CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Instructions for Acute Myelogenous Leukemia Pre-HSCT Data (Form 2010)

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

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: CIBMTRFormsManualComments@nmdp.org. Comments will be considered for future manual updates and revisions. For questions that require an immediate response, please contact your transplant center's CIBMTR liaison.

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Acute Myelogenous Leukemia Pre-HSCT Data

AML is a cancer of the blood and bone marrow. Healthy bone marrow produces immature cells (normal blasts) that then develop into white blood cells. White blood cells (neutrophils) help fight infection. In AML, the blasts do not mature normally into healthy white blood cells. Instead, the abnormal leukemic blasts reproduce rapidly, crowding out healthy white blood cells, red blood cells, and platelets that the body needs. Symptoms of AML—infections, fatigue, unusual bleeding—result from the lower-than-normal levels of these cells.

The Acute Myelogenous Leukemia Pre-HSCT Data Form is one of the Comprehensive Report Forms. This form captures AML-specific pre-HSCT data such as: the recipient's hematologic and cytogenetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HSCT treatments administered, and disease status prior to the preparative regimen.

NOTE: Cytogenetic/Cytogenetics
Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known genetic abnormality that reflects the recipient's disease. Testing/reporting methods you may see include routine chromosome analysis (karyotyping), fluorescence in-situ hybridization (FISH), or microarray comparative genomic hybridization (aCGH) testing. For more information about understanding cytogenetic testing and terminology, see Appendix R, Cytogenetic Abbreviations and Terminology.

This form must be completed for all recipients whose primary disease is reported on Form 2000, question 9, as Acute Myelogenous Leukemia (AML), Acute Nonlymphocytic Leukemia (ANLL), other acute leukemia, or atypical CML (other leukemia). If the recipient had a Myelodysplastic/Myeloproliferative Syndrome (MDS/MPS) that transformed into AML prior to transplant, both Form 2010 (Acute Myelogenous Leukemia Pre-HSCT Data) *and* Form 2014 (Myelodysplasia/Myeloproliferative Disorders Pre-HSCT Data) must be completed.

Key Fields

Accuracy of the Key Fields is essential for ensuring that:

- Data are being reported for the correct recipient.
- Transplant centers have access to their data.
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other agency.

For instructions regarding the completion of the Key Fields, see Appendix K. Key fields include all fields listed in the box found in the upper right-hand corner of the first page of the paper form, or on the "key page" in the FormsNet™ application.

Disease Assessment at Diagnosis

Question 1: What was the date of diagnosis of Acute Myelogenous Leukemia?
Report the date of the first pathological diagnosis (e.g., bone marrow biopsy) of AML. 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.

The date of diagnosis is important because the interval between diagnosis and HSCT is often a significant indicator for the recipient's prognosis post-HSCT.

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

Question 2: Was this a secondary (therapy-linked) leukemia? (*not MDS / MPS*)
Agents such as radiation or systemic therapy used to treat other diseases (e.g., Hodgkin lymphoma, non-Hodgkin lymphoma, and breast cancer) can damage the marrow and lead to a secondary malignancy, such as AML. If the diagnosis of AML is therapy-related, check "yes" and continue with question 3. If the diagnosis of AML is not therapy-related, check "no" and continue with question 10.

Do not answer this question "yes" if the recipient developed AML after an environmental exposure (e.g., exposure to benzene).

Questions 3-4: What was the recipient's prior disease (malignant or nonmalignant):

NOTE: Malignant vs. Non-malignant
Malignant diseases involve cells dividing without control, which 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. For example, a patient with rheumatoid arthritis is treated with methotrexate and then develops a secondary leukemia.

Indicate the recipient's primary disease prior to the diagnosis of AML.

If the recipient's prior disease is not listed, select "other" and specify the disease.

Question 5: What was the date of diagnosis of prior disease?
Report the date of the first pathological diagnosis (e.g., bone marrow or tissue biopsy) of the prior disease. Enter the date the sample was collected for examination. Do not report the date symptoms first appeared. This date must be prior to the AML diagnosis date entered in question 1.

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

Questions 6-9: Specify treatment(s) for prior disease
For each listed treatment, indicate "yes," "no," or "unknown." If the treatment administered was "Other treatment," specify the type of treatment given. Check all that apply; do not leave any responses blank.

