify if FISH abnormalities were identified between diagnosis and the last evaluation.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 47 – 50: Specify FISH abnormalities *(between diagnosis and last evaluation)*

Report the ISCN compatible string, if applicable. If reporting the ISCN compatible string and multiple FISH assessments were completed between diagnosis and the last evaluation, add a separate instance of the *ISCN compatible string* to report each FISH ISCN compatible string.

Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH between diagnosis and the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report “see attachment” and attach the final report(s) for any other abnormalities detected.

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Question 51: Were cytogenetics tested via karyotyping? *(between diagnosis and last evaluation)*

Specify if karyotyping studies were performed between diagnosis and the last evaluation. Report **Yes** even if there were no evaluable metaphase cells (these results will be specified below).

If karyotyping studies were not performed at this time point or it is unknown if performed, report **No**.

Question 52: Results of tests

Specify if abnormalities were detected by karyotype between diagnosis and the last evaluation.

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the Karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 53 – 56: Specify karyotype abnormalities *(between diagnosis and last evaluation)*

Report the ISCN compatible string, if applicable. If reporting the ISCN compatible string and multiple karyotype studies were completed between diagnosis and the last evaluation, add a separate instance of the *ISCN compatible string* to report each karyotype ISCN compatible string.

Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype between diagnosis and the last evaluation and select all abnormalities detected.

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If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Questions 57 – 76: Specify molecular marker results *(between diagnosis and last evaluation)*

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

The molecular markers listed below are ELN AML markers and prognostic of AML. Due to the importance of these markers, it is necessary to know if the marker was positive, negative, or not assessed.

- ASXL1
- BCOR
- BCR::ABL1
- CEBPA
- DDX41
- EZH2
- FLT3-ITD
- GATA2
- NPM1

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- RUNX1
- SF3B1
- SRSF2
- STAG2
- TP53
- U2AF1
- ZRSR2

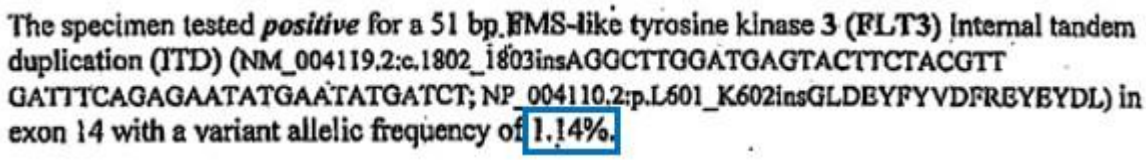
For each molecular marker, specify if the marker was **Positive** or **Negative** between diagnosis and the last evaluation and answer additional questions. If the molecular marker was not assessed between diagnosis and the last evaluation, select **Not done**.

If CEBPA was **Positive**, specify the CEBPA variant mutation and allelic expression. If the variant mutation is not documented, report the mutation as **Unknown**. If the allelic expression is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

If FLT3-ITD was **Positive**, specify the allelic ratio, if known. If the allelic ratio is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

The allelic ratio data field is intended to capture the ratio of the FLT3-ITD mutation. This data field does not collect the allelic frequency, the allelic frequency is used to calculate the allelic ratio. The FLT-3 ITD allelic ratio (or signal ratio) compares the number of ITD-mutated alleles to the number of wild-type (normal) alleles. If the allele frequency was assessed, the ITD-mutated allele frequency will be documented on the molecular report; however, the wild-type allele frequency will need to be calculated. To determine the wild-type allele frequency, subtract the ITD-mutated allele frequency from 1 (or 100.0%). After determining the wild-type allele frequency, the allelic ratio can be assessed. To calculate the allelic ratio, divide the mutant allele frequency by the wild-type (normal) allele frequency. Review example 3 below for more information:

- Example 3:


The specimen tested ***positive*** for a 51 bp FMS-like tyrosine kinase 3 (FLT3) internal tandem duplication (ITD) (NM_004119.2:c.1802_1803insAGGCTTGGATGAGTACTTCTACGTT GATTTCAGAGAATATGAATATGATCT; NP_004110.2:p.L601_K602insGLDEYFYVDFREYEYDL) in exon 14 with a variant allelic frequency of 1.14%.

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- ITD variant allele frequency: 1.14% (0.0114)
  - As documented in the molecular report
- Wild-type allele frequency: 98.86% (0.9886)
  - Determined by subtraction 1.14% from 100.0%
- FLT3-ITD allelic ratio: 0.0114 / 0.9886 = 0.0115

Report the FLT3-ITD allelic ratio as 0.0115

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 77 – 78: Specify any other positive molecular marker(s) identified *(check all that apply)*

Indicate if any other *positive* molecular markers (excluding the ELN AML molecular markers listed above), including variance of unknown significant markers, were detected between diagnosis and the last evaluation.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality, along with the amino acid change, if known.

If molecular markers were not detected between diagnosis and the last evaluation, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

Last Evaluation Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes, use the following definition when reporting for the *last evaluation* time point: Testing performed during the recipient's work-up for infusion (generally within 30 days of the start of the preparative regimen or infusion).

Question 79: Were cytogenetics tested (karyotyping or FISH)? *(at last evaluation)*

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Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate **No**.

Question 80: Were cytogenetics tested via FISH? *(at last evaluation)*

Specify if FISH studies were performed at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). If FISH studies were not performed at this time point, FISH sample was inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 81: Results of tests

Specify if FISH abnormalities were identified at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen).

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 82 – 85: Specify FISH abnormalities *(at last evaluation)*

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Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen) and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 86: Were cytogenetics tested via karyotyping? *(at last evaluation)*

Specify if karyotyping studies were performed at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). Report **Yes** even if there were no evaluable metaphase cells (these results will be specified below).

If karyotyping studies were not performed at this time point or it is unknown if performed, report **No**.

Question 87: Results of tests

Specify if abnormalities were detected by karyotype at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen).

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the Karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 88 – 91: Specify karyotype abnormalities *(at last evaluation)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

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If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen) and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Questions 92 – 111: Specify molecular marker results *(at last evaluation)*

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

The molecular markers listed below are ELN AML markers and prognostic of AML. Due to the importance of these markers, it is necessary to know if the marker was positive, negative, or not assessed.

- ASXL1
- BCOR
- BCR::ABL1
- CEBPA
- DDX41
- EZH2
- FLT3-ITD

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- GATA2
- NPM1
- RUNX1
- SF3B1
- SRSF2
- STAG2
- TP53
- U2AF1
- ZRSR2

For each molecular marker, specify if the marker was **Positive** or **Negative** at the last evaluation and answer additional questions. If the molecular marker was not assessed at the last evaluation, select **Not done**.

If CEBPA was **Positive**, specify the CEBPA variant mutation and allelic expression. If the variant mutation is not documented, report the mutation as **Unknown**. If the allelic expression is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

If FLT3-ITD was **Positive**, specify the allelic ratio, if known. If the allelic ratio is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

The allelic ratio data field is intended to capture the ratio of the FLT3-ITD mutation. This data field does not collect the allelic frequency, the allelic frequency is used to calculate the allelic ratio. The FLT-3 ITD allelic ratio (or signal ratio) compares the number of ITD-mutated alleles to the number of wild-type (normal) alleles. If the allele frequency was assessed, the ITD-mutated allele frequency will be documented on the molecular report; however, the wild-type allele frequency will need to be calculated. To determine the wild-type allele frequency, subtract the ITD-mutated allele frequency from 1 (or 100.0%). After determining the wild-type allele frequency, the allelic ratio can be assessed. To calculate the allelic ratio, divide the mutant allele frequency by the wild-type (normal) allele frequency. Review example 4 below for more information:

- Example 4:

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The specimen tested ***positive*** for a 51 bp FMS-like tyrosine kinase 3 (FLT3) internal tandem duplication (ITD) (NM_004119.2:c.1802_1803insAGGCTTGGATGAGTACTTCTACGTT GATTTCAGAGAATATGAATATGATCT; NP_004110.2:p.L601_K602insGLDEYFYVDFREYEYDL) in exon 14 with a variant allelic frequency of 1.14%.

- ITD variant allele frequency: 1.14% (0.0114)
  - As documented in the molecular report
- Wild-type allele frequency: 98.86% (0.9886)
  - Determined by subtraction 1.14% from 100.0%
- FLT3-ITD allelic ratio: 0.0114 / 0.9886 = 0.0115

Report the FLT3-ITD allelic ratio as 0.0115

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 112 – 113: Specify any other positive molecular marker(s) identified *(check all that apply)*

Indicate if any other *positive* molecular markers (excluding the ELN AML molecular markers listed above), including variance of unknown significant markers, were detected at the last evaluation.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality, along with the amino acid change, if known.

If molecular markers were not detected at the last evaluation, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

Question 114: Did the recipient have central nervous system leukemia at any time prior to the start of the preparative regimen / infusion?

Central nervous system (CNS) involvement by leukemia may be detected via pathologic examination of cerebrospinal fluid or tumor tissue as well as by radiological examinations (e.g., MRI, PET/CT, MIBG, etc.).

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Specify if the recipient had documented involvement of AML in the CNS at any time prior to the start of the preparative regimen (or infusion if no preparative regimen).

If all CNS testing was negative since the time of diagnosis, report **No**.

If testing for CNS involvement was not performed from the time of diagnosis to the time of infusion, report **Unknown**.

Question 115: What was the disease status (based on hematologic test results)?

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. Refer to the AML Response Criteria section for definitions of each response. For reporting purposes, consider complete remission with incomplete hematologic recovery (CRi) a complete remission (CR1, CR2, or CR3+).

If the recipient did not receive any treatment for AML from the time of diagnosis to the start of the preparative regimen (or infusion if no preparative regimen), report **No treatment**

Number of Induction Cycles

The intent of this question is to capture the number of induction cycles required to achieve the *first* CR (including CRi) in the recipient's disease history, regardless of if there have been prior relapses or infusions.

Question 116: How many cycles of induction therapy were required to achieve 1st complete remission (CR)? *(includes CRi)*

Chemotherapy is initially given as induction therapy intended to bring the disease into remission. Recipients usually have one to two cycles of induction therapy; disease prognosis is considered less favorable if the patient fails to achieve remission with the first induction therapy and even poorer if patients fail two or more induction therapies.1 An example of a common induction therapy for all AML subtypes (except M3) is a combination of an anthracycline and cytarabine, commonly known as "7+3." In this regimen, cytarabine is typically administered for seven days at a dose of 100 mg/m^2/day. The anthracycline (usually daunorubicin at 45 to 60 mg/m^2/day or idarubicin at 12 mg/m^2/day) is generally given on the first three days the cytarabine is given.

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The second phase of chemotherapy is known as consolidation therapy. The goal of consolidation therapy is to destroy any remaining leukemia cells and sustain remission. An example of a common consolidation therapy for all AML subtypes (except M3) is high-dose cytarabine, commonly referred to as "HiDAC." In this regimen, cytarabine is typically administered at a dose exceeding 10 g/m^2 per cycle.

Maintenance chemotherapy may follow consolidation therapy. Maintenance chemotherapy is given in lower doses and is intended to prolong a remission. Maintenance therapy is used less commonly for the treatment of AML than other malignancies. Treatment may also be administered for relapsed disease. Much like induction therapy, treatment for relapse is intended to bring the disease back into remission. Systemic therapeutic agents used to induce remission following relapse often differ from those used in the initial induction, since the disease is often resistant to many of the agents used earlier in the disease course and is considered high-risk with a poor prognosis. Allogeneic HCT is often considered the only potential "cure" for relapsed disease.

If the pre-infusion disease status is **CR1**, report the number of cycles of *induction therapy* that were required to achieve the first CR.

[1] Ravandi F, Cortes J, Faderl S, et al. (2010). Characteristics and outcome of patients with acute myeloid leukemia refractory to one cycle of high-dose cytarabine-based induction therapy. Blood, 116(26):5818-23.

Question 117: Date CR first achieved

This question is intended to capture the date when the *first clinical / hematologic CR* was achieved.

Report the date when the first CR was achieved. This should be the earliest date all international working group criteria for CR were met. Report the date the sample was collected for pathologic evaluation (i.e., bone marrow biopsy) or blood / serum assessments (i.e., CBC, peripheral blood smear).

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, General Guidelines for Completing Forms.

Question 118: Date of most recent relapse

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Enter the date of the most recent relapse prior to the start of the preparative regimen / infusion. If reporting a pathological evaluation (i.e., bone marrow) or blood / serum assessment (i.e., CBC, peripheral blood smear), enter the date the sample was collected.

If extramedullary disease was detected by radiographic examination (i.e.., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place.

If the physician determines cytogenetic or molecular relapse, enter the date the sample was collected for cytogenetic or molecular evaluation. If the physician determines evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, General Guidelines for Completing Forms.

Question 119: Specify method(s) that was used to assess measurable residual disease status *(check all that apply) (at infusion)*

Specify the method(s) how the measurable residual status was assessed at the last evaluation, approximately 30 days prior to the start of the preparative regimen / infusion. Select all that apply.

- **FISH**: A sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA. These probes are mixed with cells from the recipient's blood or bone marrow. A fluorescent "tag" is then used to visualize the binding of the probe to the diseased cells.
- **Karyotype**: A technique 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.
- **Flow cytometry**: A method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics. Its primary clinical purpose in the setting of leukemias is to quantify blasts in the peripheral blood or bone marrow, or to identify unique cell populations through immunophenotyping. Flow

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cytometry assessment may also be referred to as “MRD,” or minimal residual disease, testing.

- **PCR**: Polymerase chain reaction (PCR) amplification is a molecular assessment used to detect single specific disease markers. Testing for molecular markers is often performed using PCR based methods. Once a marker has been identified, this method can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue.
- **NGS**: Next-generation sequencing (NGS), also known as massive parallel sequencing, is another molecular assessment which is used to determine the order of nucleotides in a genome.

If testing for measurable residual status was not completed at the last evaluation, select **Not assessed**.

Question 120: Was measurable residual disease detected by FISH? *(at infusion)*

Indicate if measurable residual disease was detected by FISH at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if measurable residual disease was detected by FISH at the last evaluation.

Question 121: Was measurable residual disease detected by karyotyping assay? *(at infusion)*

Indicate if measurable residual disease was detected by karyotype at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if minimal residual disease was detected by karyotype at the last evaluation.

Question 122: Was measurable residual disease detected by flow cytometry? *(at infusion)*

Indicate if measurable residual disease was detected by flow cytometry at the last evaluation prior to the start of the preparative regimen / infusion.

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If the results are not clear, seek physician clarification to determine if minimal residual disease was detected by flow cytometry at the last evaluation.

Original vs Aberrant Phenotype

The original vs aberrant phenotype questions are currently disabled.

Questions 123 – 125: Which leukemia phenotype was used for detection? *(at infusion) (check all that apply)*

Specify which leukemia phenotype was used for detection. Select all that apply.

If the **Original leukemia immunophenotype** was used, specify the lower limit of detection, and then indicate if measurable residual disease was detected by flow cytometry at the last evaluation prior to the start of the preparative regimen / infusion.

If an **Aberrant phenotype** was used, specify the lower limit of detection, and then indicate if measurable residual disease was detected by flow cytometry at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if minimal residual disease was detected by flow cytometry at the last evaluation.

Question 126: Was measurable residual disease detected by PCR? *(at infusion)*

Indicate if measurable residual disease was detected by PCR at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if measurable residual disease was detected by PCR at the last evaluation assay at the last evaluation prior to the start of the preparative regimen / infusion.

Question 127: Was measurable residual disease detected by NGS? *(at infusion)*

Indicate if measurable residual disease was detected by NGS at the last evaluation prior to the start of the preparative regimen / infusion.

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If the results are not clear, seek physician clarification to determine if measurable residual disease was detected by NGS at the last evaluation assay at the last evaluation prior to the start of the preparative regimen / infusion.

Section Updates

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

Q128 – 194: Acute Lymphoblastic Leukemia

Acute Lymphoblastic Lymphoma
Due to the aggressive nature of precursor T- and precursor B-cell lymphoblastic lymphoma (or lymphoma / leukemia), the primary disease reported for recipients with these malignancies should be acute lymphoblastic leukemia (T-cell lymphoblastic leukemia / lymphoma or B-lymphoblastic leukemia / lymphoma, NOS).

Acute Lymphoblastic Leukemia (ALL) is a cancer of the white blood cells. It is characterized by the rapid proliferation of abnormal, immature lymphocytes, known as lymphoblasts, in the bone marrow. This accumulation of blasts in the marrow prevents the formation of healthy red blood cells, white blood cells and/or platelets. Normal lymphoblasts develop into B and T lymphocytes that fight infection. In ALL, the leukemic lymphoblasts do not fully develop and therefore cannot fight infection. The symptoms of ALL are caused by the replacement of normal bone marrow with leukemic cells, resulting in a drop in red blood cells, platelets, and normal white blood cells. It is estimated that 80-85% of ALL cases occur in children, with peak incidence of pediatric ALL at age 5. Biologically, adult and pediatric ALL are very different. Pediatric cases are more often characterized by favorable prognostic indicators including a precursor B-cell population, TEL / AML1 fusion gene, and/or hyperdiploidy; adult cases are more often characterized by poor prognostic indicators including a precursor T-cell population and / or BCR / ABL fusion gene.[1]

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[1] Sallan S. Myths and Lessons from the Adult/Pediatric Interface in Acute Lymphoblastic Leukemia. ASH Education Book, 1st edition. 2006:128-32.

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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 exact diagnosis date is not known, use the process described in General Instructions, Guidelines for Completing Forms

Question 128: Specify ALL classification

CIBMTR captures the classification of ALL based on the World Health Organization (WHO) 2022 but also recognizes International Consensus Classification (ICC) 2022 and those classifications are also included, when applicable. Indicate the disease classification at diagnosis.

Due to the aggressive nature of precursor T- and precursor B-cell lymphoblastic lymphoma (or lymphoma / leukemia), the primary disease reported for recipients with these malignancies should be acute lymphoblastic leukemia.

Report the most specific entity that applies to the recipient. If the cytogenetic or molecular abnormalities present are listed on the form, check the sub-type rather than **B-lymphoblastic leukemia / lymphoma, NOS**.

In some cases, disease specific cytogenetic and / or molecular abnormalities are not identified at the initial diagnosis but identified at some point prior to the infusion, report the most disease specific entity. Review the example below for further clarification:

- Example 1: A recipient diagnosed with ALL had only a bone marrow biopsy and FISH testing for BCR-ABL performed at diagnosis. The bone marrow identified B-lymphoblastic leukemia / lymphoma and FISH was negative for BCR-ABL. Induction began and additional molecular testing completed after starting treatment which identified ETV6-RUNX1 fusion. The disease classification should

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be reported as **B-lymphoblastic leukemia / lymphoma with ETV6::RUNX1 fusion**.

Subsequent Infusion and Predisposing Conditions

If this is a subsequent infusion for the same disease, *Did the recipient have a predisposing condition* question is disabled.

Question 129: Did the recipient have a predisposing condition?

A predisposing condition is a condition that contributes to the susceptibility of developing leukemia. Therefore, diagnosis of the condition increases the likelihood that the recipient will develop leukemia.

Indicate if the recipient has a documented history of predisposing condition. If there is no history of a predisposing condition or it is not known, indicate **No** or **Unknown**, respectively.

Questions 130 – 131: Specify condition

Indicate the recipient's predisposing condition prior to the diagnosis of leukemia. If the recipient has a documented history of a predisposing condition but it is not listed as an option, select **Other condition** and specify the condition.

Question 132: Were tyrosine kinase inhibitors given for therapy at any time prior to the start of the preparative regimen / infusion? (e.g., imatinib mesylate, dasatinib, etc.)

Report if the recipient received *any* tyrosine kinase inhibitor from the diagnosis of ALL to the start of the preparative regimen (or infusion if no preparative regimen). Examples include, Imatinib mesylate is also known as Gleevec, Glivec, STI-571, or CGP57148B.

If tyrosine kinase inhibitors were not given at any time prior to the preparative regimen / infusion, or is unknown, report **No**.

Questions 133 – 134: Specify tyrosine kinase inhibitors *(check all that apply)*

Select all tyrosine kinase inhibitors given prior to the start of the preparative regimen (or infusion if no preparative regimen).

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If tyrosine kinase inhibitor was given but is not listed as an option on the form, select **Other** specify the drug.

Subsequent Infusion and At Diagnosis Time Point
If this is a subsequent infusion for the same disease, the *At Diagnosis* time point is disable.

At Diagnosis Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes, use the following definition when reporting for the *at diagnosis* time point: Any testing performed closest to (before or after) the date of diagnosis (question 1) and prior to the start of any treatment for ALL.

Question 135: Were cytogenetics tested (conventional or FISH)? *(at diagnosis)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at diagnosis. If cytogenetic studies were obtained, select **Yes**. If no cytogenetic studies were obtained, or it is unknown if chromosome studies were performed, select **No** or **Unknown**, respectively.

Table 1. Examples of ALL Cytogenetic Findings Categorized by Prognosis (Adult Precursor B-cell ALL)

Favorable	Intermediate	Poor	Very Poor
High hyperdiploidy (51-65 chromosomes)	Normal 11q abnormalities del(6q) del(17p)	-7/del(7p) +8 11q23 abnormalities/MLL	≥ 5 abnormalities t(4;11) t(8;14)

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	del(9p) del(12p) -13/del(13q) t(14q32) t(10;14) Low hyperdiploidy (47-50 chromosomes) Tetraploidy (> 80 chromosomes)	t(1;19) t(17;19) t(5;14) t(9;22)	

[2] Pullarkat V, Slovak ML, Kopecky KJ, Forman SJ, Appelbaum FR. Impact of cytogenetics on the outcome of adult acute lymphoblastic leukemia: results of Southwest Oncology Group 9400 study. *Blood*. 2008;111(5):2563-72.

Question 136: Were cytogenetics tested via FISH? *(at diagnosis)*

Specify if FISH studies were performed at diagnosis. If FISH studies were not performed at diagnosis or FISH samples were inadequate, report **No**. If it is not known if it was performed, report **Unknown**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 137: Results of tests

Specify if FISH abnormalities were identified at diagnosis.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 138 – 141: Specify FISH abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable.