NOTE:
In question 6, specify all chemotherapy drugs administered. In question 9, do *not* list individual chemotherapy drugs.

Question 10: Did the recipient have a documented antecedent hematologic disorder (preleukemia or myelodysplastic syndrome)?
AML often evolves from MDS or MPS. This transformation is typically distinguished by the percentage of blasts in the bone marrow. AML that transforms from MDS or MPS has a lower survival prognosis because of the association with unfavorable chromosomal 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, or JMML cells, accumulate in the bone marrow and interfere with the production of normal white blood cells, red blood cells, and platelets.

If there is documentation of an antecedent (prior) hematological disorder, check "yes" and continue with question 11.

If MDS is suspected, but not confirmed by documented laboratory or pathologic findings, or if there is documentation of MDS concurrent with AML, check "yes, MDS suspected and/or concurrent with AML diagnosis" and continue with question 13.

If the recipient does not have a documented antecedent hematologic disorder, check "no" and continue with question 13.

Question 11: What was the date of diagnosis of antecedent hematologic disorder?
Report the date of the first pathological diagnosis (e.g., bone marrow biopsy, laboratory results, or cytogenetic findings) of the antecedent hematologic disorder. Enter the date the sample was collected for examination. Do not report the date symptoms first appeared. If the source documentation does not include the exact pathological diagnosis date of the antecedent hematologic disorder, enter the AML diagnosis date in this field.

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

Question 12: What was the classification of hematologic disorder at diagnosis?
Indicate the classification of the hematologic disorder at diagnosis.

Table 1.
Myelodysplastic / Myeloproliferative Disorder Subtypes

CLASSIFICATION	DESCRIPTION
Refractory Anemia (RA)	• Unilineage dysplasia in >10% of red blood cell precursors (i.e., erythroid dysplasia only) • <5% blasts in the bone marrow • <15% ringed sideroblasts
Refractory Anemia with Ringed Sideroblasts (RARS)	• Unilineage dysplasia in >10% of red blood cell precursors (i.e., erythroid dysplasia only) • <5% blasts in the bone marrow • ≥15% ringed sideroblasts in the bone marrow
Refractory Anemia with Excess Blasts (RAEB-1) *WHO classification terminology:* Refractory Anemia with Excess Blasts-1 (RAEB-1)	• 5-9% blasts in the bone marrow and <5% blasts in the peripheral blood • Or, if <5% blasts in bone marrow, then there must be 2-4% blasts in the peripheral blood • No Auer rods
Refractory Anemia with Excess Blasts in Transformation (RAEB-2) *WHO classification terminology:* Refractory Anemia with Excess Blasts-2 (RAEB-2)	• Unilineage or multilineage dysplasia • 10-19% blasts in the bone marrow • And/or 5-19% blasts in the peripheral blood • Auer rods may be seen

CLASSIFICATION	DESCRIPTION
Refractory Cytopenia with Multilineage Dysplasia (RCMD)	• 2 or more blood cytopenias • Dysplasia in >10% in 2 or more myeloid lineages in bone marrow • <5% blasts in the bone marrow • No Auer rods • <15% ringed sideroblasts
Refractory Anemia with Ringed Sideroblasts with Dysplasia (RCMD-RS) *WHO classification terminology:* Refractory Anemia with Multilineage Dysplasia and Ringed Sideroblasts (RCMD-RS)	• Same criteria as RCMD except with >15% ringed sideroblasts
5q-Syndrome *WHO classification terminology:* Myelodysplastic Syndrome with Isolated Del(5q)	• Associated with macrocytic anemia often thrombocytosis, erythroblastopenia, megakaryocyte hyperplasia with nuclear hypolobation • <5% blasts in bone marrow • Deletion of part of the long arm (q arm) of chromosome 5 in bone marrow cells • No Auer rods