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If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at diagnosis and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 142: Were cytogenetics tested via karyotyping? *(at diagnosis)*

Specify if karyotyping studies were performed at diagnosis. Report **Yes** even if there were no evaluable metaphase cells / failed (these results will be specified below).

If karyotyping studies were not performed at diagnosis or it is unknown if performed, report **No** or **Unknown**, respectively.

Question 143: Results of tests

Specify if abnormalities were detected by karyotype at diagnosis.

If karyotyping failed, select **No evaluable metaphases**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 144 – 147: Specify karyotype abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at diagnosis and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

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Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 148 – 149: Specify any other positive molecular marker(s) identified *(check all that apply)*

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

Indicate if any other *positive* molecular markers, including variance of unknown significant markers, were detected at diagnosis.

If a molecular marker was detected, but not listed as an option, select **Other** and specify the abnormality.

If molecular markers were not detected at diagnosis, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

In Between Diagnosis and Last Evaluation Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes, use the following definition when reporting for the *in between* time point: Any pre-

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infusion testing which cannot be reported as part of *at diagnosis* or *last evaluation*. For subsequent infusions, any testing performed after the prior infusion until the last evaluation for the current infusion should be reported here. For example, if relapse / progression occurred after the previous infusion but prior to Last Evaluation of the current infusion, report the relapse / progression abnormalities at the In Between timepoint.

Question 150: Were cytogenetics tested (karyotyping or FISH)? *(between diagnosis and last evaluation)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were performed between diagnosis and the last evaluation. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate **No**.

Question 151: Were cytogenetics tested via FISH? *(between diagnosis and last evaluation)*

Specify if FISH studies were performed between diagnosis and the last evaluation. If FISH studies were not performed at this time point, FISH sample was inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 152: Results of tests

Specify if FISH abnormalities were identified between diagnosis and the last evaluation.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH

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The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 153 – 156: Specify FISH abnormalities *(between diagnosis and last evaluation)*

Report the ISCN compatible string, if applicable. If reporting the ISCN compatible string and multiple FISH assessments were completed between diagnosis and the last evaluation, add a separate instance of the *ISCN compatible string* to report each FISH ISCN compatible string.

Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH between diagnosis and the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 157: Were cytogenetics tested via karyotyping? *(between diagnosis and last evaluation)*

Specify if karyotyping studies were performed between diagnosis and the last evaluation. Report **Yes** even if there were no evaluable metaphase cells (these results will be specified below).

If karyotyping studies were not performed at this time point or it is unknown if performed, report **No**.

Question 158: Results of tests

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Specify if abnormalities were detected by karyotype between diagnosis and the last evaluation.

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the Karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 159 – 162: Specify karyotype abnormalities *(between diagnosis and last evaluation)*

Report the ISCN compatible string, if applicable. If reporting the ISCN compatible string and multiple karyotype studies were completed between diagnosis and the last evaluation, add a separate instance of the *ISCN compatible string* to report each karyotype ISCN compatible string.

Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype between diagnosis and the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Submitting Molecular Marker Documentation

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CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 163 – 164: Specify molecular marker results *(between diagnosis and last evaluation)*

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

Indicate if any other *positive* molecular markers, including variance of unknown significant markers, were detected between diagnosis and the last evaluation.

If a molecular marker was detected, but not listed as an option, select **Other** and specify the abnormality.

If molecular markers were not detected between diagnosis and the last evaluation, the sample failed, testing was not completed or unknown if completed between diagnosis and the last evaluation report **None**.

Last Evaluation Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes, use the following definition when reporting for the *last evaluation* time point: Testing performed during the recipient's work-up for infusion (generally within 30 days of the start of the preparative regimen or infusion).

Question 165: Were cytogenetics tested (karyotyping or FISH)? *(at last evaluation)*

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Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate **No**.

Question 166: Were cytogenetics tested via FISH? *(at last evaluation)*

Specify if FISH studies were performed at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). If FISH studies were not performed at this time point, FISH sample was inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 167: Results of tests

Specify if FISH abnormalities were identified at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen).

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 168 – 171: Specify FISH abnormalities *(at last evaluation)*

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Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen) and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 172: Were cytogenetics tested via karyotyping? *(at last evaluation)*

Specify if karyotyping studies were performed at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). Report **Yes** even if there were no evaluable metaphase cells (these results will be specified below).

If karyotyping studies were not performed at this time point or it is unknown if performed, report **No**.

Question 173: Results of tests

Specify if abnormalities were detected by karyotype at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen).

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the Karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 174 – 177: Specify karyotype abnormalities *(at last evaluation)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

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If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen) and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 178 – 179: Specify any other positive molecular marker(s) identified *(check all that apply)*

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

Indicate if any other *positive* molecular markers, including variance of unknown significant markers, were detected at the last evaluation.

If a molecular marker was detected, but not listed as an option, select **Other** and specify the abnormality.

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If molecular markers were not detected at the last evaluation, the sample failed, testing was not completed or unknown if completed at the last evaluation report **None**.

Question 180: Did the recipient have central nervous system leukemia at any time prior to the start of the preparative regimen / infusion?

Central nervous system (CNS) involvement by leukemia may be detected via pathologic examination of cerebrospinal fluid or tumor tissue as well as by radiological examinations (e.g., MRI, PET/CT, MIBG, etc.).

Specify if the recipient had documented involvement of AML in the CNS at any time prior to the start of the preparative regimen (or infusion if no preparative regimen).

If all CNS testing was negative since the time of diagnosis, report **No**.

If testing for CNS involvement was not performed from the time of diagnosis to the time of infusion, report **Unknown**.

Question 181: What was the disease status? *(based on hematological test results) (at infusion)*

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. Refer to the ALL Response Criteria section for definitions of each response. For reporting purposes, consider complete remission with incomplete hematologic recovery (CRi) a complete remission (CR1, CR2, or CR3+).

If the recipient did not receive any treatment for AML from the time of diagnosis to the start of the preparative regimen (or infusion if no preparative regimen), report **No treatment**

Number of Induction Cycles

The intent of this question is to capture the number of induction cycles required to achieve the *first* CR (including CRi) the recipient's disease history, regardless of if there have been prior relapses or infusions.

Question 182: How many cycles of induction therapy were required to achieve CR? *(includes CRi)*

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Chemotherapy is initially given as induction therapy intended to bring the disease into remission. Recipients usually have one to two cycles of induction therapy. An example of a common induction therapy for precursor B-cell ALL in children with higher-risk prognostic indicators is a combination of vincristine, prednisone, an anthracycline, and L-asparaginase given over 4-6 weeks. Patients with a rapid response, defined as < 5% blasts within 7 to 14 days of starting induction, have improved outcomes.[1]

[1] Gaynon PS, Desai AA, Bostrom BC, et al. Early response to therapy and outcome in childhood acute lymphoblastic leukemia: a review. Cancer. 1997;80(9):1717-26.

The second phase of chemotherapy is known as consolidation therapy. The goal of consolidation therapy is to destroy any remaining leukemia cells and sustain remission. An example of a consolidation therapy for precursor B-cell ALL in children is daunorubicin and cytarabine; several studies support the use of consolidation therapy in ALL.

Maintenance therapy typically involves daily doses of mercaptopurine and weekly doses of methotrexate. Treatment continues for 2-3 years for most children with ALL. Treatment may also be administered for relapsed disease. Much like induction therapy, treatment for relapse is intended to bring the disease back into remission. Systemic therapeutic agents used to induce remission following relapse often differ from those used during initial induction, since the disease is considered high-risk with a poor prognosis and is often resistant to many of the agents used earlier in the disease course. Allogeneic HCT is often considered the only potential “cure” for relapsed disease, if the patient has not already been transplanted.

If the pre-infusion disease status is **CR1**, report the number of cycles of *induction therapy* that were required to achieve the first CR.

Question 183: Date CR first achieved

This question is intended to capture the date when the *first clinical / hematologic CR* was achieved.

Report the date when the first CR was achieved. This should be the earliest date all international working group criteria for CR were met. Report the date the sample was collected for pathologic evaluation (i.e., bone marrow biopsy) or blood / serum assessments (i.e., CBC, peripheral blood smear).

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If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, General Guidelines for Completing Forms.

Question 184: Date of most recent relapse

Enter the date of the most recent relapse prior to the start of the preparative regimen / infusion. If reporting a pathological evaluation (i.e., bone marrow) or blood / serum assessment (i.e., CBC, peripheral blood smear), enter the date the sample was collected.

If extramedullary disease was detected by radiographic examination (i.e.., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place.

If the physician determines cytogenetic or molecular relapse, enter the date the sample was collected for cytogenetic or molecular evaluation. If the physician determines evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, General Guidelines for Completing Forms.

Question 185: Specify method(s) that was used to assess measurable residual disease status *(check all that apply) (at infusion)*

Specify the method(s) how the minimal residual status was assessed at the last evaluation, approximately 30 days prior to the start of the preparative regimen / infusion. Select all that apply.

- **FISH**: A sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA. These probes are mixed with cells from the recipient's blood or bone marrow. A fluorescent "tag" is then used to visualize the binding of the probe to the diseased cells.
- **Karyotype**: A technique 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

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bands and reconfigurations can be seen. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease.

- **Flow cytometry**: A method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics. Its primary clinical purpose in the setting of leukemias is to quantify blasts in the peripheral blood or bone marrow, or to identify unique cell populations through immunophenotyping. Flow cytometry assessment may also be referred to as “MRD,” or minimal residual disease, testing.
- **PCR**: Polymerase chain reaction (PCR) amplification is a molecular assessment used to detect single specific disease markers. Testing for molecular markers is often performed using PCR based methods. Once a marker has been identified, this method can be repeated to detect minimal residual disease (MRD) in the recipient’s blood, marrow, or tissue.
- **NGS**: Next-generation sequencing (NGS), also known as massive parallel sequencing, is another molecular assessment which is used to determine the order of nucleotides in a genome.
- **ClonoSEQ**: A type of measurable residual disease testing, which identifies and quantifies the number of cancer cells.[1]

If testing for measurable residual status was not completed at the last evaluation, select **Not assessed**.

[1] clonoSEQ® by Adaptive Biotechnologies. (n.d.). ClonoSEQ. https://www.clonoseq.com/hcp-home/?gad_source=1&gclid=CjwKCAjwuMC2BhA7EiwAmJKRrCLoK5aZwMM5jAHZu3o3GBCYmIAK4Z0-OSyM9up8GkCWAw7-J1O9BRoCShYQAvD_BwE&utm_source=google&utm_medium=cpc&utm_campaign=hcp_priority&utm_medium=cpc&utm_campaign=hcp_priority

Question 186: Was measurable residual disease detected by FISH? *(at infusion)*

Indicate if measurable residual disease was detected by FISH at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if measurable residual disease was detected by FISH at the last evaluation.

Question 187: Was measurable residual disease detected by karyotyping assay? *(at infusion)*

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Indicate if measurable residual disease was detected by karyotype at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if measurable residual disease was detected by karyotype at the last evaluation.

Question 188: Was measurable residual disease detected by flow cytometry? *(at infusion)*

Indicate if measurable residual disease was detected by flow cytometry at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if minimal residual disease was detected by flow cytometry at the last evaluation.

Original vs Aberrant Phenotype

The original vs aberrant phenotype questions are currently disabled.

Questions 189 – 191: Which leukemia phenotype was used for detection? *(check all that apply) (at infusion)*

Specify which leukemia phenotype was used for detection. Select all that apply.

If the **Original leukemia immunophenotype** was used, specify the lower limit of detection, and then indicate if minimal residual disease was detected by flow cytometry at the last evaluation prior to the start of the preparative regimen / infusion.

If an **Aberrant phenotype** was used, specify the lower limit of, and then indicate if minimal residual disease was detected by flow cytometry at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if minimal residual disease was detected by flow cytometry at the last evaluation.

Question 192: Was measurable residual disease detected by PCR? *(at infusion)*

Indicate if measurable residual disease was detected by PCR at the last evaluation prior to the start of the preparative regimen / infusion.

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If the results are not clear, seek physician clarification to determine if measurable residual disease was detected by PCR at the last evaluation assay at the last evaluation prior to the start of the preparative regimen / infusion.

Question 193: Was minimal residual disease detected by NGS? *(at infusion)*

Indicate if minimal residual disease was detected by NGS at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if minimal residual disease was detected by NGS at the last evaluation assay at the last evaluation prior to the start of the preparative regimen / infusion.

Question 194: Was minimal residual disease detected by ClonoSEQ? *(at infusion)*

Indicate if minimal residual disease was detected by ClonoSEQ at the last evaluation prior to the start of the preparative regimen / infusion.

If the results are not clear, seek physician clarification to determine if minimal residual disease was detected by ClonoSEQ at the last evaluation assay at the last evaluation prior to the start of the preparative regimen / infusion.

Section Updates

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

Q195 – 301: Acute Leukemias of Mixed or Ambiguous Lineage

Question 1: Date of diagnosis of primary disease for infusion

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Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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 exact diagnosis date is not known, use the process described in General Instructions, Guidelines for Completing Forms

Question 195: Specify acute leukemias of mixed or ambiguous lineage

CIBMTR captures the classification of ambiguous lineage and other myeloid neoplasms based on the World Health Organization (WHO) 2022. Report the disease classification at diagnosis.

Report the most specific entity that applies to the recipient.

- **Acute undifferentiated leukemia** is a type of AML characterized by immature predominating cells that cannot be classified.
- Biphenotypic, bilineage, hybrid, or mixed leukemias have characteristics representative of both myeloid and lymphoid lineages.
- Mast cell leukemia is characterized by an increased number of tissue mast cells in the peripheral blood.

In some cases, disease specific cytogenetic and / or molecular abnormalities are not identified at the initial diagnosis but identified at some point prior to the infusion, report the most disease specific entity. Review the example below for further clarification:

- Example 1: A recipient diagnosed with mixed-phenotype acute leukemia had only a bone marrow biopsy and FISH testing for BCR-ABL performed at diagnosis. The bone marrow identified mixed-phenotype acute leukemia and FISH was negative for BCR-ABL. Induction began and additional molecular testing completed after starting treatment which identified KMT2A rearrangement. The disease classification should be reported as **Mixed phenotype acute leukemia with KMT2A rearrangement**.

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Subsequent Infusion and At Diagnosis Time Point
If this is a subsequent infusion for the same disease, the *At Diagnosis* time point is disable.

At Diagnosis Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes, use the following definition when reporting for the *at diagnosis* time point: Any testing performed closest to (before or after) the date of diagnosis (question 1) and prior to the start of any treatment for ALL.

Question 196: Were cytogenetics tested (conventional or FISH)? *(at diagnosis)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at diagnosis. If cytogenetic studies were obtained, select **Yes**. If no cytogenetic studies were obtained, or it is unknown if chromosome studies were performed, select **No** or **Unknown**, respectively.

Question 197: Were cytogenetics tested via FISH? *(at diagnosis)*

Specify if FISH studies were performed at diagnosis. If FISH studies were not performed at diagnosis or FISH samples were inadequate, report **No**. If it is not known if it was performed, report **Unknown**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 198: Results of tests

Specify if FISH abnormalities were identified at diagnosis.

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International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 199 – 202: Specify FISH abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at diagnosis and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 203: Were cytogenetics tested via karyotyping? *(at diagnosis)*

Specify if karyotyping studies were performed at diagnosis. Report **Yes** even if there were no evaluable metaphase cells / failed (these results will be specified below).

If karyotyping studies were not performed at diagnosis or it is unknown if performed, report **No** or **Unknown**, respectively.

Question 204: Results of tests

Specify if abnormalities were detected by karyotype at diagnosis.

If karyotyping failed, select **No evaluable metaphases**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

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Questions 205 – 208: Specify karyotype abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at diagnosis and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Questions 209 – 228: Specify molecular marker results *(at diagnosis)*

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

The molecular markers listed below are ELN AML markers and prognostic of leukemia. Due to the importance of these markers, it is necessary to know if the marker was positive, negative, or not assessed.

- ASXL1
- BCOR

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- BCR::ABL1
- CEBPA
- DDX41
- EZH2
- FLT3-ITD
- GATA2
- NPM1
- RUNX1
- SF3B1
- SRSF2
- STAG2
- TP53
- U2AF1
- ZRSR2

For each molecular marker, specify if the marker was **Positive** or **Negative** at diagnosis and answer and additional questions. If the molecular marker was not assessed at diagnosis, select **Not done**.

If CEBPA was **Positive**, specify the CEBPA variant mutation and allelic expression. If the variant mutation is not documented, report the mutation as **Unknown**. If the allelic expression is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

If FLT3-ITD was **Positive**, specify the allelic ratio, if known. If the allelic ratio is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

The allelic ratio data field is intended to capture the ratio of the FLT3-ITD mutation. This data field does not collect the allelic frequency, the allelic frequency is used to calculate the allelic ratio. The FLT-3 ITD allelic ratio (or signal ratio) compares the number of ITD-mutated alleles to the number of wild-type (normal) alleles. If the allele frequency was assessed, the ITD-mutated allele frequency will be documented on the molecular report; however, the wild-type allele frequency will need to be calculated. To determine the wild-type allele frequency, subtract the ITD-mutated allele frequency from 1 (or 100.0%). After determining the wild-type allele frequency, the allelic ratio can be

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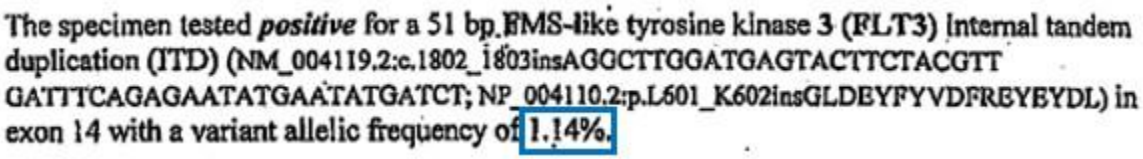
assessed. To calculate the allelic ratio, divide the mutant allele frequency by the wild-type (normal) allele frequency. Review example 2 below for more information:

- Example 2:


The specimen tested ***positive*** for a 51 bp FMS-like tyrosine kinase 3 (FLT3) internal tandem duplication (ITD) (NM_004119.2:c.1802_1803insAGGCTTGGATGAGTACTTCTACGTT GATTTCAGAGAATATGAATATGATCT; NP_004110.2:p.L601_K602insGLDEYFYVDFREYEYDL) in exon 14 with a variant allelic frequency of 1.14%.

  - ITD variant allele frequency: 1.14% (0.0114)
    - As documented in the molecular report
  - Wild-type allele frequency: 98.86% (0.9886)
    - Determined by subtraction 1.14% from 100.0%
  - FLT3-ITD allelic ratio: 0.0114 / 0.9886 = 0.0115

Report the FLT3-ITD allelic ratio as 0.0115

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 229 – 230: Specify any other positive molecular marker(s) identified *(check all that apply)*

Indicate if any other *positive* molecular markers (excluding the ELN AML molecular markers listed above), including variance of unknown significant markers, were detected at diagnosis.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality.

If molecular markers were not detected at diagnosis, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

In Between Diagnosis and Last Evaluation Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes,

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use the following definition when reporting for the *in between* time point: Any pre-infusion testing which cannot be reported as part of *at diagnosis* or *last evaluation*. For subsequent infusions, any testing performed after the prior infusion until the last evaluation for the current infusion should be reported here. For example, if relapse / progression occurred after the previous infusion but prior to Last Evaluation of the current infusion, report the relapse / progression abnormalities at the In Between timepoint.

Question 231: Were cytogenetics tested (karyotyping or FISH)? *(between diagnosis and last evaluation)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were performed between diagnosis and the last evaluation. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate **No**.

Question 232: Were cytogenetics tested via FISH? *(between diagnosis and last evaluation)*

Specify if FISH studies were performed between diagnosis and the last evaluation. If FISH studies were not performed at this time point, FISH sample was inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 233: Results of tests

Specify if FISH abnormalities were identified between diagnosis and the last evaluation.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH

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The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 234 – 237: Specify FISH abnormalities *(between diagnosis and last evaluation)*

Report the ISCN compatible string, if applicable. If reporting the ISCN compatible string and multiple FISH assessments were completed between diagnosis and the last evaluation, add a separate instance of the *ISCN compatible string* to report each FISH ISCN compatible string.

Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH between diagnosis and the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 238: Were cytogenetics tested via karyotyping? *(between diagnosis and last evaluation)*

Specify if karyotyping studies were performed between diagnosis and the last evaluation. Report **Yes** even if there were no evaluable metaphase cells (these results will be specified below).

If karyotyping studies were not performed at this time point or it is unknown if performed, report **No**.

Question 239: Results of tests

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Specify if abnormalities were detected by karyotype between diagnosis and the last evaluation.

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the Karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 240 – 243: Specify karyotype abnormalities *(between diagnosis and last evaluation)*

Report the ISCN compatible string, if applicable. If reporting the ISCN compatible string and multiple karyotype studies were completed between diagnosis and the last evaluation, add a separate instance of the *ISCN compatible string* to report each karyotype ISCN compatible string.

Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype between diagnosis and the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Questions 244 – 263: Specify molecular marker results *(between diagnosis and last evaluation)*

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Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

The molecular markers listed below are ELN AML markers and prognostic of leukemia. Due to the importance of these markers, it is necessary to know if the marker was positive, negative, or not assessed.

- ASXL1
- BCOR
- BCR::ABL1
- CEBPA
- DDX41
- EZH2
- FLT3-ITD
- GATA2
- NPM1
- RUNX1
- SF3B1
- SRSF2
- STAG2
- TP53
- U2AF1
- ZRSR2

For each molecular marker, specify if the marker was **Positive** or **Negative** between diagnosis and the last evaluation and answer additional questions. If the molecular marker was not assessed between diagnosis and the last evaluation, select **Not done**.

If CEBPA was **Positive**, specify the CEBPA variant mutation and allelic expression. If the variant mutation is not documented, report the mutation as **Unknown**. If the allelic

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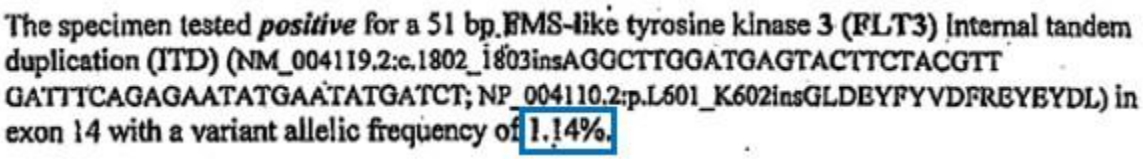
expression is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

If FLT3-ITD was **Positive**, specify the allelic ratio, if known. If the allelic ratio is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

The allelic ratio data field is intended to capture the ratio of the FLT3-ITD mutation. This data field does not collect the allelic frequency, the allelic frequency is used to calculate the allelic ratio. The FLT-3 ITD allelic ratio (or signal ratio) compares the number of ITD-mutated alleles to the number of wild-type (normal) alleles. If the allele frequency was assessed, the ITD-mutated allele frequency will be documented on the molecular report; however, the wild-type allele frequency will need to be calculated. To determine the wild-type allele frequency, subtract the ITD-mutated allele frequency from 1 (or 100.0%). After determining the wild-type allele frequency, the allelic ratio can be assessed. To calculate the allelic ratio, divide the mutant allele frequency by the wild-type (normal) allele frequency. Review example 3 below for more information:

- Example 3:


The specimen tested ***positive*** for a 51 bp FMS-like tyrosine kinase 3 (FLT3) internal tandem duplication (ITD) (NM_004119.2:c.1802_1803insAGGCTTGGATGAGTACTTCTACGTT GATTTCAGAGAATATGAATATGATCT; NP_004110.2:p.L601_K602insGLDEYFYVDFREYEYDL) in exon 14 with a variant allelic frequency of 1.14%.

  - ITD variant allele frequency: 1.14% (0.0114)
    - As documented in the molecular report
  - Wild-type allele frequency: 98.86% (0.9886)
    - Determined by subtraction 1.14% from 100.0%
  - FLT3-ITD allelic ratio: 0.0114 / 0.9886 = 0.0115

  Report the FLT3-ITD allelic ratio as 0.0115

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3℠, refer to the Training Guide.

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Questions 264 – 265: Specify any other positive molecular marker(s) identified *(check all that apply)*

Indicate if any other *positive* molecular markers (excluding the ELN AML molecular markers listed above), including variance of unknown significant markers, were detected between diagnosis and the last evaluation.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality.

If molecular markers were not detected between diagnosis and the last evaluation, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

Last Evaluation Assessments
Assessments performed *at diagnosis*, *last evaluation* and *in between* questions ask about testing performed at different time points prior to infusion. For reporting purposes, use the following definition when reporting for the *last evaluation* time point: Testing performed during the recipient's work-up for infusion (generally within 30 days of the start of the preparative regimen or infusion).

Question 266: Were cytogenetics tested (karyotyping or FISH)? *(at last evaluation)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen. If cytogenetic studies were not obtained at this time point or it is not known whether chromosome studies were performed, indicate **No**.

Question 267: Were cytogenetics tested via FISH? *(at last evaluation)*

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Specify if FISH studies were performed at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). If FISH studies were not performed at this time point, FISH sample was inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 268: Results of tests

Specify if FISH abnormalities were identified at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen).

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 269 – 272: Specify FISH abnormalities *(at last evaluation)*

Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen) and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report “see attachment” and attach the final report(s) for any other abnormalities detected.

Question 273: Were cytogenetics tested via karyotyping? *(at last evaluation)*

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Specify if karyotyping studies were performed at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). Report **Yes** even if there were no evaluable metaphase cells (these results will be specified below).

If karyotyping studies were not performed at this time point or it is unknown if performed, report **No**.

Question 274: Results of tests

Specify if abnormalities were detected by karyotype at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen).

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the Karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 275 – 278: Specify karyotype abnormalities *(at last evaluation)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen) and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402)

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form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Questions 279 – 298: Specify molecular marker results *(at last evaluation)*

Molecular markers for disease refer to specific genetic sequences which are believed to be associated with the recipient's primary disease. Testing for these sequences is often performed using PCR based methods. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

The molecular markers listed below are ELN AML markers and prognostic of leukemia. Due to the importance of these markers, it is necessary to know if the marker was positive, negative, or not assessed.

- ASXL1
- BCOR
- BCR::ABL1
- CEBPA
- DDX41
- EZH2
- FLT3-ITD
- GATA2
- NPM1
- RUNX1
- SF3B1
- SRSF2
- STAG2
- TP53
- U2AF1
- ZRSR2

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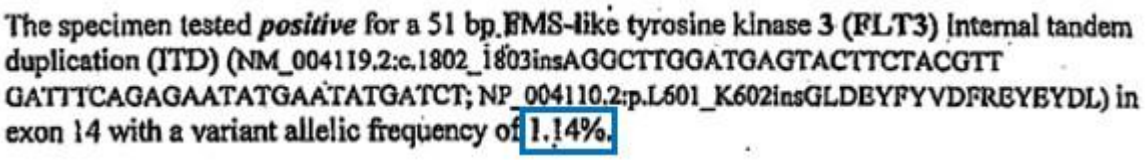
For each molecular marker, specify if the marker was **Positive** or **Negative** at the last evaluation and answer additional questions. If the molecular marker was not assessed at the last evaluation, select **Not done**.

If CEBPA was **Positive**, specify the CEBPA variant mutation and allelic expression. If the variant mutation is not documented, report the mutation as **Unknown**. If the allelic expression is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

If FLT3-ITD was **Positive**, specify the allelic ratio, if known. If the allelic ratio is not documented, confirm with the lab if this information can be determined prior to reporting **Unknown**.

The allelic ratio data field is intended to capture the ratio of the FLT3-ITD mutation. This data field does not collect the allelic frequency, the allelic frequency is used to calculate the allelic ratio. The FLT-3 ITD allelic ratio (or signal ratio) compares the number of ITD-mutated alleles to the number of wild-type (normal) alleles. If the allele frequency was assessed, the ITD-mutated allele frequency will be documented on the molecular report; however, the wild-type allele frequency will need to be calculated. To determine the wild-type allele frequency, subtract the ITD-mutated allele frequency from 1 (or 100.0%). After determining the wild-type allele frequency, the allelic ratio can be assessed. To calculate the allelic ratio, divide the mutant allele frequency by the wild-type (normal) allele frequency. Review example 4 below for more information:

- Example 4:


The specimen tested ***positive*** for a 51 bp FMS-like tyrosine kinase 3 (FLT3) internal tandem duplication (ITD) (NM_004119.2:c.1802_1803insAGGCTTGGATGAGTACTTCTACGTT GATTTCAGAGAATATGAATATGATCT; NP_004110.2:p.L601_K602insGLDEYFYVDFREYEYDL) in exon 14 with a variant allelic frequency of 1.14%.

  - ITD variant allele frequency: 1.14% (0.0114)
    - As documented in the molecular report
  - Wild-type allele frequency: 98.86% (0.9886)
    - Determined by subtraction 1.14% from 100.0%
  - FLT3-ITD allelic ratio: 0.0114 / 0.9886 = 0.0115

Report the FLT3-ITD allelic ratio as 0.0115

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Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 299 – 300: Specify any other positive molecular marker(s) identified *(check all that apply)*

Indicate if any other *positive* molecular markers (excluding the ELN AML molecular markers listed above), including variance of unknown significant markers, were detected at the last evaluation.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality.

If molecular markers were not detected at the last evaluation, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

Question 301: What was the disease status? *(based on hematological test results) (at infusion)*

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. Refer to table 1 below for definitions of each response.

Table 1. Disease Status of Acute Leukemia

Disease Status	Definition
Primary Induction Failure (PIF)	The recipient received treatment for acute leukemia **but never achieved complete remission at any time**. PIF is not limited by the number of unsuccessful treatments; this disease status only applies to recipients who have *never been in complete remission.*
Complete Remission (CR)	Hematologic complete remission is defined as meeting **all** of the following response criteria for at least four weeks. • < 5% blasts in the bone marrow • Normal maturation of all cellular components in the bone marrow

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	• No extramedullary disease (e.g., CNS, soft tissue disease) • Neutrophils ≥ 1,000/µL • Platelets ≥ 100,000/µL • Transfusion independent In some cases, there may not be a four-week interval between completion of therapy and the pre-transplant disease assessment; in this case, CR should still be reported as the status at transplant, since it represents the "best assessment" prior to infusion. This is an exception to the criteria that CR be durable beyond four weeks; the pre-transplant disease status should not be changed based on early relapse or disease assessment post-transplant. Include recipients with persistent cytogenetic or molecular abnormalities who meet the above CR criteria for hematologic CR. Include recipients meeting the above CR criteria regardless of how many courses of therapy were required to achieve CR. The number of this complete remission can be determined by using the following guidelines: • 1st CR: no prior relapse • 2nd CR: one prior relapse • 3rd or higher: two or more prior relapses
Relapse (REL)	Relapse is defined as the recurrence of disease after CR, meeting the following criteria: • ≥ 5% blasts in the marrow or peripheral blood • Extramedullary disease • Reappearance of cytogenetic and/or molecular abnormalities associated with diagnosis that, in the judgment of a physician, are at a level representing relapse • Disease presence determined by a physician upon clinical assessment The number of this relapse can be determined by using the following guidelines: • 1st relapse: one prior CR • 2nd relapse: two prior CRs • 3rd or higher: three or more CRs Do not include a partial response (PR) when determining

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	number of relapse. Recipients who achieve a PR to treatment should be classified as either PIF or relapse; PR in acute leukemia is generally of short duration and is unlikely to predict clinical benefit.
No Treatment	The recipient was diagnosed with acute leukemia and never received therapeutic agents; include recipients who have received only supportive therapy, including growth factors and/or blood transfusions.

Section Updates

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

Q302 – 308: Chronic Myelogenous Leukemia

Chronic myelogenous leukemia (CML) is a slow-progressing cancer of the myeloid white blood cells. It is characterized by increased proliferation of immature white blood cells (granulocytes) with damaged DNA, or blasts, which accumulate in the blood and bone marrow. Normal blasts develop into white blood cells that fight infection. The symptoms of CML are caused by the replacement of normal bone marrow with leukemic cells, resulting in fewer red blood cells, platelets, and normal white blood cells.

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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.

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

Question 302: Was therapy given prior to this infusion?

Specify if therapy to treat CML was given prior to the current infusion. If treatment was not given prior to the current infusion or it is unknown, report **No**. If this is a subsequent infusion and treatment was not given prior to the subsequent infusion (i.e., only given prior to the previous infusion), report **No**.

Questions 303 – 304: Specify the therapy for CML *(check all that apply)*

Select all the therapy given to treat CML prior to the current infusion.

If the recipient's treatment consisted of a combination of chemotherapeutic agents, check the **Combination chemotherapy** box **and** each drug included in the combination from the list provided.

If a drug was given but not listed as an option on the form, select **Other therapy** and specify.

- Example 1: If the recipient received a combination of interferon and cytarabine, check all of the following: **Combination chemotherapy, Interferon-α**, and **Other therapy** – specify 'cytarabine'.

Question 305: What was the disease status?

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. Refer to the CML Response Criteria section for definitions of each response.

Question 306: Specify level of response

If the recipient's best response to therapy is **Complete hematologic remission (CHR)** or **Chronic phase (CP)**, specify the cytogenetic / molecular response. Refer to table 1 below for definitions of cytogenetic and molecular responses.

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The responses below are listed from most favorable (complete molecular remission) to least favorable (no cytogenetic response). Report the most favorable response achieved.

- Example 2: If a recipient has achieved a major molecular remission by PCR testing as well as a complete cytogenetic response by karyotyping / FISH, report the response as **Major molecular remission**.

Table 1. Definitions of Cytogenetic and Molecular Responses to Therapy

Response	Definition
Complete molecular remission *(most favorable)*	0% BCR / ABL transcripts detected in peripheral blood or bone marrow
Major molecular remission	> 0 – 0.1% BCR / ABL transcripts detected in peripheral blood or bone marrow
Complete cytogenetic response	0% Ph+ cells detected in bone marrow
Partial cytogenetic response	> 0 – 35% Ph+ cells in bone marrow
Minor cytogenetic response	> 35 – 65% Ph+ cells in bone marrow
Minimal cytogenetic response	> 65 – 95% Ph+ cells in bone marrow
No cytogenetic response *(least favorable)*	> 95% Ph+ cells in bone marrow.

Definitions taken from Hughes, T. P., Ross, D. M. & Melo, J. V. Handbook of chronic myeloid leukemia. (Adis, 2014).

Question 307: Specify blast phase phenotype

Assessments performed on the bone marrow or peripheral blood may be used to determine the blast phenotype at the time of the pre-infusion disease status.

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Indicate the phenotype detected prior to infusion. If phenotype cannot be determined, seek clinician clarification prior to report **Unknown**.

Question 308: Number

Indicate the number of times the recipient has been in the disease phase reported above.

Section Updates

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

Q309 – 378: Myelodysplastic Diseases

Transformation to AML
If the recipient is receiving an infusion for AML that has transformed from MDS, the primary disease for infusion must be reported as **AML**. Disease Classification questions must be completed for both AML and MDS.

The **myelodysplastic syndromes** (**MDS**) are a group of clonal hematopoietic stem cell diseases characterized by cytopenia(s), dysplasia (abnormal growth or development leading to an alteration in size, shape, and organization of the cell) in one or more of the major myeloid cell lines (WBC, RBC, and/or platelets), ineffective hematopoiesis, and an increased risk of developing acute myelogenous leukemia (AML). MDS occurs primarily in older adults, with a median age of 70 years. The majority of recipients present with symptoms related to cytopenias. Most recipients present with anemia requiring RBC transfusions.

Primary or *de novo* MDS occurs without a known history of chemotherapy or radiation exposure. Some inherited hematologic disorders, such as Fanconi anemia, dyskeratosis

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congenita, Shwachman-Diamond syndrome, and Diamond-Blackfan syndrome are associated with an increased risk of MDS.

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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's MDS progressed to from a lower grade MDS to a higher grade MDS, report the diagnosis date of the original MDS diagnosis (i.e., the lower MDS grade). The transformation date (i.e., diagnosis of the higher grade) is captured below.

If the recipient's MDS transformed to AML prior to HCT, report the diagnosis date of AML and ensure the primary disease for infusion is reported as **AML**. Ensure the AML section of the Disease Classification Form is completed appropriately. The MDS diagnosis date is captured below.

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

Atypical CML
Atypical CML is no longer reported as **Other leukemia** and should be reported as **MDS** as of October 2024. If the primary disease for infusion is 'atypical CML' report the disease classification as **Myelodysplastic / myeloproliferative neoplasm with neutrophilia**.

Question 309: What was the MDS subtype at diagnosis?

CIBMTR captures the MDS classification based on the World Health Organization (2022) WHO classification. Indicate the MDS subtype at diagnosis.

Report the most specific entity that applies to the recipient. For example, if the recipient was classified using both defining genetic abnormalities and differentiation, the defining genetic abnormality classification should be reported for classification purposes.

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Additionally, if the recipient meets the criteria for MDS-5q, MDS-SF3B1, and MDS-biTP53 report the disease subtype as **MDS-biTP53**.

In some cases, disease specific cytogenetic and / or molecular abnormalities are not identified at the initial diagnosis but identified at some point prior to the infusion, report the most disease specific entity. Review the example below for further clarification:

- Example 1: A recipient diagnosed with MDS had only a bone marrow biopsy and karyotyping performed at diagnosis. The bone marrow identified MDS with low blasts and karyotyping was normal. Induction began and additional FISH testing for deletion 5q was completed after starting treatment which identified deletion 5q. The disease classification should be reported as **Myelodysplastic syndrome with low blasts and isolated 5q deletion**.

Subsequent Infusion and Therapy Related and Predisposing Conditions
If this is a subsequent infusion for the same disease, the *Was the disease therapy related* and *Did the recipient have predisposing condition* questions are disabled.

Question 310: Was the disease (MDS) therapy related?

Agents such as radiation or systemic therapy used to treat other diseases (e.g., Hodgkin lymphoma, non- Hodgkin lymphoma, or breast cancer) can damage the marrow and lead to a secondary malignancy, such as MDS.

Specify if the diagnosis of MDS is therapy related. If the diagnosis of MDS is not therapy-related or it is not known, select **No** or **Unknown**, respectively. If documentation is not clear if MDS was therapy related, seek clinician clarification.

Do not report **Yes** if the recipient developed MDS after an environmental exposure (e.g., exposure to benzene).

ET or PCV to MDS Transformation
In the rare event MDS transformed from ET or PCV, report **Yes** there was a predisposing condition and specify the condition as **Essential thrombocythemia** or **Polycythemia vera**. Do not report there was a disease transformation below.

Question 311: Did the recipient have a predisposing condition?

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A predisposing condition contributes to the susceptibility of developing MDS. Therefore, diagnosis of the condition increases the likelihood that the recipient will develop MDS. If the recipient has a documented history of predisposing condition, select **Yes**. If there is no history of predisposing condition or if predisposition is unknown, indicate **No** or **Unknown**.

Questions 312 – 313: Specify MDS predisposing condition

Specify the recipient's predisposing condition.

If the recipient had a predisposing condition not listed above, select **Other condition** and specify the condition.

A list of entities that would fall into the **Other condition** category include: ETV6-related familial thrombocytopenia, ANKRD26-related familial thrombocytopenia, SRP72-related familial aplastic anemia/MDS, MBD4-related familial leukemia, Bloom Syndrome, Noonan Syndrome, Neurofibromatosis, Downs Syndrome, ATG2B/GSKIP duplication (chromosome 14q32.2), MECOM-associated syndrome.

Subsequent Infusions and Assessments At Diagnosis
If this is a subsequent infusion for the same disease, the assessments reported at diagnosis are disabled.

Laboratory Studies at Diagnosis of MDS
Report laboratory results closest to the diagnosis date and prior to the start of first treatment of the primary disease for which the infusion is being performed. If the recipient's MDS transformed, report the studies from the original diagnosis.

Reporting Blasts Percentage
If the bone marrow pathology report states a range for blasts, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
If the report indicates "sheets of blasts" or "packed marrow," report 100%.
If the report states > n% blasts, enter (n+1)% on the form. For example, if the laboratory report indicates > 90% blasts, report 91%.
If the report states < n% blasts, enter (n-1)% on the form. For example, if the laboratory report indicates < 5% blasts, report 4%.

Questions 314 – 315: Blasts in bone marrow *(at diagnosis)*

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Indicate whether the percentage of blasts in the bone marrow was known at diagnosis. If **Known**, report the percentage documented on the laboratory report.

If the lab was assessed multiple times prior to starting treatment, report the values closest to the diagnosis date.

If multiple methods were used to detect the percentage of blasts in the bone marrow, the aspirate differential is the preferred method; followed by flow cytometry and IHC (immunohistochemical staining).

Questions 316 – 324: Complete blood count (CBC) results available *(check all that apply) (at diagnosis)*

These questions are intended to capture the laboratory studies performed at the initial diagnosis of MPN. Report the date of the CBC completed closest to the diagnosis date and select all lab values assessed on the reported date. All values must reflect testing performed prior to the start of the first treatment of the primary disease for infusion. If the recipient's MDS transformed, report the studies from the original diagnosis. If labs were assessed multiple times prior to starting treatment, report the values closest to the diagnosis date.

- **WBC**: The white blood cell count is a value that represents all of the white blood cells in the blood. If the count is too high or too low, the ability to fight infection may be impaired. If known, specify the value and units of measurement as documented on the lab report.
- **Neutrophils**: Neutrophils are a subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage or an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. Neutrophils are also known as polymorphonuclear leukocytes (PMNs). If known, specify the percentage as documented on the lab report.
- **Blasts in blood**: Blasts are not typically found in the peripheral blood; however, can appear for various reasons, including infection, blood cancer, or blood disorder. If known, report the percentage of blasts detected in the blood.
    - If a differential was performed and the percentage of plasma cells are not listed, report **0%**.
- **Hemoglobin**: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered "anemia" and

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blood transfusions, or growth factors may be required to increase the hemoglobin level. If known, specify the value and units of measurement as documented on the lab report. Additionally, indicate if red blood cells were transfused ≤ 30 days prior to the CBC date reported above.

Transfusions temporarily increase the red blood cell count, and it is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

- **Platelets**: Platelets are formed elements within the blood that help with coagulation. A low platelet count, called thrombocytopenia, may lead to easy bleeding or bruising. Thrombocytopenia may require platelet transfusions. If known, specify the value and unites of measurement as documented on the lab report. Additionally, indicate if platelets were transfused ≤ seven days prior to the CBC date reported above.

  Transfusions temporarily increase the platelet count, and it is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

If a CBC was not completed at diagnosis or unknown if completed, select **None**.

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

Question 325: Were cytogenetics tested (karyotyping or FISH)? *(at diagnosis)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at diagnosis. If cytogenetic studies were obtained, select **Yes**. If no cytogenetic studies were obtained, or it is unknown if chromosome studies were performed, select **No** or **Unknown**, respectively.

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Question 326: Were cytogenetics tested via FISH? *(at diagnosis)*

Specify if FISH studies were performed at diagnosis. If FISH studies were not performed at diagnosis or FISH samples were inadequate, report **No**. If it is not known if it was performed, report **Unknown**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 327: Sample source

The cytogenetic sample source is important for MDS research. Indicate if the sample was from **Bone marrow** or from **Blood**. If FISH studies were performed on multiple samples at diagnosis, the bone marrow results are the preferred sample source to report.

Question 328: Results of tests

Specify if FISH abnormalities were detected at diagnosis.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 329 – 332: Specify FISH abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at diagnosis and select all abnormalities detected.

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If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 333: Were cytogenetics tested via karyotyping? *(at diagnosis)*

Specify if karyotyping studies were performed at diagnosis. Report **Yes** even if there were no evaluable metaphase cells / failed (these results will be specified below).

If karyotyping studies were not performed at diagnosis or it is unknown if performed, report **No** or **Unknown**, respectively.

Question 334: Sample source

The cytogenetic sample source is important for MDS research. Indicate if the sample was from **Bone marrow** or from **Blood**. If karyotype analyses were performed on multiple samples at diagnosis, the bone marrow results are the preferred sample source to report.

Question 335: Results of test

Specify if abnormalities were detected by karyotype at diagnosis.

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Question 336 – 339: Specify karyotype abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at diagnosis and select all abnormalities detected.