CLASSIFICATION	DESCRIPTION
MDS Unclassifiable, Not Otherwise Specified (MDS-U)	• MDS that cannot be classified into defined category due to one or more atypical features Examples: • <5% blasts in the bone marrow and Auer rods present • Hypocellular MDS • MDS with myelofibrosis • Megakaryocyte dysplasia with fibrosis • Refractory cytopenia with unilineage dysplasia (RCUD), or refractory cytopenia with multilineage dysplasia (RCMD) but with 1% blasts in blood • MDS with unilineage dysplasia associated with pancytopenia • Unequivocal dysplasia in <10% of cells in one or more myeloid cell lines accompanied by a chromosomal abnormality considered as presumptive evidence for a diagnosis of MDS (e.g., +8, -7, -5, etc.)
Chronic Myelomonocytic Leukemia (CMML)	• <20% blasts (myeloblasts or monoblasts) in the peripheral blood or bone marrow • >1 x10^9 /L monocytes in the peripheral blood • No Philadelphia chromosome or BCR/ABL fusion gene present • Dysplasia in one or more myeloid lineages. If dysplasia is absent or minimal, the diagnosis of CMML may still be made if other requirements are met.

CLASSIFICATION	DESCRIPTION
Chronic MPS Disorder, Not Otherwise Specified WHO classification terminology: Myeloproliferative neoplasm, unclassifiable (MPN, U)	• MPS that cannot be classified into defined category due to one or more atypical features Most cases of "Myeloproliferative neoplasm, unclassifiable" will fall into one of three groups: 1. Early stages of polycythemia vera (PV), primary myelofibrosis (PMF) or essential thrombocythemia (ET) in which the characteristics are not yet fully developed; 2. Advanced stage of MPN, in which pronounced myelofibrosis, osteosclerosis, or transformation to a more aggressive stage (i.e., increased blasts and/or dysplasia) obscures the underlying disorder; or, 3. Patients with convincing evidence of an MPN in whom a coexisting neoplastic or inflammatory disorder obscures some of the diagnostic clinical and/or morphological features.
Chronic Neutrophilic Leukemia	• WBC >25x10^9/L • Persistent neutrophilia in peripheral blood (neutrophils + bands must be >80% of WBC) • Myeloid hyperplasia in bone marrow (increased myeloid:erythroid ratio of 20:1 or greater) • Hepatosplenomegaly • Absence of the Philadelphia chromosome or BCR/ABL fusion gene

CLASSIFICATION	DESCRIPTION
Chronic Eosinophilic Leukemia and Hypereosinophilic Syndrome	• Chronic Eosinophilic Leukemia • Eosinophil count >1.5x10^9/L • 5-19% blasts in bone marrow • No Philadelphia chromosome present • Hypereosinophilic Syndrome • Elevated eosinophil count (≥1500 eosinophils/mm^3) persisting for at least six months without any known etiology • Multiple organ damage (e.g., involvement of either the heart, nervous system, or bone marrow) • No evidence of eosinophil clonality
Polycythemia Vera (PCV)	• Overproduction of erythrocytes (red blood cells) by the bone marrow Diagnostic criteria: • Increased hemoglobin (>18.5 gm/dl in men & >16.5 gm/dl in women); presence of JAK2 mutation • Bone marrow showing hypercellularity with trilineage growth (erythroid, granulocytic & megakaryocytic proliferation) • Increased platelet or white blood count • Low erythropoietin (EPO) level

CLASSIFICATION	DESCRIPTION
Chronic Idiopathic Myelofibrosis (with Extramedullary Hematopoiesis), Myelofibrosis with Myeloid Metaplasia, Acute Myelofibrosis or Myelosclerosis WHO classification terminology: Primary Myelofibrosis (PMF)	• Myeloproliferative syndrome of unknown etiology • Myeloid proliferation • Reactive fibrosis in the bone marrow • Extramedullary hematopoiesis (formation and development of blood cells outside of the bone marrow)
Essential or Primary Thrombocythemia	• Presence of persistent (overproduction of platelets) thrombocytosis >450 x 10^9/L without an alternative cause
Juvenile Myelomonocytic Leukemia (JMML, JCML, JCMML) (no evidence of Ph[1] or BCR/ABL)	All of the following: • No Philadelphia chromosome or BCR/ABL fusion gene • Peripheral blood monocytosis >1 x 10^9/L • <20% blasts in the blood and bone marrow Two or more of the following: • Hemoglobin F increased for age • Immature granulocytes and nucleated red cells in the peripheral blood • White blood cell count >1 x10^9/L • Clonal chromosomal abnormality • GM-CSF hypersensitivity of myeloid progenitors in vitro

NOTE:
If one of the first 15 options is selected for question 12, complete Form 2014 - MDS in addition to Form 2010 - AML. Form 2014 provides more detailed information on the preleukemic or myelodysplastic syndrome prior to the recipient developing AML.