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If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Reporting Multiple Positive Molecular Markers
Complete the *Specify positive molecular marker(s) identified* questions if multiple molecular markers were detected at diagnosis by adding an additional instance in FormsNet3SM.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Disease Classification (2402) form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Disease Classification (2402) form.

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 340 – 343: Specify positive molecular marker(s) identified *(at diagnosis)*

Testing for molecular markers is often performed by using PCR based methods to assess specific genetic sequences. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

Specify all positive molecular markers detected at diagnosis and the amino acid change, if known. If molecular markers were not detected at diagnosis, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

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If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality, along with the amino acid change, if known.

Transformation to AML
If the recipient is being transplanted for AML that has transformed from MDS, the primary disease for infusion must be reported as **AML**. Disease Classification questions must be completed for both AML and MDS.

Question 344: Did the recipient progress or transform to a different MDS subtype or AML between diagnosis and the start of the preparative regimen / infusion?

Approximately one third of MDS cases transform into AML, signifying a poorer prognosis. Progression to AML is defined by an increase in blood or bone marrow blasts ≥ 20%.

MDS subtypes may also transform / progress from one into another. A progression from one subtype of MDS to another indicates that the number of cytopenias, number of blasts, and/or morphology of marrow sufficiently qualified them for a higher grade (i.e., more severe) MDS.

- Example 2: At diagnosis, the disease was classified as MDS, with low blasts (MDS-LB) and the bone marrow blast count increased to 8% during treatment. This is considered a progression and would be classified as MDS with increased blasts (MDS-IB1).

Specify if the recipient's disease progressed to AML or transformed into a different MDS subtype between diagnosis and the start of the preparative regimen / infusion. If a transformation or progression did not occur or it is unknown, select **No**.

Do not report a progression / transformation if the recipient's assessments after diagnosis show that they qualify for a lower grade (i.e., less severe MDS).

- Example 3: A recipient is diagnosed with MDS with increased blasts (MDS-IB2) and assessments show that they meet the criteria for MDS with increased blasts (MDS-IB1) as a response to treatment would not qualify as progression or transformation. In this example, the disease is lower grade (i.e., less severe), rather than a higher grade (i.e., more severe) so it should not be reported as

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progression / transformation. See the table below for guidance in determining the severity of MDS progressions and transformations.

Table 1. Grade of MDS Progression/Transformations

Lower Grade	>>>>>>	>>>>>>	>>>>>>	Higher Grade
MDS-LB	?	MDS-IB1	MDS-IB2	AML
Childhood MDS with low blasts, hypocellular or Childhood MDS with low blasts, not otherwise specified	Childhood MDS with increased blasts			AML
JMML/CMML	—	—	—	AML

Indicate if the recipient's disease progressed to AML or transformed from one MDS subtype to another. If the recipient's disease transformed or progressed, select **Yes**. If there was no documented transformation or progression, select **No**.

Question 345: Specify the MDS subtype or AML after transformation

Indicate the recipient's current MDS subtype after transformation. If the recipient experienced more than one transformation after diagnosis, report the most recent subtype.

If the disease progressed to **AML**, report the date of MDS diagnosis. If MDS progresses to AML and the recipient is on the CRF track, the AML Pre-Infusion (2010) form will also come due.

For all other progressions or transformations, continue with to specify the date of the most recent transformation.

Question 346: Specify the date of the most recent transformation

Report the date of assessment that determined the most recent disease transformation (i.e., if there were multiple transformations, report the most recent). Report the date of the pathological evaluation (i.e., bone marrow) or blood / serum assessment (i.e., CBC,

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peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 347: Date of MDS Diagnosis

If MDS transformed to AML prior to infusion, report the initial diagnosis date of MDS. If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Ensure the AML diagnosis date has been reported as the diagnosis date of the primary disease for infusion and AML is reported as the primary disease for infusion. The AML section of the Disease Classification (24020 form must be completed appropriately.

Laboratory Studies at Last Evaluation
Report the most recent laboratory values prior to the start of the preparative regimen.

Reporting Blasts Percentage
If the bone marrow pathology report states a range for blasts, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
If the report indicates “sheets of blasts” or “packed marrow,” report 100%.
If the report states > n% blasts, enter (n+1)% on the form. For example, if the laboratory report indicates > 90% blasts, report 91%.
If the report states < n% blasts, enter (n-1)% on the form. For example, if the laboratory report indicates < 5% blasts, report 4%.

Questions 348 – 349: Blasts in bone marrow *(at last evaluation)*

Indicate whether the percentage of blasts in the bone marrow was known at diagnosis. If **Known**, report the percentage documented on the laboratory report.

If the lab was assessed multiple times, report the most recent values prior to the preparative regimen / infusion. Laboratory values obtained on the first date of the preparative regimen / lymphodepleting therapy may be reported as long as the sample was collected before any administration of systemic therapy or radiation.

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Questions 350 – 356: Complete blood count (CBC) results available *(check all that apply) (at last evaluation)*

These questions are intended to capture the laboratory studies performed at the evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). Report the date of the CBC completed at the last evaluation and select all lab values assessed on the reported date. If labs were assessed multiple times prior to the preparative regimen / infusion, report the most recent lab.

Laboratory values obtained on the first date of the preparative regimen / lymphodepleting therapy may be reported as long as the sample was collected before any administration of systemic therapy or radiation.

- **WBC**: The white blood cell count is a value that represents all of the white blood cells in the blood. If the count is too high or too low, the ability to fight infection may be impaired. If known, specify the value and units of measurement as documented on the lab report.
- **Neutrophils**: Neutrophils are a subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage or an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. Neutrophils are also known as polymorphonuclear leukocytes (PMNs). If known, specify the percentage as documented on the lab report.
- **Blasts in blood**: Blasts are not typically found in the peripheral blood; however, can appear for various reasons, including infection, blood cancer, or blood disorder. If known, report the percentage of blasts detected in the blood.
    - If a differential was performed and the percentage of plasma cells are not listed, report **0%**.
- **Hemoglobin**: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered “anemia” and blood transfusions, or growth factors may be required to increase the hemoglobin level. If known, specify the value and units of measurement as documented on the lab report. Additionally, indicate if red blood cells were transfused ≤ 30 days prior to the CBC date reported above.

  Transfusions temporarily increase the red blood cell count, and it is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

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If a CBC was not completed at diagnosis or unknown if completed, select **None**.

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

Question 357: Were cytogenetics tested (karyotyping or FISH)? *(at last evaluation)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). If cytogenetic studies were obtained, select **Yes**. If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select **No**.

Question 358: Were cytogenetics tested via FISH? *(at last evaluation)*

Specify if FISH studies were performed at last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). If FISH studies were not performed at this time point, FISH sample was inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 359: Sample source

Indicate if the sample was from **Bone marrow** or from **Blood**. If FISH studies were performed on multiple samples at the last evaluation prior to the start of the preparative regimen / infusion, the bone marrow results are the preferred sample source to report.

Question 360: Results of tests

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Specify if FISH abnormalities were detected at the last evaluation.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 361 – 364: Specify FISH abnormalities *(at last evaluation)*

Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 365: Were cytogenetics tested via karyotyping? *(at last evaluation)*

Specify if karyotyping studies were performed at the last evaluation prior to the preparative regimen / infusion. Report **Yes** even if there were no evaluable metaphase cells (these results will be specified below).

If karyotyping studies were not performed at this time point or it is unknown if performed, report **No**.

Question 366: Sample source

The cytogenetic sample source is important for MPN research. Indicate if the sample was from **Bone marrow** or from **Blood**. If karyotyping analyses were performed on multiple samples at the last evaluation prior to the start of the preparative regimen / infusion, the bone marrow results are the preferred sample source to report

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Question 367: Results of tests

Specify if abnormalities were detected by karyotype at the last evaluation.

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the Karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 368 – 371: Specify karyotype abnormalities *(at last evaluation)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Reporting Multiple Positive Molecular Markers
Complete the *Specify positive molecular marker(s) identified* questions if multiple molecular markers were detected at the last evaluation by adding an additional instance in FormsNet3^{SM}.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Pre-TED Disease Classification (2402) Form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Pre-TED Disease Classification (2402) Form.

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Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 372 – 375: Specify positive molecular marker(s) identified *(at last evaluation)*

Testing for molecular markers is often performed by using PCR based methods to assess specific genetic sequences. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

Specify all positive molecular markers detected at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen and the amino acid change, if known. If molecular markers were not detected at this time point, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality, along with the amino acid change, if known.

Question 376: What was the disease status? *(at infusion)*

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. Refer to the MDS Response Criteria section for definitions of each disease response based on clinical / hematologic assessments.

Report the disease status prior to the start of the preparative regimen (or infusion if no preparative regimen).

Question 377: Specify the cell line examined to determine HI status *(check all that apply)*

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Indicate the cell line examined to determine hematologic improvement. To determine the cell line, review the Hematologic Improvement criteria listed in the MDS Response Criteria section.

Transfusion Dependence Status
If the transfusion status is between **Non-transfused** (0 RBCs in 16 weeks) and **Low-transfusion burden** (3 – 7 RBCs in 16 weeks in at least 2 transfusion episodes; maximum of 3 in 8 weeks), report the status as **Non-transfused**.

Question 378: Specify transfusion dependence *(at infusion)*

If the recipient's pre-infusion disease status included **Hematologic improvement – Erythroid (HI-E)**, indicate the transfusion dependence at the time of determining disease status at last evaluation prior to start of the preparative regimen / infusion.

Select **Non-transfused (NTD)** if the recipient was without RBC transfusions as supportive care for the disease within a period of 16 weeks prior to the start of the preparative regimen / infusion.

Select **Low-transfusion burden (LTB)** if the recipient had 3-7 RBC transfusions within a period of 16 weeks in at least 2 transfusion episodes with a maximum of 3 RBC transfusions in 8 weeks prior to the start of the preparative regimen / infusion.

Section Updates

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

Q379 – 479: Myeloproliferative Diseases

Transformation to AML

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If the recipient is receiving an infusion for AML that has transformed to MPN, the primary disease for infusion must be reported as **AML**. Disease Classification questions will be completed for both AML and MPN.

Transformation to Myelofibrosis
Report the disease at diagnosis as **Essential thrombocytopenia** or **Polycythemia vera (PCV)** for recipients who receive an infusion for post-essential thrombocythemia myelofibrosis (post-ET MF) or post-polycythemia myelofibrosis (post-PCV MF) and report **Yes** there was a disease progression or transformation.

Myeloproliferative Neoplasms (**MPN**) are characterized by the overproduction of blood cells (red blood cells, white blood cells, and/or platelets) or collagen in the bone marrow. Often the MPN will be identified because of a blood test for another condition, as some recipients are asymptomatic. Common symptoms found in the array of myeloproliferative disorders include fatigue and the enlargement of the spleen (splenomegaly).

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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's MPN progressed to from a lower grade MPN to a higher grade MPN, report the diagnosis date of the original MPN diagnosis (i.e., the lower MPN grade). The transformation date (i.e., diagnosis of the higher grade) is captured below.

If the recipient's MPN transformed to AML prior to infusion, report diagnosis date of AML and ensure the primary disease for infusion is reported as AML.
The AML section of the Disease Classification (2402) form should be completed appropriately. The MPN diagnosis date is captured below.

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

Question 379: What was the MPN subtype at diagnosis?

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CIBMTR captures the MPN classification based on the World Health Organization (WHO) 2022 classification. Indicate the MPN subtype at diagnosis.

Question 380: Specify systemic mastocytosis

Specify the systemic mastocytosis sub-type / variant.

Systemic Mastocytosis Diagnostic Criteria
The diagnosis of systemic mastocytosis can be made when the major criterion and at least 1 minor criterion are present, or when ≥ 3 minor criteria are present.

- Major criterion
  - Multifocal dense infiltrates of mast cells (≥ 15 mast cells in aggregates) detected in sections of bone marrow and/or other extracutaneous organs(s).
- Minor criteria
  - In biopsy sections of bone marrow or other extracutaneous organs, >25% of the mast cells in the infiltrate are spindle-shaped or have atypical morphology; or >25% of all mast cells in bone marrow aspirate smears are immature or atypical.
  - Detection of an activating point mutation at codon 816 of KIT in the bone marrow, blood or another extracutaneous organ.
  - Mast cells in bone marrow, blood or another extracutaneous organ express CD25, with or without CD2, in addition to normal mast cell markers.
  - Serum total tryptase is persistently >20 ng/ml, unless there is an associated myeloid neoplasm, in which case this parameter is not valid.

Systemic Mastocytosis Subtypes / Variants Diagnostic Criteria
The diagnostic criteria for the systemic mastocytosis subtypes / variants are as follows. Each sub-type / variant meets the general criteria for systemic mastocytosis with additional criteria for each.

- **Indolent systemic mastocytosis (ISM)**: Low mast cell burden; no evidence of an associated hematologic neoplasm; skin lesions are almost invariably present; no “C” findings.

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- **Smoldering systemic mastocytosis (SSM)**: ≥2 "B" findings and no "C" findings; high mast cell burden; no evidence of an associated hematologic neoplasm; does not meet criteria for mast cell leukemia
- **Systemic mastocytosis with an associated hematologic neoplasm SM-AHN)**: Meets the criteria for an associated hematologic neoplasm (i.e., MDS, MPN, AML, lymphoma or another hematological neoplasm classified as a distinct entity in the WHO classification).
- **Aggressive systemic mastocytosis (ASM)**: ≥1 "C" findings; does not meet the criteria for mast cell leukemia; skin lesions are usually absent.
- **Mast Cell leukemia (MCL)**: Bone marrow biopsy shows diffuse infiltration of atypical, immature mast cells; bone marrow aspirate smears show ≥20% mast cells. In classic cases, mast cells account for ≥10% of the peripheral blood WBC, but the aleukemic variant (in which mast cells account for <10%) is more common. Skin lesions are usually absent
- **Bone marrow mastocytosis**: Absence of skin lesions and B-findings. Additionally, the basal serum tryptase is < 125 ng / ml.

Systemic Mastocytosis Burden of Disease (B) and Cytoreduction-Requiring (C) Findings

- **"B" findings**
  - BM biopsy showing ≥30% infiltration by MC (focal, dense aggregates) and/or serum total tryptase level >200 ng/mL
  - Signs of dysplasia or myeloproliferation, in non-MC lineage(s), but insufficient criteria for definitive diagnosis of a hematopoietic neoplasm (AHNMD), with normal or slightly abnormal blood counts.
  - Hepatomegaly without impairment of liver function, and/or palpable splenomegaly without hypersplenism, and/or lymphadenopathy on palpation or imaging.

- **"C" findings**
  - Bone marrow dysfunction manifested by one or more cytopenia(s) (ANC <1.0 × 109/L, Hgb <10 g/dL, or platelets <100 × 109/L), but no obvious non-mast cell hematopoietic malignancy.
  - Palpable hepatomegaly with impairment of liver function, ascites and/or portal hypertension.
  - Skeletal involvement with large osteolytic lesions and/or pathological fractures.

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- Palpable splenomegaly with hypersplenism.
- Malabsorption with weight loss due to gastrointestinal mast cell infiltrates.

Subsequent Infusion and Constitutional Symptoms
If this is a subsequent infusion for the same disease, the *Did the recipient have constitutional symptoms* question is disabled.

Question 381: Did the recipient have constitutional symptoms in six months before diagnosis? *(symptoms are > 10% weight loss in six months, night sweats, unexplained fever higher than 37.5°C)*

Indicate if constitutional symptoms were present at diagnosis. Constitutional symptoms are often called "B" symptoms and include unexplained fever greater than 38°C (100.4°F), night sweats, or unexplained weight loss in the six months prior to diagnosis. Indicate if any constitutional symptoms were present at or six months prior to diagnosis.

If constitutional symptoms were not present at or prior to diagnosis or are not known, report **No** or **Unknown**, respectively. The **Unknown** option should be used if it is not possible to determine the presence or absence of constitutional symptoms at or six months prior to diagnosis.

Subsequent Infusion and Assessments at Diagnosis
If this is a subsequent infusion for the same disease, the assessments at diagnosis questions are disabled.

Laboratory Studies at Diagnosis of MPN
Report laboratory results closest to the diagnosis date and prior to the start of first treatment of the primary disease for which the infusion is being performed. If the recipient's MPN transformed, report the studies from the original diagnosis.

Reporting Blasts Percentage
If the bone marrow pathology report states a range for blasts, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
If the report indicates "sheets of blasts" or "packed marrow," report 100%.
If the report states > n% blasts, enter (n+1)% on the form. For example, if the laboratory report indicates > 90% blasts, report 91%.
If the report states < n% blasts, enter (n-1)% on the form. For example, if the laboratory report indicates < 5% blasts, report 4%.

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Questions 382 – 383: Blasts in bone marrow *(at diagnosis)*

Indicate whether the percentage of blasts in the bone marrow was known at diagnosis. If **Known**, report the percentage documented on the laboratory report.

If the lab was assessed multiple times prior to starting treatment, report the values closest to the diagnosis date.

Questions 384 – 392: Complete blood count (CBC) results available *(check all that apply) (at diagnosis)*

These questions are intended to capture the laboratory studies performed at the initial diagnosis of MPN. Report the date of the CBC completed closest to the diagnosis date and select all lab values assessed on the reported date. All values must reflect testing performed prior to the start of the first treatment of the primary disease for infusion. If the recipient's MPN transformed, report the studies from the original diagnosis. If labs were assessed multiple times prior to starting treatment, report the values closest to the diagnosis date.

- **WBC**: The white blood cell count is a value that represents all of the white blood cells in the blood. If the count is too high or too low, the ability to fight infection may be impaired. If known, specify the value and units of measurement as documented on the lab report.
- **Neutrophils**: Neutrophils are a subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage or an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. Neutrophils are also known as polymorphonuclear leukocytes (PMNs). If known, specify the percentage as documented on the lab report.
- **Blasts in blood**: Blasts are not typically found in the peripheral blood; however, can appear for various reasons, including infection, blood cancer, or blood disorder. If known, report the percentage of blasts detected in the blood.
    - If a differential was performed and the percentage of plasma cells are not listed, report **0%**.
- **Hemoglobin**: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered "anemia" and blood transfusions, or growth factors may be required to increase the hemoglobin level. If known, specify the value and units of measurement as documented on

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the lab report. Additionally, indicate if red blood cells were transfused ≤ 30 days prior to the CBC date reported above.

Transfusions temporarily increase the red blood cell count, and it is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

- **Platelets**: Platelets are formed elements within the blood that help with coagulation. A low platelet count, called thrombocytopenia, may lead to easy bleeding or bruising. Thrombocytopenia may require platelet transfusions. If known, specify the value and unites of measurement as documented on the lab report. Additionally, indicate if platelets were transfused ≤ seven days prior to the CBC date reported above.

  Transfusions temporarily increase the platelet count, and it is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

If a CBC was not completed at diagnosis or unknown if completed, select **None**.

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

Question 393: Were cytogenetics tested (karyotyping or FISH)? *(at diagnosis)*

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at diagnosis. If cytogenetic studies were obtained, select **Yes**. If no cytogenetic studies were obtained, or it is unknown if chromosome studies were performed, select **No** or **Unknown**, respectively.

Question 394: Were cytogenetics tested via FISH? *(at diagnosis)*

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Specify if FISH studies were performed at diagnosis. If FISH studies were not performed at diagnosis or FISH samples were inadequate, report **No**. If it is not known if it was performed, report **Unknown**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 395: Sample source

The cytogenetic sample source is important for MPN research. Indicate if the sample was from **Bone marrow** or from **Blood**. If FISH studies were performed on multiple samples at diagnosis, the bone marrow results are the preferred sample source to report.

Question 396: Results of tests

Specify if FISH abnormalities were detected at diagnosis.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 397 – 400: Specify FISH abnormalities (*at diagnosis)*

Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at diagnosis and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report “see attachment” and attach the final report(s) for any other abnormalities detected.

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Question 401: Were cytogenetics tested via karyotyping? *(at diagnosis)*

Specify if karyotyping studies were performed at diagnosis. Report **Yes** even if there were no evaluable metaphase cells / failed (these results will be specified below).

If karyotyping studies were not performed at diagnosis or it is unknown if performed, report **No** or **Unknown**, respectively.

Question 402: Sample source

The cytogenetic sample source is important for MPN research. Indicate if the sample was from **Bone marrow** or from **Blood**. If karyotype analyses were performed on multiple samples at diagnosis, the bone marrow results are the preferred sample source to report.

Question 403: Results of tests

Specify if abnormalities were detected by karyotype at diagnosis.

If karyotyping failed, select **No evaluable metaphases.**

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 404 – 407: Specify karyotype abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at diagnosis and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report “see attachment” and attach the final report(s) for any other abnormalities detected.

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CALR Testing
If CALR testing was performed and positive but the lab report does not specify the type, select **Not done** for *CALR 1* and *CALR 2*, and **Positive** for *Not defined*.

Questions 408 – 417: Were tests for driver mutations performed?

Testing for driver mutations may be performed by different methods including next generation sequencing (NGS), polymerase chain reaction (PCR), microarray, and fluorescence in situ hybridization (FISH). If testing was performed by any / all of these methods at diagnosis, report **Yes** and report the results for the most recent test(s) prior to the start of therapy.

If testing for driver mutations were not performed / sample failed or is not known if performed, report **No** or **Unknown**, respectively.

Reporting Multiple Positive Molecular Markers
Complete the *Specify positive molecular marker(s) identified* questions if multiple molecular markers were detected at diagnosis by adding an additional instance in FormsNet3^{SM}.

Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Pre-TED Disease Classification (2402) Form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Pre-TED Disease Classification (2402) Form.

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 418 – 421: Specify positive molecular marker(s) identified *(at diagnosis)*

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Testing for molecular markers is often performed by using PCR based methods to assess specific genetic sequences. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

Specify all positive molecular markers detected at diagnosis and the amino acid change, if known. If molecular markers were not detected at diagnosis, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality, along with the amino acid change, if known.

Transformation to AML
If the recipient is being transplanted for AML that has transformed from MPN, the primary disease for HCT must be reported as **AML**. Disease Classification questions must be completed for both AML and MPN.

Question 422: Did the recipient progress or transform to a different MPN subtype or AML between diagnosis and the start of the preparative regimen / infusion?