If the response to question 12 is "juvenile myelomonocytic leukemia (JMML, JCML, JCMML) (no evidence of Ph[1] or BCR/ABL)," complete Form 2015 - JMML in addition to Form 2010 - AML. Form 2015 provides more detailed information on the juvenile myelomonocytic leukemia prior to the recipient developing AML.

Question 13: Did the recipient have a predisposing condition prior to the diagnosis of leukemia?
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. If the recipient has a documented history of a predisposing condition, check "yes" and continue with question 14. If there is no history of a predisposing condition, check "no" and continue with question 16.

NOTE: Aplastic Anemia and Fanconi Anemia
If the response to question 14 is Aplastic Anemia, complete Form 2028 - APL in addition to Form 2010 - AML. This form provides detailed data specific to this disease.

If the response to question 14 is Fanconi Anemia, complete Form 2029 – FAN in addition to Form 2010 – AML. This form provides detailed data specific to this disease.

Questions 14-15: Specify condition
Aplastic anemia is a condition in which the bone marrow does not produce enough new blood cells (red blood cells, white blood cells, or platelets). The cells produced are normal, but in insufficient amounts to maintain healthy numbers of blood cells.

Bloom syndrome is a chromosomal disorder that is defined by many breaks and rearrangements in the chromosomes. It is characterized by growth deficiency and skin rash following exposure to the sun. Because of the greatly elevated rate of gene mutation, Bloom syndrome patients have a high risk of developing cancer.

Down syndrome is also a chromosomal disorder. It is characterized by an additional chromosome 21, also referred to as trisomy 21. Down syndrome patients exhibit a particular set of facial characteristics, growth deficiency, and cognitive impairment. Although Down syndrome patients have a reduced risk of developing many common malignancies, they have an increased risk of developing leukemia.

Fanconi anemia is a rare genetic blood disorder that prevents the body from producing a sufficient number of new blood cells to function properly. Abnormal blood cells may also be produced. These patients are short in stature, exhibit skeletal anomalies, and have an increased risk of developing solid tumors and leukemias.

Indicate the recipient's predisposing condition prior to the diagnosis of leukemia. If the condition was "Other," specify the condition in question 15.

Laboratory Studies at Diagnosis

Report findings prior to any treatment of the primary disease for which the HSCT is being performed.

Question 16: WBC
Indicate whether the white blood count (WBC) is "known" or "not known" at the time of AML diagnosis. If "known," report the laboratory value and unit of measure documented on the laboratory report. If "not known," continue with question 17.

Question 17: Blasts in blood
Indicate whether the percentage of blasts in the peripheral blood is "known" or "not known" at the time of AML diagnosis. If "known," report the percentage documented on the laboratory report. If "not known," continue with question 18.

NOTE:
If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and "0" can be entered on the form.

The percentage of blasts in the peripheral blood may also be identified on a flow cytometry report. A flow cytometry report may be used as source documentation when reporting this data field.

Question 18: Blasts in bone marrow
Indicate whether the percentage of blasts in the bone marrow is "known" or "not known" at the time of AML diagnosis. If "known," report the percentage documented on the laboratory report at diagnosis. If "not known," continue with question 19.

NOTE:
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 states >90% blasts, packed marrow, or sheets of blasts, enter 91% on the form.

If the report states <5% blasts, enter 4% on the form.

Question 19: Was extramedullary disease present at diagnosis?
Extramedullary refers to disease found in organs or tissue outside the bone marrow or blood stream (e.g., central nervous system, testes, skin, soft tissue, etc.). Examples of extramedullary disease in AML patients include granulocytic sarcoma, subcutaneous nodules, leukemia cutis, and meningeal leukemia. If there is evidence of extramedullary disease at the time of diagnosis, indicate "yes" and continue with question 20. If there is no evidence of extramedullary disease at the time of diagnosis, indicate "no" and continue with question 25.

Questions 20-24: Specify site(s) of disease
Indicate the site of extramedullary disease. Check "yes" or "no" for each site. If site is "Other site," specify the site in question 24. Do not leave any responses blank.