MPN subtypes may also transform / progress from one into another. Indicate if the recipient's disease progressed to AML or transformed into a different MPN subtype between initial diagnosis and the start of the preparative regimen / infusion. Progression to AML is defined by an increase in blood or bone marrow blasts $\geq$ 20%.

Specify if the recipient's disease progressed to AML or transformed into a different MPN subtype between diagnosis and the start of the preparative regimen / infusion. If a transformation or progression did not occur or it is unknown, select **No**.

Question 423: Specify the MPN subtype or AML after transformation

Indicate the recipient's current MPN subtype after transformation. If the recipient experienced more than one transformation after diagnosis, report the most recent subtype.

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If the disease progressed to **AML**, report the date of MPN diagnosis. If MPN progresses to AML and the recipient is on the CRF track, the AML Pre-Infusion (2010) form will also come due.

For all other progressions or transformations, continue with to specify the date of the most recent transformation.

Question 424: Specify the date of the most recent transformation

Report the date of assessment that determined the most recent disease transformation (i.e., if there were multiple transformations, report the most recent). Report the date of the pathological evaluation (i.e., bone marrow) or blood / serum assessment (i.e., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 425: Date of MPN Diagnosis

If the recipient's MPN transformed to AML prior to infusion, report the date of diagnosis of MPN. If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Ensure the diagnosis date for AML has been reported as the diagnosis date of the primary disease for infusion and AML is reported as the primary disease for infusion. The AML section of the Disease Classification (2402) form must be completed appropriately.

Transfusion Dependence Status
If the transfusion status is between **Non-transfused** (0 RBCs in 16 weeks) and **Low-transfusion burden** (3 – 7 RBCs in 16 weeks in at least 2 transfusion episodes; maximum of 3 in 8 weeks), report the status as **Non-transfused**.

Question 426: Specify transfusion dependence at the last evaluation prior to the start of the preparative regimen / infusion

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Indicate the transfusion dependence for the recipient at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen).

Select **Non-transfused (NTD)** if the recipient was without RBC transfusions as supportive care for the disease within a period of 16 weeks prior to the start of the preparative regimen / infusion.

Select **Low-transfusion burden (LTB)** if the recipient had 3 – 7 RBC transfusions within a period of 16 weeks in at least 2 transfusion episodes with a maximum of 3 RBC transfusions in 8 weeks prior to the start of the preparative regimen / infusion.

Select **High-transfusion burden (HTB)** if the recipient had ≥ 8 RBCs transfusions within a period of 16 weeks or ≥ 4 within 8 weeks prior to the start of the preparative regimen / infusion.

Question 427: Did the recipient have constitutional symptoms in six months before last evaluation prior to the start of the preparative regimen / infusion? *(symptoms are > 10% weight loss in 6 months, night sweats, or unexplained fever higher than 37.5°C)*

Specify if constitutional symptoms were present within six months before the last evaluation prior to the preparative regimen / infusion. Constitutional symptoms are often called “B” symptoms and include unexplained fever greater than 38°C (100.4°F), night sweats, or unexplained weight loss in the six months before the last evaluation prior to the start of the preparative regimen / infusion.

Report **No** if constitutional symptoms were not present or unknown if present at this timepoint.

Question 428: Did the recipient have splenomegaly at last evaluation prior to the start of the preparative regimen / infusion?

Indicate if the recipient had splenomegaly at the last evaluation. Splenomegaly is often documented during the physician’s physical assessment of the recipient and represents an abnormal finding. Splenomegaly can also be detected by imaging techniques such as ultrasonography, CT or MRI.

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Indicate if splenomegaly was present at the last evaluation prior to the start of the preparative regimen / infusion.

If splenomegaly was not present or is unknown if present at this timepoint, report **No**.

Select **Not applicable** if the question does not apply to the recipient (i.e., prior splenectomy).

Questions 429 – 431: Specify the method used to measure spleen size

Indicate the method used to measure the spleen size. If spleen size is measured using multiple methods, report the most accurate assessment. Ultrasound is the most specific, and preferred, assessment.

If the method selected is **Physical assessment**, specify the spleen size (in centimeters) below the left coastal margin as determined by the physical exam.

If the method selected is **Ultrasound** or **CT / MRI**, specify the spleen size (in centimeters) as determined by imaging.

Question 432: Did the recipient have hepatomegaly at last evaluation prior to the start of the preparative regimen / infusion?

Indicate if the recipient had hepatomegaly at the last evaluation prior to the start of the preparative regimen / infusion. Hepatomegaly is often documented during the physician's physical assessment of the recipient and represents an abnormal finding.

Indicate if hepatomegaly was present at the last evaluation prior to the start of the preparative regimen / infusion.

If hepatomegaly was not present or is unknown if present at this timepoint, report **No**.

Questions 433 – 435: Specify the method used to measure liver size

Indicate the method used to measure the liver size. If liver size is measured using multiple methods, report the most accurate assessment. Ultrasound is the most specific, and preferred, assessment.

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If the method selected is **Physical assessment**, report the liver size (in centimeters) below the left coastal margin as determined by the physical exam.

If the method selected is **Ultrasound** or **CT / MRI**, report the liver size (in centimeters) as determined by imaging.

Laboratory Studies at Last Evaluation
Report the most recent laboratory values prior to the start of the preparative regimen.

Reporting Blasts Percentage
If the bone marrow pathology report states a range for blasts, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
If the report indicates “sheets of blasts” or “packed marrow,” report 100%.
If the report states > n% blasts, enter (n+1)% on the form. For example, if the laboratory report indicates > 90% blasts, report 91%.
If the report states < n% blasts, enter (n-1)% on the form. For example, if the laboratory report indicates < 5% blasts, report 4%.

Questions 436 – 437: Blasts in bone marrow *(at last evaluation)*

Indicate whether the percentage of blasts in the bone marrow was known at diagnosis. If **Known**, report the percentage documented on the laboratory report.

If the lab was assessed multiple times, report the most recent values prior to the preparative regimen / infusion. Laboratory values obtained on the first date of the preparative regimen / lymphodepleting therapy may be reported as long as the sample was collected before any administration of systemic therapy or radiation.

Questions 438 – 444: Complete blood count (CBC) results available *(check all that apply) (at last evaluation)*

These questions are intended to capture the laboratory studies performed at the evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). Report the date of the CBC completed at the last evaluation and select all lab values assessed on the reported date. If labs were assessed multiple times prior to the preparative regimen / infusion, report the most recent lab.

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Laboratory values obtained on the first date of the preparative regimen / lymphodepleting therapy may be reported as long as the sample was collected before any administration of systemic therapy or radiation.

- **WBC**: The white blood cell count is a value that represents all of the white blood cells in the blood. If the count is too high or too low, the ability to fight infection may be impaired. If known, specify the value and units of measurement as documented on the lab report.
- **Neutrophils**: Neutrophils are a subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage or an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. Neutrophils are also known as polymorphonuclear leukocytes (PMNs). If known, specify the percentage as documented on the lab report.
- **Blasts in blood**: Blasts are not typically found in the peripheral blood; however, can appear for various reasons, including infection, blood cancer, or blood disorder. If known, report the percentage of blasts detected in the blood.
    - If a differential was performed and the percentage of plasma cells are not listed, report **0%**.
- **Hemoglobin**: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered “anemia” and blood transfusions, or growth factors may be required to increase the hemoglobin level. If known, specify the value and units of measurement as documented on the lab report. Additionally, indicate if red blood cells were transfused ≤ 30 days prior to the CBC date reported above.

  Transfusions temporarily increase the red blood cell count, and it is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

If a CBC was not completed at diagnosis or unknown if completed, select **None**.

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

Question 445: Were cytogenetics tested (karyotyping or FISH)? *(at last evaluation)*

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Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies were obtained at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). If cytogenetic studies were obtained, select **Yes**. If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select **No**.

Question 446: Were cytogenetics tested via FISH? *(at last evaluation)*

Specify if FISH studies were performed at last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen). If FISH studies were not performed at this time point, FISH sample was inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

Question 447: Sample source

The cytogenetic sample source is important for MPN research. Indicate if the sample was from **Bone marrow** or from **Blood**. If FISH studies were performed on multiple samples at the last evaluation prior to the start of the preparative regimen / infusion, the bone marrow results are the preferred sample source to report.

Question 448: Results of tests

Specify if FISH abnormalities were detected at the last evaluation.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

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Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 449– 452: Specify FISH abnormalities *(at last evaluation)*

Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by FISH at the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Question 453: Were cytogenetics tested via karyotyping? *(at last evaluation)*

Specify if karyotyping studies were performed at the last evaluation prior to the preparative regimen / infusion. Report **Yes** even if there were no evaluable metaphase cells (these results will be specified below).

If karyotyping studies were not performed at this time point or it is unknown if performed, report **No**.

Question 454: Sample source

The cytogenetic sample source is important for MPN research. Indicate if the sample was from **Bone marrow** or from **Blood**. If karyotype analyses were performed on multiple samples at the last evaluation prior to the start of the preparative regimen / infusion, the bone marrow results are the preferred sample source to report.

Question 455: Results of tests

Specify if abnormalities were detected by karyotype at the last evaluation.

If karyotyping failed, select **No evaluable metaphases.**

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Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 456 – 459: Specify karyotype abnormalities *(at last evaluation)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select the number of abnormalities detected by karyotype at the last evaluation and select all abnormalities detected.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

CALR Testing
If CALR testing was performed and positive but the lab report does not specify the type, select **Not done** for *CALR 1* and *CALR 2*, and **Positive** for *Not defined*.

Questions 460 – 469: Were tests for driver mutations performed? *(at last evaluation)*

Testing for driver mutations may be performed by different methods including next generation sequencing (NGS), polymerase chain reaction (PCR), microarray, and fluorescence in situ hybridization (FISH). If testing was performed by any / all of these methods at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen), report **Yes** and report the results for the most recent test(s).

If testing for driver mutations were not performed / sample was inadequate or is unknown, report **No**.

Reporting Multiple Positive Molecular Markers
Complete the *Specify positive molecular marker(s) identified* questions if multiple molecular markers were detected at the last evaluation by adding an additional instance in FormsNet3SM.

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Molecular Marker Results
Questions capturing molecular marker results are intended to capture **molecular abnormalities** identified by **molecular methods**. Additional testing methods, such as FISH and chromosomal microarray, may identify molecular marker results but should **not** be reported in the molecular section(s) of the Pre-TED Disease Classification (2402) Form. Abnormalities identified by karyotyping, FISH, or chromosomal microarray should only be reported in the cytogenetic section of the Pre-TED Disease Classification (2402) Form.

Submitting Molecular Marker Documentation
CIBMTR strongly encourages attaching the molecular report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 470 – 473: Specify positive molecular marker(s) identified *(at last evaluation)*

Testing for molecular markers is often performed by using PCR based methods to assess specific genetic sequences. Once a marker has been identified, these methods can be repeated to detect minimal residual disease (MRD) in the recipient's blood, marrow, or tissue. Molecular assessments include polymerase chain reaction (PCR) amplification to detect single specific disease markers; however, molecular methods are evolving and now include Sanger sequencing, and next generation sequencing (e.g., Illumina, Roche 454, Proton / PGM, SOLiD).

Specify all positive molecular markers detected at the last evaluation prior to the start of the preparative regimen (or infusion if no preparative regimen and the amino acid change, if known. If molecular markers were not detected at this time point, the sample failed, testing was not completed or unknown if completed at diagnosis report **None**.

If a molecular marker was detected, but not listed as an option, select **Other molecular marker** and specify the abnormality, along with the amino acid change, if known.

Question 474: What was the disease status? *(at infusion)*

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. Refer to the MPN Response Criteria section for definitions of each disease response based on clinical / hematologic assessments.

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Report the disease status prior to the start of the preparative regimen (or infusion if no preparative regimen).

Question 475: Was an anemia response achieved?

Specify if an anemia response was achieved prior to the preparative regimen / infusion.

An anemia response is characterized by a ≥ 20 g/L (or > 2.0 g/dL) increase in hemoglobin level (for transfusion-independent recipients

Spleen Response
If a spleen response does not apply to the recipient (i.e., prior splenectomy), this question will be disabled and should not be answered.

Question 476: Was a spleen response achieved?

Specify if a spleen response has been achieved prior to the preparative regimen / infusion.

A spleen response is achieved when a baseline splenomegaly that is palpable at 5 – 10 cm below the left costal margin (LCM) becomes not palpable or baseline splenomegaly that is palpable at > 10 cm below the LCM, decreases by ≥ 50%.

A baseline splenomegaly that is palpable at < 5 cm, below the LCM, is not eligible for spleen response.

A spleen response can be documented by a physician but should be confirmed by MRI / computed tomography showing ≥ 35% spleen volume reduction.

Question 477: Was a symptom response achieved?

The Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) is used to evaluate the recipient's symptom response. The MPN-SAF TSS is used to provide an accurate assessment of MPN symptom burden. The evaluation tool allows recipients with MPN to report their symptom severity at the worst level. They rate their symptom severity on a scale from zero to ten, zero being absent to

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ten being the worst imaginable. Adding the scores for all symptoms together will result in the recipient's MPN-SAF TSS. See Table 1 below for an example of this assessment:

Table 1. Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS)

Symptom	**1 to 10 (0 if absent) ranking – 1 is most favorable and 10 least favorable**
Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during the past 24 hours	(No fatigue) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Circle the one number that describes how, during the past week how much difficulty you have had with each of the following symptoms.	**—**
Filling up quickly when you eat (early satiety)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Abdominal discomfort	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Inactivity	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Problems with concentration – Compared to prior to my MPD	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Numbness / tingling (in my hands and feet)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Night sweats	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Itching (pruritus)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Bone pain (diffuse not joint pain or arthritis)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)

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Fever (>100 F)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)
Unintentional weight loss last 6 months	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst imaginable)

A symptom response is achieved when there is a ≥ 50% reduction in the Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS).

Specify if a symptom response has been achieved prior to preparative regimen / infusion.

Question 478: Specify the cytogenetic response

Specify the recipient's cytogenetic response prior to the start of the preparative regimen / infusion. Use the following guidelines when reporting the cytogenetic response:

- **Complete response (CR)**: Eradication of the previously reported abnormality
- **Partial response (PR)**: ≥ 50% reduction in abnormal metaphases
- **No response**: Mutation persists
- **Re-emergence of pre-existing cytogenetic abnormality**: Cytogenetic abnormality was eradicated and reemerged at the last evaluation.
- **Not assessed**: Cytogenetic response was not tested at the last evaluation
- **Not applicable**: Cytogenetic abnormalities were never identified
- **None of the above**: If the response was assessed at the last evaluation but does not meet the criteria for CR, PR, no response, re-emergence of pre-existing cytogenetic abnormality, and not applicable (i.e., if a new cytogenetic abnormality is identified but there is also eradication of a previous abnormality)

Below is an example of how to report **Partial response**:

- Example 1: A recipient had 10 abnormal metaphases (out of 20) at diagnosis. At the last evaluation prior to the start of the preparative regimen, they had 2 abnormal metaphases (out of 20). As this is a ≥ 50% reduction in abnormal metaphases, Partial Remission (PR) should be reported.

Question 479: Specify the molecular response

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Specify the recipient's molecular response prior to the start of the preparative regimen / infusion, based on the four drive mutations (JAK2, CALR, MPL, and CSF3R). Use the following guidelines when reporting the molecular response:

- **Complete response (CR)**: Eradication of the previously reported driver mutation (JAK2, CALR, MPL, and/or CSF3R)
- **Partial response (PR)**: ≥ 50% decrease in allele burden of the driver mutation (JAK2, CALR, MPL, and/or CSF3R). Refer to example 2 for more information.
- **No response**: Mutation persists
- **Re-emergence of pre-existing molecular abnormality**: Molecular abnormality (JAK2, CALR, MPL, and/or CSF3R) was eradicated and reemerged at the last evaluation.
- **Not assessed**: Molecular response (JAK2, CALR, MPL, CSF3R) was not tested at the last evaluation
- **Not applicable**: JAK2, CALR, MPL, and CSF3R were never identified
- **None of the above**: If the response was assessed at the last evaluation but does not meet the criteria for CR, PR, no response, re-emergence of pre-existing molecular abnormality, and not applicable (i.e., if a new cytogenetic abnormality is identified but there is also eradication of a previous abnormality)

Below is an example of how to report **Partial response**:

- Example 2: A recipient was found to have a molecular mutation identified (JAK2, CALR, MPL, and/or CSF3R) in 80% of cells examined at diagnosis. At their last evaluation prior to transplant, the molecular mutation was only identified in 40% of cells examined. The number of cells with the molecular mutation identified decreased from 80% to 40%, which is a 50% reduction. In this case, "Partial Remission" should be reported as their molecular response.

Section Updates

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

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Q480 – 483: Other Leukemia

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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 other leukemia is CLL and CLL transformed to DLBCL (Richter syndrome), report the diagnosis date of DLBCL and the primary disease for infusion as **Non-Hodgkin lymphoma** above. Ensure the Hodgkin / Non- Hodgkin Lymphoma section is completed. The CLL diagnosis is captured in the Hodgkin / Non-Hodgkin Lymphoma section.

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

Questions 480 – 481: Specify the other leukemia classification

CIBMTR captures the classification of other leukemia based on the World Health Organization (WHO) 2022. Report the other leukemia disease classification at diagnosis. See below for general information about the other leukemia classifications listed on the form:

- **CLL**, or chronic lymphocytic leukemia, is characterized by ≥ 5 × 10[^9]/L monoclonal lymphocytes with a CLL phenotype (usually co-expressed CD5 and CD23). The term SLL, or small lymphocytic lymphoma, is used for non-leukemic cases with the tissue morphology and immunophenotype of CLL.
- **Hairy cell leukemia** is characterized by the presence of abnormal B-lymphocytes in the bone marrow, peripheral blood, and spleen.
- PLL, or prolymphocytic leukemia, is a type of CLL and is characterized by increased presence of immature prolymphocytes in the bone marrow and peripheral blood.

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If the subtype is not listed, report as **Other leukemia** and specify the disease.

Question 482: Was any 17p abnormality detected?

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence *in situ* hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate if cytogenetic studies detected any 17p abnormality at any time prior to the start of the preparative regimen (or infusion if no preparative regimen was given).

If cytogenetic studies did not detect any 17p abnormality at any time prior to the start of the preparative regimen (or infusion if no preparative regimen was given) or is unknown, select **No**.

CLL with Richter's Transformation
If the recipient is receiving an infusion for CLL and there was a Richter's transformation to lymphoma, the primary disease for infusion should be reported as lymphoma.

Question 483: What was the disease status?

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. If the primary disease for infusion is **CLL** or **CLL / SLL**, refer to the CLL Response Criteria section for definitions of each response based on clinical / hematologic assessment. If the primary disease for infusion is **Hairy Cell Leukemia**, refer to the response criteria provided below. If the primary disease is not CLL, CLL / SLL, or Hairy Cell Leukemia, use the criteria for the leukemia that most closely resembles the disease for which this form is being completed. For questions, contact the CIBMTR Customer Service Center.

Disease Status of Hairy Cell Leukemia[1]

Complete remission (CR)

- Disappearance of all evidence of disease.
- Requires **all** the following:
  - Neutrophils ≥ 1.5×10^9

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- Hemoglobin ≥ 11.0 g/dL (without transfusion)
- Platelets ≥ 100 × 10^9/L
- Absence of hairy cells on peripheral blood smear and on bone marrow examination
- No palpable lymphadenopathy or hepatosplenomegaly

Partial remission (PR)

- Requires **all** the following:
  - ≥ 50% reduction in the absolute hairy cell count in the peripheral blood and the bone marrow
  - ≥ 50% improvement of all cytopenias
  - ≥ 50% reduction in abnormal lymphadenopathy or hepatosplenomegaly

Stable disease (SD)

- Not meeting the criteria for any of the other disease response criteria.

Progressive disease (Prog)

- Requires one or more of the following:
  - ≥ 25% increase in the absolute hairy cell count in the peripheral blood and/or bone marrow
  - ≥ 25% decrease in any of the hematologic parameters (i.e., neutrophils, hemoglobin or platelets)
  - ≥ 25% increase in abnormal lymphadenopathy or hepatosplenomegaly

No treatment

- The recipient was diagnosed with hairy cell leukemia and never treated.

Relapse (untreated)

Relapse after CR:

- Reappearance of hairy cells in the peripheral blood smear and/or bone marrow (regardless of the degree of infiltration)
- Development of peripheral blood cytopenias
- Splenomegaly

Relapse after PR:

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- ≥ 50% increase of residual hairy cells in the marrow
- Development of cytopenias
- Splenomegaly insufficient to qualify as PR
  OR
- Reappearance of hairy cells in the bone marrow of those patients who had been classified as partial responders based on residual splenomegaly only

1 Saven, A., Burian, C., Koziol, J. A., & Piro, L. D. (1998). Long-term follow-up of patients with hairy cell leukemia after cladribine treatment. *Blood*, 92(6), 1918-1926.

Other leukemia

To determine the disease status, use the criteria for the leukemia that most closely resembles the disease for which this form is being completed. For questions, contact the CIBMTR Customer Service Center.

Section Updates

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

Q484 – 500: Hodgkin and Non-Hodgkin Lymphoma

Hodgkin lymphoma (HL or Hodgkin disease) is a cancer of the immune system that is marked by the presence of a type of cell called the Reed-Sternberg cell. The two major types of Hodgkin lymphoma are classical Hodgkin lymphoma (90-95% of cases) and nodular lymphocyte-predominant Hodgkin lymphoma (5-10% of cases).

Classical Hodgkin lymphoma can be further subdivided into four histologic subtypes: nodular sclerosis (NS), mixed cellularity (MC), lymphocyte deplete (LD), and lymphocyte rich (LR). Symptoms include the painless enlargement of lymph nodes, spleen, or other immune tissue. Generalized pruritus is also common and may precede the diagnosis by months. The most common sites of involvement include cervical, supraclavicular, and

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mediastinal lymph nodes. Central nervous system involvement may occur in rare cases. Other symptoms include fever, weight loss, fatigue, and/or night sweats.

Non-Hodgkin lymphoma (NHL) is a large group of cancers derived from lymphocytes (white blood cells). Non-Hodgkin lymphomas can occur at any age and are often marked by enlarged lymph nodes, fever, night sweats and weight loss. There are many different types of non-Hodgkin lymphoma. These types can be divided into aggressive (fast-growing), intermediate, or indolent (slow-growing) and can develop from either B-cells or T-cells.

Lymphomas that occur after bone marrow or stem cell transplantation are usually B-cell non-Hodgkin lymphomas and are collectively known as **post-transplant lymphoproliferative disorders (PTLD)**.

Acute Lymphoblastic Leukemia / Lymphoma
Due to the aggressive nature of precursor B- and precursor T-cell lymphoblastic lymphoma (or lymphoma / leukemia), the primary disease to report for recipients with these malignancies should be acute lymphoblastic leukemia (B-cell lymphoblastic leukemia / lymphoma or early T-cell precursor lymphoblastic leukemia.

Hodgkin Lymphoma (HL) and non-Hodgkin Lymphoma (NHL) are WHO disease classification subtypes of lymphoma. HL and NHL can transform into other disease subtypes. NHL can transform into other NHL subtypes, or into HL subtypes, but HL will rarely transform into NHL. Additionally, HL and NHL can occur at the same time and most likely classified as “B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma”.

In order to complete the correct Disease Classification questions for a recipient who has a history of both HL and NHL, **it is important to determine which disease is active prior to the start of the preparative regimen. A physician must make this determination.**

The following two scenarios are examples of data reporting practice for recipients with a combination of HL and NHL.

- Example 1: A recipient is being transplanted for active NHL but has a history of HL that is in remission at the start of the preparative regimen. Report the

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active NHL on the Disease Classification questions, and report HL as a prior malignancy on the Pre-TED Form (Form 2400) or Pre-CTED (Form 4000).

- Example 2: A recipient is being transplanted for both active NHL and active HL. Report this as NHL using **Other B-cell Lymphoma** and specify. Complete the Disease Classification questions for NHL. This only applies when the NHL and HL have been diagnosed at different times (i.e., two primaries).

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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 lymphoma transformed from CLL, report the diagnosis date of the lymphoma. The CLL diagnosis will be captured below.

If the lymphoma transformed from a less severe lymphoma to a more severe lymphoma, report the diagnosis date of the more severe lymphoma. The initial lymphoma (i.e., less severe type) will be captured below.

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

DLBCL and Relapse with Follicular Lymphoma
In some scenarios, a recipient may be diagnosed with DLBCL and then later, relapses with Follicular lymphoma prior to infusion. In these cases, it is important to determine the primary disease for infusion with the physician. If the primary disease for infusion is **Follicular lymphoma**, report the diagnosis date as the date when the recipient was diagnosed with Follicular lymphoma (i.e., the relapse date) and report the lymphoma histology for infusion as 'Follicular lymphoma.' If the primary disease for infusion is **DLBCL**, report the diagnosis date as the date the recipient was diagnosed with DLBCL and report the lymphoma histology for infusion as 'DLBCL.'

Follicular Lymphoma Grade Progression
Follicular lymphoma may progress to a more severe grade prior to infusion (i.e., follicular lymphoma grade I to follicular lymphoma grade II); however, progression of the

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grade of follicular lymphoma should not be reported as a transformation. In cases where the follicular grade progresses, report the *most severe* follicular lymphoma grade (i.e., the follicular grade after progression) as the histology for infusion and report **No**, there was not a transformation – the initial follicular grade at diagnosis will not be captured on the Disease Classification (2402) Form.

Composite Lymphoma
If a recipient is diagnosed with a composite lymphoma (i.e., a combination of Hodgkin lymphoma and non-Hodgkin lymphoma), it is important to determine the primary disease for infusion with the physician. If the primary disease for infusion is **Hodgkin lymphoma**, report that as the disease classification and the non-Hodgkin lymphoma as a prior malignancy on the Pre-TED (2400) Form. If the primary disease for infusion is **non-Hodgkin lymphoma**, report that as the disease classification and the Hodgkin lymphoma as a prior malignancy on the Pre-TED (2400) Form. Do not report there was a disease transformation on the Disease Classification (2402) Form.

Double-Hit or Tripe-Hit Lymphomas
Rearrangements of MYC and BCL2 and/or BCL6 constitute a single category in the updated WHO classification and should be reported as **Diffuse large B-cell lymphoma / high grade B-cell lymphoma with MYC and BCL2 rearrangement**, **Diffuse large B-cell lymphoma / high grade B-cell lymphoma with MYC and BCL6 rearrangement**, or as **Diffuse large B-cell lymphoma / high grade B-cell lymphoma with MYC, BCL2 and BCL6 rearrangements**.

Questions 484 – 485: Specify the lymphoma histology (at infusion)

CIBMTR captures the lymphoma histology based on the World Health Organization (WHO) 2022 classification. Specify the histology for which the recipient is receiving a transplant or cellular therapy. If the histology is **Other B-cell lymphoma** or **Other T-cell / NK-cell lymphoma**, specify the histology.

If the recipient is diagnosed with a primary large B-cell lymphoma of immune-privileged sites and multiple sites are affected (i.e., CNS and the vitreoretinal), report the more predominant disease as the classification.

Question 486: Assignment of DLBCL (germinal center B-cell type vs activated B-cell type) subtype was based on

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DLBCL subtypes may be identified using different techniques including immunohistochemistry (IHC) and gene expression profiling. IHC involves staining a tissue sample and determining the presence of cell surface markers via microscopy. Gene expression profiling utilizes molecular techniques.

Report the method used to determine the DLBCL subtype. Indicate **Unknown method** if the method cannot be determined from the available source documentation.

Question 487: Is the lymphoma histology reported at transplant a transformation from CLL?

In some cases, CLL may evolve into a more aggressive diffuse large B-cell lymphoma (DLBCL). This is commonly referred to as Richter's syndrome or Richter's transformation. In a sub-set of CLL cases, the transformation may be to Hodgkin lymphoma (HL).

Specify if the histology reported at infusion is a transformation from CLL.
If the histology reported at infusion is not a transformation from CLL or is unknown, indicate **No**.

Question 488: Was any 17p abnormality detected?

Specify if an abnormality was ever detected (by any method) on the short arm of chromosome 17 since the date of diagnosis of CLL. This includes any 17p abnormality detected after transformation to lymphoma. If a 17p abnormality was not detected or it is unknown, report **No**.

DLBCL and Relapse with Follicular Lymphoma
In some scenarios, a recipient may be diagnosed with DLBCL and then later, relapses with Follicular lymphoma prior to infusion. In these cases, it is important to determine the primary disease for infusion with the physician. If primary disease for infusion is **Follicular lymphoma**, report **No** there was not a transformation. However, on the Pre-TED (2400) form, report there was a previous malignancy of lymphoma. If the primary disease for infusion is **DLBCL**, report **Yes** there was a transformation and the date of the original lymphoma diagnosis as the date when the recipient was diagnosed with DLBCL (i.e., question 1 and question 494 will be the same) as it is presumed Follicular lymphoma was present all along.

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Follicular Lymphoma Grade Progression
Follicular lymphoma may progress to a more severe grade prior to infusion (i.e., follicular lymphoma grade I to follicular lymphoma grade II); however, progression of the grade of follicular lymphoma should not be reported as a transformation. In cases where the follicular grade progresses, report the *most severe* follicular lymphoma grade (i.e., the follicular grade after progression) as the histology for infusion and report **No**, there was not a transformation – the initial follicular grade at diagnosis will not be captured on the Disease Classification (2402) Form.

Question 489: Is the lymphoma histology reported at transplant a transformation from a different lymphoma histology? *(not CLL)*

Transformation may occur when a slow-growing lymphoma with an indolent clinical history change to a more aggressive lymphoma histologically and clinically. An example of a common transformation would include follicular lymphoma evolving to a diffuse large B-cell lymphoma (DLBCL).

If a histological transformation occurs after or concurrently with diagnosis, report **Yes**. If a histological transformation did not occur or unknown if occurred, report **No**.

Questions 490 – 491: Specify the original lymphoma histology *(prior to transformation)*

Report the histology of the recipient's primary disease at diagnosis. If the histology is **Other B-cell lymphoma** or **Other T-cell / NK-cell lymphoma**, specify the histology.

Question 492: Date of original lymphoma diagnosis *(report the date of diagnosis of original lymphoma subtype)*

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

Cellular Therapy and PET (or PET / CT) at Last Evaluation
For cellular therapy infusions, report the last PET (or PET / CT) completed within three months before starting lymphodepleting therapy regardless of any treatment or procedures occurring after the scan (i.e., bridging therapy, leukapheresis, additional treatment).

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Question 493: Was a PET (or PET / CT) scan performed? *(at last evaluation prior to the start of the preparative regimen / infusion)*

Report if a PET scan was performed within three months prior to the start of the preparative regimen / lymphodepleting therapy (or infusion if no preparative regimen / lymphodepleting therapy) and meets the following criteria:

- Was performed within three months prior to the start of the preparative regimen / infusion and
- Was performed after the last pre-infusion line of therapy started

Combination PET / CT may also be reported, but a CT scan alone should not be captured here. Centers may report a PET scan performed during the most recent line of therapy so long as it is the most recent scan and was done within noted period.

If a PET scan was not performed within this period or it is unknown if completed, select **No**.

Question 494: Was the PET (or PET / CT) scan positive for lymphoma involvement at any disease site?

Specify if the most recent PET (or PET / CT) scan prior to the start of the preparative regimen / lymphodepleting therapy (or infusion if no preparative regimen / lymphodepleting therapy) detected the recipient's primary disease.

If the results are unclear, seek clinician clarification.

Questions 495 – 496: Date of PET scan

If the date of this PET scan is known, report **Known** and specify the date. If the date is only partially known (e.g., the month and year are known, but not the day) report **Known**, and use the process described in General Instructions, General Guidelines for Completing Forms. If the date cannot be determined / estimated, report **Unknown**.

Questions 497 – 498: Deauville (five-point) score of the PET (or PET/CT) scan

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Report whether the five-point PET score is known. This information is typically documented in the PET report. Consult the appropriate transplant physician if the results are unclear. If **Known**, report the score. Otherwise, report **Unknown**. If the PET scan result is only documented as an 'X', report this as **Unknown**.

If multiple scores are documented, report the highest. If a score is not documented within the PET (or PET/CT) scan report **Unknown** or work with the physician / radiologist to determine if a score can be reported. Do not determine Deauville scores without seeking physician / radiologist clarification.

DLBCL and Relapse with Follicular Lymphoma
In some scenarios, a recipient may be diagnosed with DLBCL and then later, relapses with Follicular lymphoma prior to infusion. In these cases, it is important to determine the primary disease for infusion with the physician. If primary disease for infusion is **Follicular lymphoma**, report the pre-infusion disease status since the diagnosis of the Follicular lymphoma (not since the diagnosis of DLBCL). If the primary disease for infusion is **DLBCL**, report the pre-infusion disease status since the original diagnosis of DLBCL.

Question 499: What was the disease status?

The recipient's pre-infusion disease status may be evaluated by a PET scan, CT scan, or both. If possible, report the disease status using the metabolic (PET) criteria provided in the Lymphoma Response Criteria section of the manual. If it is not possible to use metabolic criteria to report the recipient's disease (e.g., insufficient PET scan(s), non-PET-avid disease), use the radiographic criteria instead.

If metabolic criteria are used to determine the pre-infusion disease status, per the IWG criteria, normal morphology of the bone marrow is not required for reporting complete remission.

Indicate the disease status at the last evaluation prior to the start of the preparative regimen / lymphodepleting therapy (or infusion if no preparative regimen / lymphodepleting therapy).

When determining the disease status, compare the restaging assessments immediately prior to the preparative regimen to the assessments at baseline. "Baseline" is defined as the disease at diagnosis or at relapse / progression.

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When a transformation has occurred (e.g., follicular lymphoma (FL) transformed to DLBCL), count the response number (CR1, REL2, etc.) beginning with the transformed lymphoma (in this case the DLBCL). Do not include the responses to the lymphoma sub-type prior to the transformation.

The table below provides guidance on which option choice to report using the lymphoma response criteria:

Lymphoma Response Criteria	Disease Status Option
Complete remission	CR
Partial response	PIF – sensitive REL – sensitive
Stable disease	PIF – resistant (if stable on treatment)
Progressive disease / relapse disease	PIF – resistant (if progressive on treatment) PIF – unknown REL – resistant REL – unknown

Question 500: Total number of lines of therapy received (between diagnosis and HCT / infusion)

A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.). If a recipient's disease status changes resulting in a change to treatment, this should be considered a new line of therapy. Additionally, if therapy is changed because a favorable disease response was not achieved, this should be considered a new line of therapy. Do not include surgery when determining the number of lines of therapy.

Report the total number of lines of therapy received since the original lymphoma diagnosis up until the start of the preparative regimen / infusion, regardless of if the recipient has received a prior infusion. If there was a transformation (lymphoma transformation or Richter's transformation), include lines of therapy given to treat the original lymphoma histology or CLL prior to transformation.

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- Example 3: A recipient received a line of induction and achieved CR. However, following induction, the recipient relapsed and received a line of re-induction with no response. After re-induction, the recipient transformed, received a different line of re-induction followed by consolidation and achieved CR2 prior to infusion. This would be considered as four separate lines of therapy and the total number of lines of therapy reported in this example would be **3+ lines**.
- Example 4: A recipient received a line of induction, achieved CR, and then went to HCT. Post-infusion, the recipient transformed, received a line of re-induction followed by a line of consolidation and achieved CR2 prior to the second infusion. In this scenario, the recipient received three lines of therapy, and **3+ lines** would be reported.

Section Updates

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

Q501 – 558: Multiple Myeloma / Plasma Cell Disorder

One kind of white blood cell, the plasma cell (also called plasma B cells, plasmocytes, or effector B cells), produces proteins called antibodies or immunoglobulins (Igs) that are part of our defense system against foreign substances (called antigens). Antibodies are produced in response to such things as viruses, bacteria, and other infectious agents.

Multiple myeloma is a cancer that leads to the proliferation of malignant plasma cells (myeloma cells). Myeloma cells usually proliferate in the bone marrow. When myeloma cells grow into isolated masses in other sites, these masses are called plasmacytomas. Health problems caused by multiple myeloma can affect the bones, immune system, kidneys, and red blood cell count.

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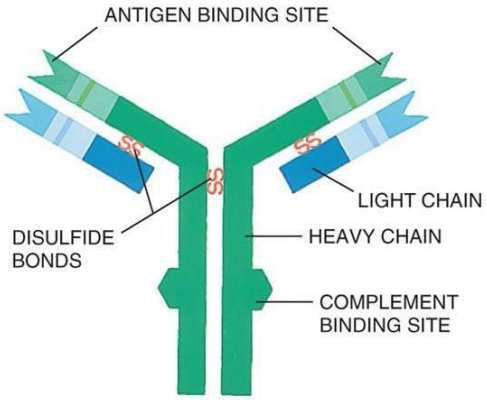
The immunoglobulins (antibodies) produced by healthy plasma cells are composed of pairs of heavy chains and light chains (see graphic below). Healthy plasma cells create many kinds of immunoglobulins that are classified by their heavy chain type into five categories (IgG, IgA, IgM, IgD, or IgE). The light chain types are designated kappa (κ) or lambda (λ). The whole Ig molecule is then labeled IgG kappa, IgG lambda, IgA kappa, IgA lambda, etc. These protein levels can be measured in blood serum and/or urine.

Structure of an Immunoglobulin (Antibody)



Secretory Multiple Myeloma

Healthy plasma cells make immunoglobulins (antibodies) of all types. With the proliferation of malignant plasma cells, the level of one immunoglobulin type increases in the blood and/or urine. This abnormal immunoglobulin type is called the monoclonal immunoglobulin, monoclonal protein (M-protein/M-spike/M-component), or paraprotein. In most cases, normal immunoglobulins are reciprocally depressed. Patients with this condition are said to have *secretory myeloma*.

Some myeloma patients make only an excess of the light chain portion of the immunoglobulin molecule (i.e., only monoclonal kappa or lambda light chains). The light chain is also called Bence Jones protein. In most patients whose myeloma cells only make light chains, this paraprotein may not be detectable in the blood, but only in the urine. These patients are said to have *light-chain-only disease*. Ninety-seven percent of patients diagnosed with multiple myeloma have a detectable paraprotein in the blood serum and / or urine.

Distribution of Monoclonal Proteins in Secretory Multiple Myeloma[1,2]

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Monoclonal Proteins at Diagnosis	Percent
Source of monoclonal proteins	
Serum monoclonal proteins	80%
Urine monoclonal proteins	75%
Type of monoclonal proteins	
IgG	50-54%
IgA	20%
Monoclonal light chain (light-chain-only disease)	20%
IgD	2%

[1] Kyle RA, et al. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc*. 2003;78(1):21-33.

[2] International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group. *Br J Haem*. 2003;121(5):749-57.

Nonsecretory Multiple Myeloma

In some myeloma patients, the malignant plasma cells do not produce an excess of the heavy chain or light chain portion of the immunoglobulin molecule; therefore, a paraprotein is not detectable in the serum or urine. These patients are said to have nonsecretory myeloma (i.e., the absence of a paraprotein on immunofixation). Immunofixation detects the specific immunoglobulins after separating the proteins into bands on an electrophoresis gel. Nonsecretory myeloma accounts for 3% of myeloma cases.

Amyloidosis

Amyloidosis is a disease in which abnormally folded proteins build up in different tissues of the body. In the most common amyloidosis, AL amyloidosis, the abnormally folded protein is the light chain component of an immunoglobulin. These light chains may build up in a variety of tissues, but the most common sites of build-up are the heart, kidneys, liver and nerves. According to the Amyloidosis Foundation, AL Amyloidosis is a relatively rare disorder, with 1200-3200 new cases reported each year in the United States. The disease mostly impacts men and people over 40.[3]

[3] Amyloidosis Foundation. Amyloidosis – Primary AL. 15 Apr. 2013. Accessed at: http://www.amyloidosis.org/TreatmentInformation/primaryAL.html
Accessibility verified on October 21, 2013.

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Question 1: Date of diagnosis of primary disease for infusion

Report the diagnosis date as the first date when all diagnostic criteria for the multiple myeloma / PCD subtype is met. Refer to the criteria listed below for symptomatic multiple myeloma. For other multiple myeloma / PCD subtypes, refer to the guidelines listed in the Disease Assessments at Diagnosis section of the PCD Pre-Infusion manual.

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

Multiple Myeloma (symptomatic)[4]
Diagnostic criteria for symptomatic multiple myeloma require clonal bone marrow plasma cells in ≥ 10% or biopsy proven bony or extramedullary plasmacytoma and any one or more of the following myeloma-defining events:

1. Evidence of end organ damage (i.e., CRAB features) that can be attributed to the underlying plasma cell proliferative disorder, specifically:

- Hypercalcemia: serum calcium >1 mg/dL (> 0.25 mmol/L) higher than the ULN or > 11 mg/dL (> 2.75 mmol/L)
- Renal insufficiency: creatinine clearance < 40 ml/min or serum creatinine > 2 mg/dL (> 177 µmol/L)
- Anemia: hemoglobin > 2 g/dL (> 20 g/L) below the LLN or a hemoglobin < 10 g/dL (< 100 g/L)
- Bone lesions: one or more osteolytic lesions on skeletal x-ray, CT or PET-CT

2. Any one or more of the following biomarkers of malignancy:

- Clonal bone marrow plasma cell percentage ≥ 60%
- Involved : uninvolved serum free light chain ratio ≥ 100
- > 1 focal lesions on MRI studies (each lesion must be ≥ 5 mm in size)

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[4] (2015, October 29). International Myeloma Working Group (IMWG) Criteria for the Diagnosis of Multiple Myeloma. Retrieved February 15, 2017, from http://imwg.myeloma.org/international-myeloma-working-group-imwg-criteria-for-the-diagnosis-of-multiple-myeloma/

Submitting Disease Classification Documentation
If the primary disease for infusion is MGRS, CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 501 – 507: Specify the multiple myeloma / plasma cell disorder (PCD) classification

CIBMTR captures the classification of multiple myeloma and PCDs based on the World Health Organization (WHO) 2022, but also recognizes International Consensus Classification (ICC) 2022 and those classifications are also included, when applicable. Indicate the multiple myeloma / plasma cell disorder (PCD) disease classification for infusion. If the subtype is not listed, report as **Other plasma cell disorder** and specify the reported disease.

Plasma Cell Disorders and Characteristics

Multiple Myeloma (symptomatic)[4]
Diagnostic criteria for symptomatic multiple myeloma requires clonal bone marrow plasma cells in ≥ 10% or biopsy proven bony or extramedullary plasmacytoma and any one or more of the following myeloma-defining events:

1. Evidence of end organ damage (i.e., CRAB features) that can be attributed to the underlying plasma cell proliferative disorder, specifically:

- Hypercalcemia: serum calcium >1 mg/dL (> 0.25 mmol/L) higher than the ULN or > 11 mg/dL (> 2.75 mmol/L)
- Renal insufficiency: creatinine clearance < 40 ml/min or serum creat >2 mg/dL (> 177 µmol/L)
- Anemia: hemoglobin > 2 g/dL (> 20 g/L) below the LLN or a hemoglobin <10 g/dL (< 100 g/dL)
- Bone lesions: one or more osteolytic lesions on skeletal x-ray, CT or PET-CT

2. Any one or more of the following biomarkers of malignancy:

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- Clonal bone marrow plasma percentage ≥ 60%
- Involved **:** uninvolved serum free light chain ratio ≥ 100
- > 1 focal lesion on MRI studies (each lesion must be ≥ 5 mm in size)

[4] (2015, October 29). International Myeloma Working Group (IMWG) Criteria for the Diagnosis of Multiple Myeloma. Retrieved February 15, 2017, from http://imwg.myeloma.org/international-myeloma-working-group-imwg-criteria-for-the-diagnosis-of-multiple-myeloma/

Plasma Cell Leukemia

- Peripheral blood absolute plasma cell count of at least 2.0×10^9/L (2,000 cells/mm^3)
- ≥ 20% plasma cells in the peripheral differential white blood cell count.[5]

Multiple Plasmacytomas
If the recipient has greater than one plasmacytoma but has not been diagnosed with another plasma cell disorder, select **Other plasma cell disorder** and specify how many plasmacytomas are present and if each is bone derived or extramedullary.