Question 25: Were cytogenetics tested (conventional or FISH)?
Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. FISH is categorized with cytogenetics.

Examples of AML cytogenetic findings categorized by prognosis

Favorable	Intermediate	Poor
t(15; 17)	normal	Complex (≥3 abnormalities)
t(8; 21)	+8	5- or 5q-
inv(16) or t(16; 16)	t(9;11)	7- or 7q-
	everything else	t(9;22)

Indicate if cytogenetic studies were obtained at the time the recipient was diagnosed with AML and/or at any time prior to the start of the preparative regimen.

If cytogenetic studies were obtained, check "yes" and continue with question 26.

If cytogenetic studies were obtained but there were not adequate cells (metaphases) to determine the results, check "yes," and specify "no evaluable metaphases" in questions 26 and/or 27.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, indicate "no" or "unknown" and continue with question 91.

Question 26: Results of test at diagnosis
Indicate if any chromosomal abnormalities were identified at the time the recipient was diagnosed with AML.

If "yes abnormalities identified," continue with question 27. Also, complete questions 28-58.

If "no evaluable metaphases" or "no abnormalities," continue with question 27 and leave questions 28-58 blank.

Question 27: Results of tests after diagnosis and prior to the preparative regimen
Indicate if any chromosomal abnormalities were identified at any time after AML diagnosis and prior to the start of the preparative regimen.

If "yes abnormalities identified," complete questions 59-89.

If "no evaluable metaphases" or "no abnormalities," leave questions 59-89 blank and continue with question 90.

Questions 28-89: Specify abnormalities identified

NOTE:
If ≥3 cytogenetic abnormalities are identified **at diagnosis**, select "yes" for question 56 (*complex (≥3 distinct abnormalities))* and specify the corresponding abnormalities in questions 28-55. If any of these abnormalities are not listed among 28-55, report them in question 57 (*other abnormality*). For example, if the karyotype included -7, +8, and -13, report "yes" for questions 29 (-*7*), 35 (+*8*), 56 (*complex (≥3 distinct abnormalities)*) and 57/58 (*other abnormality, -13*).

If ≥3 cytogenetic abnormalities are identified **between diagnosis and the start of the preparative regimen**, select "yes" for question 87 (*complex (≥3 distinct abnormalities)*) and specify the corresponding abnormalities in questions 59-86. If any of these abnormalities are not listed among 59-86, report them in question 88 (*other abnormality*). For example, if the karyotype included -7, +8 and -13, report "yes" for questions 60 (*-7*), 66 (*+8*), 87 (*complex (≥3 distinct abnormalities)*), and 88/89 (*other abnormality, -13*).

Questions 28-58: Indicate "yes" or "no" for each cytogenetic abnormality identified at the time of AML diagnosis. If ≤2 distinct abnormalities are identified, and one or both of the abnormalities is/are "other abnormality," specify the abnormality or abnormalities identified in question 58. If ≥3 cytogenetic abnormalities are identified at diagnosis, refer to the "NOTE" box above. Do not leave any response blank.

Questions 59-89: Indicate "yes" or "no" for each cytogenetic abnormality identified at any time after AML diagnosis and prior to the start of the preparative regimen. If ≤2 distinct abnormalities are identified, and one or both of the abnormalities is/are "other abnormality," specify the abnormality or abnormalities identified in question 89. If ≥3 cytogenetic abnormalities are identified at any time after AML diagnosis and prior to the start of the preparative regimen, refer to the "NOTE" box above. Do not leave any response blank.

For more information regarding cytogenetic terminology and nomenclature, see Appendix R, Cytogenetic Abbreviations and Terminology.

Question 90: Is a copy of the cytogenetic or FISH report attached?
Indicate if a copy of the cytogenetic or FISH report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the cytogenetic or FISH report. Attaching a copy of the report may prevent additional queries.

Question 91: Was a flt-3 ligand mutation present at diagnosis?
FLT-3 is a protein receptor which has an important role in hematopoietic stem cell survival and proliferation. A gene mutation, expressed in the blast cells of approximately one-third of AML patients, activates FLT-3. These FLT-3 mutations result in low cure rates and high relapse rates. Indicate if an FLT-3 ligand mutation was present at the time of AML diagnosis.

NOTE:
FLT-3 mutations are identified by molecular analysis (e.g., PCR). The molecular assessment will indicate if the mutation is present. The absence of an FLT-3 mutation following a molecular assessment in which the FLT-3 mutation was previously present would indicate molecular remission.

Currently, the only genetic mutation the CIBMTR collects for AML is FLT-3. This is a recognized limitation and the addition of other genetic mutations, such as C-KIT, is under consideration.

Pre-HSCT Treatment for Acute Myelogenous Leukemia

When submitting the paper version of the form for more than two lines of therapy, copy the "Pre-HSCT for Acute Myelogenous Leukemia" section and complete a "Line of Therapy" section for each line of therapy administered. The FormsNet™ application allows multiple lines of therapy to be reported. Complete a "Line of Therapy" section for each line of therapy administered prior to the start of the preparative regimen.

Question 92: Was therapy given between diagnosis and the start of the preparative regimen?
Indicate if the recipient received treatment for AML after the time of diagnosis and before the start of the preparative regimen. If "yes," continue with question 93. If "no", continue with question 151.

Questions 93 & 122: Purpose of therapy
The first cycles of chemotherapy are called induction chemotherapy. Recipients usually have one or two cycles of induction chemotherapy. The goal is to bring the disease into remission. Induction therapy usually lasts one week, followed by three or more weeks for the patient to recover from the treatment. The second phase of chemotherapy is often called consolidation chemotherapy. The goal of consolidation chemotherapy is to destroy any remaining leukemia cells and sustain remission. Maintenance chemotherapy may follow consolidation chemotherapy and is given in lower doses to assist in prolonging a remission. Treatment may also be administered for relapse of disease after a remission is achieved.

Indicate the purpose of the therapy administered between the time of AML diagnosis and the start of the preparative regimen.

Questions 94 & 123: Systemic/Intrathecal Therapy
Systemic therapy is delivered to the whole body and may be injected into a vein or given orally. These drugs enter the bloodstream and reach all areas of the body. Intrathecal therapy is administered through an injection into the space around the spinal cord, or spinal canal.

Indicate "yes" if the therapy administered was systemic or intrathecal, and continue with question 95 or 124.

Indicate "no" if the therapy administered was not systemic or intrathecal, and continue with question 112 or 141.

Questions 95 & 124: Date therapy started
Enter the first date the recipient received the line of therapy.

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 96 & 125: Date therapy stopped
Enter the last date the recipient received the line of therapy.

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 97 & 126: Number of cycles
Chemotherapy is usually administered in cycles, with rest periods between them. This enables the attack of cancer cells at vulnerable times and provides healthy cells adequate time to recover from the damage. A cycle can last one or more days, and may repeat weekly, bi-weekly, or monthly. A chemotherapy course may consist of multiple cycles. Enter the number of chemotherapy cycles the recipient received during the line of therapy being reported, or check "unknown/not applicable."

Questions 98-111 & 127-140: Treatment
Chemotherapy treatments vary based on protocol and may be administered in inpatient or outpatient settings. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. Indicate "yes" or "no" for each chemotherapy treatment drug administered for the line of therapy being reported. Do not leave any responses blank. If the recipient received a chemotherapy treatment that is not listed, check "yes" for "other chemotherapy" and specify the treatment in question 111 or 140.

NOTE: Reporting Cytarabine doses (Questions 99, 100 and 128, 129)
In some cases the dose of cytarabine administered for treatment may not be available. Generally, if cytarabine is given for induction therapy, it is administered in doses ≤2g/m^2/day. If cytarabine is given for consolidation therapy, it is often administered in doses >2g/m^2/day.

NOTE: Reporting Intrathecal Therapy (Questions 106 and 135)
Any intrathecal therapy administered as part of a pre-HSCT line of therapy should be reported only in the "intrathecal therapy" category (Q106/Q135) and not in its corresponding drug category. For example, if intrathecal Ara-C is administered as part of a pre-HSCT line of therapy, questions 99-100 or 128-129 are answered "no", and question 106 or 135 is answered "yes." If intrathecal methotrexate is administered as part of a pre-HSCT line of therapy, question 110 or 139 is answered "no", and question 106 or 135 is answered "yes."