Plasmacytoma (in absence of bone marrow findings diagnostic for multiple myeloma or plasma cell leukemia)

- Extraosseous plasmacytoma
  - No M-protein in serum and/or urine
  - Extramedullary tumor of clonal plasma cells
  - Normal bone marrow
  - Normal skeletal survey
  - No related organ or tissue impairment (end organ damage including bone lesions)

- Solitary plasmacytoma of bone
  - No M-protein in serum and/or urine
  - Single area of bone destruction due to clonal plasma cells
  - Bone marrow not consistent with multiple myeloma
  - Normal skeletal survey (and MRI of spine and pelvis if done)
  - No related organ or tissue impairment (no end organ damage other than solitary bone lesion)[5]

[5] The International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma, and related disorders: a report of the international myeloma working group. *Brit J Haematol*. 2003;121(5):749-57.

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Immuno-globulin-related (AL) amyloidosis

Immuno-globulin-related (AL) amyloidosis is the buildup of abnormally folded proteins in various tissues of the body. Affected tissues may include the kidneys, heart, liver, gastrointestinal tract, etc. In the most common type of Immuno-globulin-related (AL) amyloidosis, "AL amyloidosis," light chains from antibodies function as the amyloid protein, building up within organs and disrupting organ function. Serum and urine tests are useful for evaluating amyloidosis, but tissue biopsy is the best way to diagnose the condition.

POEMS Syndrome

POEMS syndrome is poorly understood, but generally refers to **P** olyneuropathy, **O** rganomegaly, **E** ndocrinopathy, **M** protein, and **S** kin changes. Diagnosis may be made using the presence of the major criteria and one minor criteria below

- Major Criteria (both of the following)
  - Polyneuropathy
  - Monoclonal plasmaproliferative disorder
- Minor Criteria (at least one of the following)
  - Sclerotic bone lesions[6]
  - Castleman disease[6]
  - Organomegaly (splenomegaly, hepatomegaly, lymphadenopathy)
  - Edema (edema, pleural effusion, or ascites)
  - Endocrinopathy (adrenal, thyroid[7], pituitary, gonadal, parathyroid, pancreatic[7])
  - Skin changes (hyperpigmentation, hypertrichosis, plethora, hemangiomata, white nails)
  - Papilledema

[6] Osteosclerotic lesion or Castleman disease is usually present.

[7] Because of the high prevalence of diabetes mellitus and thyroid abnormalities, this diagnosis alone is not sufficient to meet this minor criterion. Dispenzieri A, Kyle RA, Lacy MQ, et al. POEMS syndrome: definitions and long-term outcome. *Blood*. 2003;101(7):2496-506.

Monoclonal gammopathy of renal significance (MGRS)

Monoclonal gammopathy of renal significance (MGRS), similar to monoclonal gammopathies of unknown significance (MGUS), represent a group of disorders in which a monoclonal immunoglobulin is secreted by a non-malignant ore pre-malignant B cell or plasma cell clone. MGRS is characterized by demonstrated renal damage

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attributable to the underlying M-protein, unlike MGUS recipients who exhibit no end-organ damage. By definition and classification criteria, these disorders differ from symptomatic myeloma and lymphoproliferative disorders. Recipients diagnosed with MGRS are at risk of developing progressive renal disease in addition to other hematologic disorders.[8]

[8]The Hematologist: ASH News and Reports. Monoclonal Gammopathy of Renal Significance. 16 Oct. 2018. Accessed at: https://www.hematology.org/Thehematologist/Ask/9059.aspx Accessibility verified on November 4, 2019.

Specifying Disease Sub-Classification

Multiple myeloma

- If the recipient's disease classification is one of the following listed below, specify heavy and / or light chain type, select all that apply. Only report more than one heavy and / or light chain if the recipient is diagnosed with bi-clonal multiple myeloma.
    - Multiple myeloma – IgG
    - Multiple myeloma – IgA
    - Multiple myeloma – IgD
    - Multiple myeloma – IgE
    - Multiple myeloma – IgM (not Waldenstrom macroglobulinemia)
    - Multiple myeloma – light chain only

Immuno-globulin-related (AL) amyloidosis

- Specify the amyloidosis classification as one of the following:
    - **AL amyloidosis** (light-chain amyloidosis): This is the most common type of amyloidosis where the abnormally folded protein is the light chain component of an immunoglobulin. Misfolded proteins can deposit in the nervous system, heart, kidneys, or digestive tract; however, they can often affect more than one organ.[9]
    - **AH amyloidosis** (heavy-chain amyloidosis): This is a rare type of amyloidosis where the abnormally folded protein is the heavy chain component of an immunoglobulin.[9]
    - **AHL amyloidosis** (heavy- and light-chain amyloidosis): This is a rare type of amyloidosis where the abnormally folded protein is composed of fragments of both the Ig heavy chain and light chain.[10]

[9] "AL Amyloidosis." Amyloidosis Foundation, http://amyloidosis.org/facts/al/.

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[10] Nasr, S. H. (2013). The diagnosis and characteristics of renal heavy-chain and heavy/light-chain amyloidosis and their comparison with renal light-chain amyloidosis. Kidney International, 83(3), 463–470. https://doi.org/10.1038/ki.2012.414

Monoclonal gammopathy of renal significance (MGRS)

- Specify the MGRS classification.
  - If the MGRS classification is **Monoclonal immunoglobulin deposition disease (MIDD)**, then the MIDD subtype must be specified.

Multiple Plasmacytomas

If the recipient has greater than one plasmacytoma but has not been diagnosed with another plasma cell disorder, select **Other plasma cell disorder** and specify how many plasmacytomas are present and if each is bone derived or extramedullary.

Plasmacytoma

- Specify the type of plasmacytoma as **Extraosseous plasmacytoma** (i.e., extramedullary) or **Solitary plasmacytoma of bone** (i.e., bone derived). Refer to the Plasma Cell Characteristics above for additional information regarding the characteristics of each type.

Other plasma cell disorder

- If the recipient's disease classification is not listed, specify the disease.

Question 508: Did the recipient have a preceding or concurrent plasma cell disorder?

Indicate if the recipient had a concurrent or preceding plasma cell disorder. Many recipients progress to symptomatic myeloma from a preceding condition or have concurrent plasma cell disorder, such as amyloidosis.

- Example 1 If a recipient has smoldering myeloma (asymptomatic) and then develops symptomatic multiple myeloma, **Multiple myeloma** should be reported as the primary diagnosis and **Smoldering myeloma** should be reported as the preceding / concurrent disorder.
- Example 2: If a recipient has smoldering myeloma (asymptomatic) and amyloidosis, **Immuno-globulin-related (AL) amyloidosis** should be reported as the primary diagnosis and **Smoldering myeloma** should be reported as the preceding / concurrent disorder.
- Example 3: If the recipient has symptomatic multiple myeloma and amyloidosis, **Multiple myeloma** should be reported as the primary diagnosis and **Immuno-**

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globulin-related (AL) amyloidosis should be reported as the preceding / concurrent disorder.

Reporting More Than One Concurrent or Preceding Disorder
Copy *Specify preceding / concurrent disorder* and *Date of diagnosis of preceding / concurrent disorder* questions to report more than one concurrent or preceding disorder.

Questions 509 – 510: Specify preceding / concurrent disorder

Indicate the preceding or concurrent disorder. See the Plasma Cell Characteristics information above for descriptions of diseases and the previous question for examples of situations with preceding or concurrent disorders. If the recipient has a preceding or concurrent plasma cell disorder that is not listed, select **Other plasma cell disorder (PCD)** and specify the type.

Question 511: Date of diagnosis or preceding / concurrent disorder

Report the date the recipient was first diagnosed with the preceding or concurrent plasma cell disorder. Enter the date the blood/urine was collected for the laboratory evaluations (e.g., serum/urine protein electrophoresis (SPEP / UPEP, respectively), or serum / urine immunofixation) or enter the date of the first pathological diagnosis (e.g., bone marrow biopsy, plasmacytoma, tissue). Enter the date the sample was collected for examination.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Questions 512 – 521: Laboratory studies at diagnosis for the disease for which the infusion is being done *(check all that apply)*

This section is only enabled if this is the *first* CIBMTR reported infusion of the primary disease for infusion.

These questions are intended to determine the clinical status of the recipient and disease staging of the primary disease for infusion at diagnosis. Select all lab values known at diagnosis. All values reported must reflect testing performed prior to the start of treatment. If labs were assessed multiple times prior to starting treatment, report the values closest to the diagnosis date.

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- **Serum calcium**: Calcium is an essential mineral for bodily functions. It is assessed to identify or monitor certain diseases (including bone, kidney, and parathyroid diseases). Hypercalcemia is common in recipients with multiple myeloma as it can cause extra bone resorption, resulting in release of calcium in excessive amounts. If known, specify the value and units of measurement as documented on the lab report.
- **Serum creatinine**: Creatinine is a normal metabolic waste that is primarily filtered from the blood by the kidneys and then excreted in the urine. Since it is generally produced at a constant rate, the clearance rate and the serum level are widely used as indicators of kidney function. If known, specify the value and units of measurement as documented on the lab report.
- **Hemoglobin**: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered “anemia” and blood transfusions, or growth factors may be required to increase the hemoglobin level. If known, specify the value and units of measurement as documented on the lab report.
- **LDH**: Lactate dehydrogenase is an enzyme found in the cytoplasm of almost all tissues, which converts L-lactate into pyruvate, or pyruvate into L-lactate depending on the oxygen level. For some diseases, high levels indicate active disease (e.g., lymphoma and multiple myeloma). If known, specify the value, units of measurement, and the upper limit of normal as documented on the lab report.
- **Serum albumin**: Serum albumin is a protein found in the blood. Levels are most often reported on a chemistry panel but may occasionally be found in a separate liver function test report. If known, specify the value and units of measurement as documented on the lab report.
- **Serum β2-microglobulin**: Serum β2 microglobulin is a protein found in the blood and urine and can also be found on the surface of various cells. If known, specify the value and units of measurement as documented on the lab report.
- **Plasma cells in peripheral blood by morphologic assessment**: Plasma cells are not typically detected in the peripheral blood; however, can appear for various reasons, including infection, certain diseases, like multiple myeloma, post-immunization. If known, report the percentage of plasma cells detected in the blood by morphologic assessment and / or the absolute number as documented and units of measurement as on the lab report.
    - If a differential was performed and the percentage of plasma cells are not listed, report **0%**.

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- If only the percentage of plasma cells is available, the absolute number of plasma cells can be determined by multiplying the percentage of plasma cells by the white blood count (WBC).

If the labs values listed above were not assessed at diagnosis or unknown if completed, select **None**.

Questions 522 – 523: Plasma cells in peripheral blood by flow cytometry

This question is only enabled if this is the *first* CIBMTR reported infusion of the primary disease for infusion.

Indicate if plasma cells in the peripheral blood by flow cytometry was known at the time of diagnosis of the primary disease for infusion. If **Known**, report the percentage of plasma cells detected in the blood by flow cytometry documented on the flow cytometry report.

If this lab was assessed multiple times prior to starting treatment, report the values closest to the diagnosis date.

Question 524: I.S.S. stage *(at diagnosis)*

This question is only enabled if this is the *first* CIBMTR reported infusion of the primary disease for infusion *and* none of the components needed to calculate the I.S.S. staging is not reported elsewhere on the Disease Classification (2402) form.

Report the recipient's I.S.S. stage of myeloma at diagnosis.

Table 1. I.S.S. Staging System for Multiple Myeloma[11]

Stage	Description
Stage 1	Serum β2-microglobulin < 3.5 mg/L and serum albumin ≥ 3.5 g/dL
Stage 2	Not fitting stage 1 or 3; serum β2-microglobulin < 3.5 mg/L and serum albumin < 3.5 g/dL OR Serum β2-microglobulin 3.5 to <5.5 mg/dL irrespective of serum albumin level
Stage 3	Serum β2-microglobulin ≥ 5.5 mg/L irrespective of serum albumin level

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[11] Greipp, P. R., San Miguel, J., Durie, B. G., Crowley, J. J., Barlogie, B., Bladé, J., … & Westin, J. (2005). International staging system for multiple myeloma. *Journal of Clinical Oncology*, 23(15), 3412-3420.

Question 525: R – I.S.S. stage *(at diagnosis)*

This question is only enabled if this is the *first* CIBMTR reported infusion of the primary disease for infusion *and* none of the components needed to calculate the R-I.S.S. staging is not reported elsewhere on the Disease Classification (2402) form.

The Revised International Staging System (R-I.S.S.) includes variables included in the original ISS (serum beta-2 microglobulin and serum albumin), while also including the additional prognostic information obtained from serum LDH and high-risk chromosomal abnormalities detected by interphase fluorescent in situ hybridization (iFISH) after CD138 plasma cell purification.[12] High risk chromosomal abnormalities identified by iFISH include:

- Deletion 17p / 17p-
- t(4;14)
- t(14;16)

Report the recipient's R-I.S.S. stage of myeloma at diagnosis.

Table 2. R-I.S.S. Staging System for Multiple Myeloma[12]

Stage	Description
Stage I	Requires all the following: • I.S.S. stage 1 • No high-risk cytogenetic abnormalities by FISH (deletion 17p / 17p-, t(4;14), t(14;16)) • Normal LDH levels
Stage II	Not R-ISS stage I or III
Stage III	Requires all the following: • I.S.S. stage 3 • High-risk cytogenetic abnormalities by FISH (deletion 17p / 17p-, t(4;14), t(14;16)) *or* high LDH levels

[12] Palumbo, A. et al (2015). Revised International Staging System for Multiple Myeloma: A Report From International Myeloma Working Group. J Clin Oncol, 33(26), 2863-9. doi: 10.1200/JCO.2015.61.

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Questions 526 – 527: Durie-Salmon stage and sub classification *(at diagnosis)*

This question is only enabled if this is the *first* CIBMTR reported infusion of the primary disease for infusion, the I.S.S. stage is not reported *and* none of the components needed to calculate the Durie-Salmon staging is not reported elsewhere on the Disease Classification (2402) form.

Indicate Durie-Salmon stage and sub classification at diagnosis. If the Durie-Salmon stage and / or sub classification is not documented in the medical record, use the table below to determine the appropriate stage.

If the Durie-Salmon stage is unknown and cannot be determined using the table below, select **Unknown**.

Table 3. Durie-Salmon Staging System for Multiple Myeloma[13]

Stage	Criteria
I	• Requires all the following: Hemoglobin > 10 g/dL Serum calcium normal (< 10.5 mg/dL) On radiograph, normal bone structure or solitary bone plasmacytoma only Low M-component production rate (IgG < 5 g/dL, IgA < 3 g/dL) • Urinary light chain M-component on electrophoresis (< 4 g/24 h)
II	Fitting neither stage I nor stage III
III	• Requires one or more of the following: • Hemoglobin < 8.5 g/dL • Serum calcium > 12 mg/dL • Advanced lytic bone lesions (three or more lytic lesions) • High M-component product rate (IgG > 7 g/dL, IgA > 5 g/dL), • Urinary light chain M-component on electrophoresis (> 12 g/24 h)

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Sub-classification	(either A or B) A: Relatively normal renal function (serum creatinine < 2.0 mg/dL) B: Abnormal renal function (serum creatinine ≥ 2.0 mg/dL)

[13] Adapted from Durie BG, Salmon SE: A clinical staging system for multiple myeloma: Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. *Cancer*. 1975;36:842-54.

Question 528: Were cytogenetics tested (karyotyping or FISH)? *(at diagnosis)*

This question is only enabled if this is the *first* CIBMTR reported infusion of the primary disease for infusion.

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality which reflects the recipient's disease.

Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate whether cytogenetic studies were performed at diagnosis. If cytogenetic studies were performed at diagnosis, check **Yes**. If cytogenetic studies were not obtained at diagnosis, or it is not known whether chromosome studies were performed, indicate **No** or **Unknown**, respectively.

Questions 529 – 530: Were cytogenetics tested via FISH? *(at diagnosis)*

Specify if FISH studies were performed at diagnosis. If **Yes**, indicate whether clonal abnormalities were detected. If FISH studies were not performed at diagnosis or FISH samples were inadequate, report **No**. If it is unknown if performed, report **Unknown**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation

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CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 531 – 533: Specify FISH abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select all cytogenetic abnormalities identified by FISH assessments at diagnosis.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Questions 534 – 535: Were cytogenetics tested via karyotyping? *(at diagnosis)*

Specify if karyotyping studies were performed at diagnosis. If **Yes**, indicate if abnormalities were detected. If the karyotype failed, select **No evaluable metaphases**.

If karyotyping studies were not performed at diagnosis or is unknown if performed, report **No** or **Unknown**, respectively.

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 536 – 538: Specify karyotype abnormalities *(at diagnosis)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select all cytogenetic abnormalities identified by karyotype at diagnosis.

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If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Questions 539 – 543: Laboratory studies at last evaluation prior to the start of the preparative regimen *(for subsequent infusion) (check all that apply)*

This question is only enabled if this is a *subsequent* infusion reported to CIBMTR for the *same* primary disease for infusion.

These questions are intended to determine the clinical status of the recipient and disease staging of the primary disease at the last evaluation prior to the subsequent infusion. Select all lab values known at the last evaluation. Do not report any values from the initial diagnosis. If labs were assessed multiple times, report the most recent values prior to the start of the preparative regimen / lymphodepleting therapy (or infusion if preparative regimen / lymphodepleting therapy was not given). Laboratory values obtained on the first date of the preparative regimen / lymphodepleting therapy may be reported as long as the sample was collected before any administration of systemic therapy or radiation.

- **Serum creatinine**: Creatinine is a normal metabolic waste that is primarily filtered from the blood by the kidneys and then excreted in the urine. Since it is generally produced at a constant rate, the clearance rate and the serum level are widely used as indicators of kidney function. If known, specify the value and units of measurement as documented on the lab report.
- **Hemoglobin**: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered "anemia" and blood transfusions, or growth factors may be required to increase the hemoglobin level. If known, specify the value and units of measurement as documented on the lab report.
- **Plasma cells in peripheral blood by morphologic assessment**: Plasma cells are not typically detected in the peripheral blood; however, can appear for various reasons, including infection, certain diseases, like multiple myeloma, post-immunization. If known, report the percentage of plasma cells detected in the blood by morphologic assessment and / or the absolute number as documented and units of measurement as on the lab report.
    - If a differential was performed and the percentage of plasma cells are not listed, report **0%**.

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- If only the percentage of plasma cells is available, the absolute number of plasma cells can be determined by multiplying the percentage of plasma cells by the white blood count (WBC).

If the labs values listed above were not assessed at the last evaluation or unknown if completed, select **None**.

Questions 544 – 545: Plasma cells in peripheral blood by flow cytometry

This question is only enabled if this is a *subsequent* infusion reported to CIBMTR for the *same* primary disease for infusion

Indicate if plasma cells in the peripheral blood by flow cytometry was known the last evaluation prior to the subsequent infusion. If **Known**, report the percentage of plasma cells detected in the blood by flow cytometry documented on the flow cytometry report.

If labs were assessed multiple times, report the most recent values prior to the start of the preparative regimen / lymphodepleting therapy (or infusion if preparative regimen / lymphodepleting therapy was not given). Laboratory values obtained on the first date of the preparative regimen / lymphodepleting therapy may be reported as long as the sample was collected before any administration of systemic therapy or radiation.

Question 546: Were cytogenetics tested (karyotyping or FISH)? *(for subsequent infusion, at last evaluation)*

This question is only enabled if this is a *subsequent* infusion reported to CIBMTR for the *same* primary disease for infusion

Cytogenetic analysis is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality which reflects the recipient's disease.

Testing methods you may see include conventional chromosome analysis (karyotyping) or fluorescence in situ hybridization (FISH). For more information about cytogenetic testing and terminology, see Appendix C.

Indicate whether cytogenetic studies were performed at the last evaluation prior to the subsequent infusion. If cytogenetic studies were performed, check **Yes**. If cytogenetic

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studies were not obtained, or it is not known whether chromosome studies were performed, indicate **No**.

Questions 547 – 548: Were cytogenetics tested via FISH? *(for subsequent infusion, at last evaluation)*

Specify if FISH studies were performed at the last evaluation prior to the subsequent infusion. If **Yes**, indicate whether clonal abnormalities were detected. If FISH studies were not performed, FISH samples were inadequate, or it is unknown if performed, report **No**.

Report chromosomal microarrays / chromosomal genomic arrays as FISH assessments.

International System for Human Cytogenetic Nomenclature (ISCN) for FISH
The International System for Human Cytogenetic Nomenclature (ISCN) compatible string is disabled for FISH and cannot be answered at this time.

Submitting FISH Documentation
CIBMTR strongly encourages attaching the FISH report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 549 – 551: Specify FISH results *(for subsequent infusion, at last evaluation)*

Report the ISCN compatible string, if applicable.

If the ISCN compatible string is not reported, then select all cytogenetic abnormalities identified by FISH assessments at the last evaluation prior to the subsequent infusion.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report “see attachment” and attach the final report(s) for any other abnormalities detected.

Questions 552 – 553: Were cytogenetics tested via karyotyping? *(for subsequent infusion, at last evaluation)*

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Specify if karyotyping studies were performed at the last evaluation prior to the subsequent infusion. If **Yes**, indicate if abnormalities were detected. If the karyotype failed, select **No evaluable metaphases**.

If karyotyping studies were not performed at the last evaluation or is unknown if performed, report **No**.

Submitting Karyotype Documentation
CIBMTR strongly encourages attaching the karyotype report when abnormalities are identified. For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 554 – 556: Specify karyotyping results *(for subsequent infusion, at last evaluation)*

Report the ISCN compatible string, if applicable. Refer to Appendix C for more information on how to report using the ISCN functionality.

If the ISCN compatible string is not reported, then select all cytogenetic abnormalities identified by karyotype at the last evaluation prior to the subsequent infusion.

If a clonal abnormality is detected, but not listed as an option, select **Other abnormality** and specify the abnormality. If multiple other abnormalities were detected, report "see attachment" and attach the final report(s) for any other abnormalities detected.

Treatment Never Given for Myeloma
If treatment was never given, then report the disease status as **No response (NR) / stable disease (SD)**.

Question 557: What was the disease status? *(at infusion)*

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. Refer to the Multiple Myeloma Response Criteria section for multiple myeloma and solitary plasmacytoma disease status definitions and Plasma Cell Leukemia Response Criteria for plasma cell leukemia disease status definitions.

Report the disease status prior to the start of the preparative regimen / lymphodepleting therapy (or infusion if no preparative regimen / lymphodepleting therapy).

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If the recipient relapsed prior to the infusion and did not receive additional therapy following the relapse, select **Relapse from CR (Rel) (untreated)**.

Treatment Never Given for Amyloidosis
If treatment was never given, then report the disease status as **No response (NR) / stable disease (SD)**.

Question 558: Specify amyloidosis hematologic response *(for Amyloid patients only) (at infusion)*

This data field is intended to capture the pre-infusion disease status, based on clinical / hematologic assessments. Refer to the Amyloidosis Response Criteria section for disease status definitions.

Report the disease status prior to the start of the preparative regimen / lymphodepleting therapy (or infusion if no preparative regimen / lymphodepleting therapy).

If the recipient relapsed prior to the infusion and did not receive additional therapy following the relapse, select **Relapse from CR (Rel) (untreated)**.

Section Updates

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

Q559 – 561: Solid Tumors

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center, and no documentation of a pathological or

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

Questions 559 – 560: Specify the solid tumor classification

CIBMTR captures the classification for solid tumors based on the World Health Organization (WHO) 2022 classification. Indicate the solid tumor disease classification at the time of diagnosis. Germ cell tumors that originate in the ovary or testes should be reported as ovarian or testicular, respectively. If the subtype is not listed, report as **Other solid tumor** and specify the reported malignancy.

If a certain disease becomes a common indication for infusion, the CIBMTR will add the disease as a separate category.

Question 561: What was the disease status? *(neuroblastoma only)*

If the primary disease for infusion is neuroblastoma, specify the disease status using the response criteria provided below:

- **Complete remission (CR)**: TBD
- **Partial response**: TBD
- **Stable disease**: TBD
- **Progressive disease**: TBD

Section Updates

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

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Q562 – 564: Severe Aplastic Anemia

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease. Enter the date the sample was collected for examination. 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 exact diagnosis date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

Questions 562 – 564: Specify the aplastic anemia classification

Indicate the aplastic anemia classification of the primary disease for infusion.

If the primary disease for infusion is any of the classifications listed below, specify the severity as either **Severe / Very Severe** or **Not Severe** at the time of diagnosis using the criteria also provided below:

- **Acquired AA, not otherwise specified**
- **Acquired AA secondary to chemotherapy**
- **Acquired AA secondary to hepatitis *(any form of hepatitis)***
- **Acquired AA secondary to immunotherapy or immune effector cell therapy**
- **Acquired AA secondary to toxin / other drug**

Severe / Very Severe or Not Severe Criteria:

- **Severe / Very Severe** Requires both of the following[1]:
    - Bone marrow cellularity < 25% (or 25% to 50% if < 30% of residual cells are hematopoietic)
      and
    - At least two of the following:
        - Peripheral blood absolute neutrophil count (ANC) < 500 / µL (<0.5 x 10^9/L)
        - Peripheral blood platelet count < 20,000 / µL
        - Peripheral blood reticulocyte count < 20,000 / µL

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- **Not severe**: Does not meet the criteria for **Severe / Very Severe**

[1] Olson, T. S. (2019, July 18). Aplastic anemia: pathogenesis, clinical manifestations, and diagnosis. UpToDate. https://www-uptodate-com/contents/aplastic-anemia-pathogenesis-clinical-manifestations-and-diagnosis?search=aplastic+anemia&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H683870569.

Select **Acquired AA secondary to chemotherapy** only when a recipient develops acquired AA after receiving chemotherapy. See example below:

- Example 1: A female recipient in her 50's was diagnosed with Stage IV breast cancer and received dose-dense chemotherapy with doxorubicin and cyclophosphamide every other week, followed by weekly Taxol. After receiving four cycles, the recipient became neutropenic requiring red blood cell and platelet transfusions. The chemotherapy was discontinued but the blood counts remained low. After three months of persistent neutropenia, the decision was made to proceed with transplant and the recipient was diagnosed with acquired AA secondary to chemotherapy.

If the classification is not listed, select **Other acquired cytopenic syndrome** and specify the other acquired cytopenic syndrome.

Section Updates

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

Q565: Inherited Bone Marrow Failure Syndromes

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of genetic / molecular testing. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center, and no

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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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date. If the exact diagnosis date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

Primary Disease for Infusion
If the recipient was diagnosed with an inherited bone marrow failure syndrome and developed MDS or AML, report the primary disease for infusion as MDS or AML, respectively.

Question 565: Specify the inherited bone marrow failure syndrome classification

Indicate the inherited bone marrow failure syndrome classification of the primary disease for infusion.

If the primary disease for infusion is not listed, select **Other inherited bone marrow failure syndrome.**

Section Updates

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

Q566 – 599: Hemoglobinopathies

Question 1: Date of diagnosis of primary disease for infusion

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Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of genetic / molecular testing. Enter the date the sample was collected for examination. 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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date.

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

Erythropoietic protoporphyria (EPP)
If the primary disease for infusion is erythropoietic protoporphyria, report the disease classification as **Other hemoglobinopathy** and specify as erythropoietic protoporphyria.

Questions 566 – 568: Specify the hemoglobinopathy classification

Indicate the hemoglobinopathy classification of the primary disease for infusion.

- **Sickle cell disease:** A group of disorders that adversely affect the body's production of hemoglobin, the component in red blood cells that delivers oxygen throughout the body. Individuals with these disorders possess atypical hemoglobin molecules, called hemoglobin "S," which can distort the red blood cell morphology into a sickle, or crescent, shape.
- **Transfusion dependent thalassemia:** Previously described as "beta thalassemia major" on CIBMTR forms. Transfusion-dependent thalassemia is a blood disorder that reduces the production of hemoglobin in the body and is defined as requiring eight or more transfusion events per year for two years or more for treatment of symptomatic anemia.

If **Transfusion dependent thalassemia** is selected, specify if the disease is **Transfusion dependent beta thalassemia** (known as "beta thalassemia major" on prior CIBMTR forms) or **Other transfusion dependent thalassemia**.

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If the recipient is diagnosed with a hemoglobinopathy other than sickle cell disease or transfusion dependent thalassemia, select **Other hemoglobinopathy** and specify the type.

Questions 569 – 571: Was tricuspid regurgitant jet velocity (TRJV) measured by echocardiography?

Tricuspid regurgitant jet velocity (TRJV) measurements are used in determining the pulmonary artery pressure for patients with hemolytic disorders. An elevated TRJV is an indication of pulmonary hypertension, a condition common in adults with hemolytic diseases. TRJV can be determined by echocardiography (ECHO); this information is typically documented in the echocardiogram report.

Report whether the TRJV was measured by echocardiography prior to the start of the preparative regimen / infusion. Seek physician clarification, as needed, if the results are unclear.

If the TRJV was measured by echocardiography, select **Yes** and indicate if the TRJV value is known. If **Known**, specify the TRJV value documented in the laboratory report. If the TRJV was measured multiple times prior to the start of the preparative regimen / infusion by an echocardiography, report the most recent value.

If the TRJV was not measured or it is not known if measured by echocardiography, report **No** or **Unknown**, respectively.

Questions 572 – 574: Was liver iron content (LIC) tested within 6 months prior to infusion?

Transfusion support for hemolytic diseases can often lead to iron build up or accumulation in the liver and other target organs. Liver iron content (LIC) is commonly used to measure total iron storage for recipients at risk of hemosiderosis. LIC is a more sensitive method of testing for measuring the level of iron in the liver. Common methods include, but are not limited to, liver biopsy, T2*MRI, and FerriScan.

Specify if the liver iron content was assessed within six months prior to the start of the preparative regimen / infusion. If **Yes**, report the value, unit of measure documented in

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the laboratory report, and the method used to estimate the LIC. If the method of assessment is not listed, select **Other**.

Report **No** if liver iron content was not assessed or it is not known if assessed within six months prior to the start of the preparative regimen / infusion.

Questions 575 – 576: Is the recipient red blood cell transfusion dependent?

Indicate if the recipient is red blood cell transfusion dependent at any time prior to the start of the preparative regimen / infusion. In this context, “red blood cell transfusion dependent” is defined as requiring transfusions to maintain hemoglobin 9 – 10 d / dL.

If the recipient the recipient was red blood cell transfusion dependent at any time prior to the start of the preparative regimen / infusion, report **Yes** and specify the year of the first transfusion (since diagnosis).

If the recipient was never red blood cell transfusion dependent at any time prior to the start of the preparative regimen / infusion or it is unknown, report **No**.

Question 577: Was iron chelation therapy given at any time since diagnosis?

Iron chelation therapy is commonly used for recipients to prevent or reduce iron overload. Iron chelation therapy is the removal of excess iron from the body using drugs such as Deferrioxamine (Desferal) or Deferasirox (Jadenu, Exjade).

Specify if iron chelation therapy was given at any time since diagnosis. If iron chelation was not given or it is unknown whether iron chelation therapy was given, select **No** or **Unknown**, respectively.

Question 578: Did iron chelation therapy meet the following criteria: initiated within 18 months of the first transfusion and administered for at least 5 days / week (either oral or parenteral iron chelation medication)

Indicate if the iron chelation therapy was initiated within 18 months of the first transfusion and administered for at least five days a week (either oral or parenteral iron chelation medication).

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If iron chelation therapy met the criteria listed above, report **Yes, iron chelation therapy given as specified**.

If iron chelation therapy was given but does not meet the specified criteria, report **No, iron chelation therapy given, but does not meet criteria**.

If iron chelation therapy was given but administration details are unavailable, report **Iron chelation therapy given, but details of administration unknown**.

Questions 579 – 580: Specify reason criteria not met

If iron chelation therapy was given but does not meet the criteria specified above, indicate why the criteria was not met. If the reason is not listed, report **Other** and specify the reason criteria were not met.

Questions 581 – 582: Year iron chelation therapy started

Indicate if the year iron chelation therapy was started is known. If **Known**, specify the year when iron chelation therapy began.

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

Questions 583 – 584: Did the recipient have hepatomegaly?

Indicate if the recipient had hepatomegaly (i.e. abnormal enlargement of the liver) at the last evaluation prior to the start of the preparative regimen / infusion. Hepatomegaly is often documented during the physician's physical assessment of the recipient and represents an abnormal finding. If **Yes**, report the liver measurement (in centimeters below the right costal margin).

If hepatomegaly was not present or is not known if it was present at the last evaluation prior to the start of the preparative regimen, select **No.**

Submitting Source Documentation
CIBMTR strongly encourages attaching the liver biopsy in FormsNet3^{SM}. For further instructions on how to attach documents, refer to the Training Guide.

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Questions 585 – 587: Was a liver biopsy performed at any time since diagnosis?

Evaluation of liver tissue may be necessary to determine the extent of the recipient's disease. Indicate if a liver biopsy was performed at any time since diagnosis.

If **Yes**, report if the assessment date was known and if **Known**, the date of the liver biopsy. If multiple liver biopsies were performed since diagnosis, report the date of the most recent biopsy.

If the date of the liver biopsy is partially known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms; check the box **Date estimated**.

If a liver biopsy was not performed or it is unknown if a biopsy was performed at any time since diagnosis, report **No**.

Question 588: Was there evidence of liver cirrhosis?

Indicate if the liver biopsy performed on the date reported above showed evidence / characteristics of liver cirrhosis. If the results are unclear, seek physician clarification.

Select **Unknown** if no information is available to determine if the biopsy showed characteristics of liver cirrhosis.

Questions 589 – 590: Was there evidence of liver fibrosis?

Indicate if the liver biopsy performed on the date reported above showed evidence / characteristics of liver fibrosis. If the results are unclear, seek physician clarification. If **Yes**, specify the type of fibrosis observed.

- **Bridging:** Bands of fibrous tissue and collagen which span portal spaces and/or centrilobular spaces creating a "bridge-like" appearance
- **Periportal:** Fibrous expansion of portal fields with fibrosis extending along the terminal portal veins
- **Other:** Select this option if the type of fibrosis present is not listed as an option.

Select **Unknown** if no information is available to determine if the biopsy showed characteristics of liver fibrosis.

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Question 591: Was there evidence of chronic hepatitis?

Indicate if the liver biopsy performed on the date reported above showed evidence / characteristics of chronic hepatitis. If the results are unclear, seek physician clarification.

Select **Unknown** if no information is available to determine if the biopsy showed characteristics of chronic hepatitis or if the results were inconclusive.

Question 592: Is there evidence of abnormal cardiac iron deposition based on an MRI of the heart at time of infusion? *(within 60 days of infusion)*

A cardiac MRI may be performed to assess cardiac iron deposition. This information is typically listed within the MRI interpretation of the report.

Indicate if cardiac MRI shows evidence of abnormal cardiac iron deposition at the time of infusion (within 60 days of infusion). If multiple MRIs were performed, report the results based on the most recent scan prior to the start of the preparative regimen / infusion.

Question 593: Did the recipient have a splenectomy?

Indicate if the recipient had a splenectomy prior to the start of the preparative regimen / infusion. If unknown, select **No**.

Laboratory studies at last evaluation
Complete the serum iron, TIBC, and total serum bilirubin questions based on the most recent testing prior to the start of the preparative regimen / infusion. Tests can be performed on different days. Laboratory values obtained on the first day of the preparative regimen may be reported as long as the sample was collected before administration of any systemic therapy or radiation.

Questions 594 – 599: Laboratory studies at last evaluation prior to start of preparative regimen *(check all that apply)*

The questions are intended to determine the clinical status of the recipient prior to the preparative regimen (or infusion if a preparative regimen was not given). Select all lab values assessed at the last evaluation prior to the start of the preparative regimen.

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- **Serum iron**: A serum iron test is used to determine how much iron is in the serum. If the serum iron level is lower than normal, it indicates the body's iron stores are low (iron deficiency). If the serum iron level is higher than normal, it could indicate hemochromatosis, a condition that causes the body to store too much iron. If the serum iron was assessed at the last evaluation, report the value and unit of measurement as documented on the lab report.
- **TIBC** (total iron binding capacity): Total iron binding capacity (TIBC) is a test used to gauge the total amount of iron in the blood. If the TIBC was assessed at the last evaluation, report the value and unit of measurement as documented on the lab report.
- **Direct bilirubin**: Also known as conjugated bilirubin. If the direct bilirubin was assessed at the last evaluation, report the value and unit of measurement as documented on the lab report.
- **Total serum bilirubin**: Bilirubin is a pigment that is formed from the breakdown of hemoglobin in red blood cells. Serum bilirubin is a test of liver function that reflects the ability of the liver to take up, process, and secrete bilirubin. Total bilirubin includes the direct (conjugated) and indirect (unconjugated) bilirubin values. If the lab reports direct and indirect separately, add the two together to report the total serum bilirubin. If the total serum bilirubin was assessed at the last evaluation, report the value, unit of measurement, and the upper limit of normal as documented on the laboratory report.

If none of the lab values listed above were assessed, select **none**.

Section Updates

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

Q600: Paroxysmal Nocturnal Hemoglobinuria (PNH)

Question 1: Date of diagnosis of primary disease for infusion

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Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of genetic / molecular / other blood testing. Enter the date the sample was collected for examination. 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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date.

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

Question 600: DID PNH co-occur with aplastic anemia?

Specify if there was a concurrent occurrence of PNH and aplastic anemia. If PNH did not co-occur or it is unknown, select **No**.

Section Updates

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

Q601 – 608: Disorders of the Immune System

Question 1: Date of diagnosis of primary disease for infusion

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Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of genetic / molecular / other blood testing. Enter the date the sample was collected for examination. 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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date.

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

Questions 601 – 603: Specify disorder of immune system classification

CIBMTR captures some classifications of the disorders of immune system using on the International Union of Immunological Societies (IUIS) 2022. Indicate the disorder of the immune system's disease classification at diagnosis. If the subtype is not listed, report as **Other SCID (with known genetic mutation)** or **Other immunodeficiency** and specify the reported disease.

If **Other SCID (with known genetic mutation)** is selected, specify any known mutations in addition to the subtype.

If a certain disease becomes a common indication for infusion, the CIBMTR will add the disease as a separate category.

Questions 604 – 605: Did the recipient have an active or recent infection with a viral pathogen within 60 days of infusion?

Viral infections are 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).

Report **Yes** if the recipient had an active or recent infection with a viral pathogen within 60 days of HCT and specify the viral pathogens causing the infection. Check all that apply.

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If the recipient did not have an active or recent infection with a viral pathogen or it is unknown, report **No**.

Question 606: Has the recipient ever been infected with PCP/PJP

PCP Pneumocystis is a common fungal infection commonly affecting the lungs. Indicate if the recipient has ever been infected with PCP/PJP.

Question 607: Does the recipient have GVHD due to maternal cell engraftment pre-infusion? *(SCID only)*

Recipients with SCID often have presence of maternal T lymphocytes (T cells) in the circulation. This is a complication that results from maternal-fetal transfusion and the failure in SCID patients to recognize and to reject foreign cells, allowing maternal T cells to engraft. This is also known as maternal engraftment. This engraftment can induce graft-versus-host disease (GVHD).

Report **Yes** if the recipient has a history of or current manifestations of GVHD due to maternal cell engraftment at the last evaluation prior to the preparative regimen and continue to signature line.

If the recipient does not have GVHD due to maternal cell engraftment pre-infusion, report **No** and submit the form.

Question 608: Was the recipient identified based on an abnormal newborn screen *(SCID only)*

SCID may be identified via a blood screen which measures a T-cell marker to identify the risk for SCID. This blood test is available as part of newborn screening. Infants are often diagnosed at birth or *in utero*.

Specify if the recipient was diagnosed with SCID based on abnormal newborn screen. If it is unknown whether the recipient was diagnosed via an abnormal newborn screen, report **Unknown**. This option should be used sparingly and only when no information exists regarding SCID screening as an infant.

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Section Updates

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

Q609 – 610: Inherited Abnormalities of Platelets

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of genetic testing. Enter the date the sample was collected for examination. 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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date.

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

Questions 609 – 610: Specify inherited abnormalities of platelets classification

Indicate the inherited abnormalities of platelets disease classification at diagnosis. If the subtype is not listed, report as **Other inherited platelet abnormality** and specify the reported disease.

If a certain disease becomes a common indication for infusion, the CIBMTR will add the disease as a separate category.

Section Updates

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

Q611 – 613: Inherited Disorders of Metabolism

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of genetic testing. Enter the date the sample was collected for examination. 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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date.

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

Questions 611 – 612: Specify inherited abnormalities of metabolism classification

Indicate the inherited abnormalities of metabolism disease classification at diagnosis. If the subtype is not listed, report as **Other inherited metabolic disorder** and specify the reported disease.

If a certain disease becomes a common indication for infusion, the CIBMTR will add the disease as a separate category.

Question 613: Report the Loes composite score *(Adrenoleukodystrophy (ALD) only)*

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The Loes composite score is often used to assess disease/progression for recipients with ALD. The Loes composite score is a rating from 0-34, this signifies the severity of abnormalities detected in the brain after evaluation of MRI. Report the Loes composite score. If the score is unknown, check with a transplant physician to determine this value.

Section Updates

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

Q614 – 619: Histiocytic Disorders

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of molecular testing. Enter the date the sample was collected for examination. 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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date.

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

Questions 614 – 616: Specify the histiocytic disorder classification

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CIBMTR captures the classification of histiocytic disorders based on the International Union of Immunological Societies (IUIS) 2022. Indicate the histiocytic disorder disease classification at diagnosis. If the subtype is not listed, report as **Other pigmentary dilution disorder** or **Other histiocytic disorder** and specify the reported disease.

If a certain disease becomes a common indication for infusion, the CIBMTR will add the disease as a separate category.

Questions 617 – 618: Did the recipient have an active or recent infection with a viral pathogen within 60 days of infusion?

Viral infections are 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). Report **Yes** if the recipient had an active or recent infection with a viral pathogen within 60 days of infusion and specify the viral pathogen causing the infection. Check all that apply.

If the recipient did not have an active or recent infection with a viral pathogen or it is unknown, report **No**.

Question 619: Has the recipient ever been infected with PCP/PJP

PCP Pneumocystis is a common fungal infection commonly affecting the lungs. Indicate if the recipient has ever been infected with PCP/PJP.

Section Updates

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

Q620 – 623: Autoimmune Diseases

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Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of molecular / autoimmune testing. Enter the date the sample was collected for examination. 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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date.

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

Questions 620 – 623: Specify autoimmune disease classification

CIBMTR captures the classification of autoimmune diseases based on the International Union of Immunological Societies (IUIS) 2022. Indicate the autoimmune disease classification at diagnosis. If the subtype is not listed, report as **Other autoimmune disease**, **Other autoimmune cytopenia**, or **Other autoimmune bowl disorder**, and specify the reported disease.

If a certain disease becomes a common indication for infusion, the CIBMTR will add the disease as a separate category.

Section Updates

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

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Q624 – 625: Tolerance Induction Associated with Solid Organ Transplant

Question 1: Date of diagnosis of primary disease for infusion

Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy). Enter the date the sample was collected for examination. 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 exact diagnosis date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

Questions 624 – 625: Specify transplanted organ *(check all that apply)*

In an effort to achieve organ tolerance and potentially avoid long term systemic immunosuppression, a recipient may receive an infusion of cells prior to a subsequent solid organ transplant. Indicate the transplanted organ, if organ is not listed, report as **Other organ** and specify.

Section Updates

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

Q626: Other Disease

Question 1: Date of diagnosis of primary disease for infusion

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Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the disease or the date of molecular / genetic testing. Enter the date the sample was collected for examination. 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 diagnosed *in utero*, report the date of birth as the diagnosis date.

For any congenital diseases, the date of birth should be reported as the diagnosis date.

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

Question 626: Specify other disease

Before using this category, check with a transplant physician to determine whether the disease can be classified as one of the listed options in the Disease Classification questions. An example of another disease is dystrophic epidermolysis bullosa (DEB).

Section Updates

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

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