Questions 112 & 141: Radiation Therapy
Radiation therapy utilizes high-energy radiation to kill cancer cells. For AML, external-beam radiation is the type of radiation used most frequently. In this method, a beam of radiation is delivered to a specific part of the body. Radiation is used to treat leukemia that has spread to the brain, spinal fluid, or testicles, or to reduce pain in a bone area that has been invaded by leukemia. Indicate if the recipient received radiation therapy between the time of diagnosis and the start of the preparative regimen. If "yes," continue with question 113 or 142. If "no," continue with question 118 or 147.

Questions 113 & 142: Date therapy started
Enter the date the line of radiation therapy began.

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 114 & 143: Date therapy stopped
Enter the date the line of radiation therapy ended.

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 115 & 144: Central nervous system
As stated above, radiation therapy may be used to treat leukemia that has spread to the brain or spinal cord. Indicate if the recipient received radiation therapy to the central nervous system.

Questions 116-117 & 145-146: Other site
Radiation may also be utilized to shrink a tumor pressing on the trachea, reduce pain in an area of bone in which leukemic cells are evident, or treat leukemia that has spread to the testicles. Indicate if the recipient received radiation therapy to any site other than the central nervous system. If "yes," specify the site.

Questions 118 & 147: Best response to line of therapy
Complete hematologic response (CR) criteria are as follows:

A treatment response where **all** of the following criteria are met for at least four weeks:

- <5% blasts in the bone marrow
- Normal maturation of all cellular components in the bone marrow
- No blasts with Auer rods
- No extramedullary disease (e.g., central nervous system or soft tissue involvement)
- ANC of >1,000/µL

- Platelets ≥100,000/µL
- Transfusion independent

Include recipients with persistent cytogenetic or molecular testing abnormalities who otherwise meet all criteria of hematologic CR. Do not include recipients with extramedullary disease. They should be considered to have persistent disease, or to be in relapse.

Indicate the recipient's best response to the line of therapy being reported.

Questions 119 & 148: Date response established
Enter the date the best response to the line of therapy was established. Report the date of the pathological evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for examination for pathological and/or laboratory evaluations. If the recipient was treated for extramedullary disease and a radiological assessment (e.g., X-ray, CT scan, MRI scan, PET scan) was performed to assess disease response, enter the date the imaging took place for radiologic assessments. If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically assessed the recipient's response.

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 120 & 149: Did the recipient relapse following this line of therapy?
Relapse is the recurrence of disease after CR. AML relapse is demonstrated by one or more of the following findings:

- >5% blasts in the marrow and/or peripheral blood
- Extramedullary disease evident upon radiographic examination
- Reappearance of cytogenetic abnormalities and/or molecular markers associated with the diagnosis that, in the judgment of a physician, are at a level representing relapse
- Disease presence determined by a physician upon clinical assessment at an office visit

Indicate if relapse occurred following the line of therapy being reported.

Questions 121 & 150: Date of relapse
Enter the assessment date that relapse was established following the line of therapy. Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for examination for pathological and laboratory evaluations. If extramedullary disease is detected upon radiographic examination (e.g., 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 of sample collection 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 described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 151: Did the recipient have central nervous system leukemia at any time between diagnosis and the start of the preparative regimen?
Central nervous system leukemia is a disease of the membranes that surround the brain and spinal cord, or leptomeninges. Indicate if the recipient had central nervous system leukemia at any time between the AML diagnosis and prior to the start of the preparative regimen.

Laboratory Studies Prior to the Start of the Preparative Regimen

These questions are intended to determine the hematological status of the recipient prior to the preparative regimen. Testing may be performed multiple times within the 30 days prior to the preparative regimen, report the most recent laboratory value. 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.

Question 152: WBC
Indicate whether the white blood count (WBC) is “known” or “not known” just prior to the start of the preparative regimen. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “not known,” continue with question 153.

Question 153: Blasts in blood
Indicate whether the percentage of blasts in the peripheral blood is “known” or “not known” just prior to the start of the preparative regimen.

If “known,” report the percentage documented on the laboratory report. If “not known,” continue with question 154.

NOTE:
If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.

The percentage of blasts in the peripheral blood may also be identified on a flow cytometry report. A flow cytometry report may be used as source documentation when reporting this data field.

Question 154: Blasts in bone marrow
Indicate whether the percentage of blasts in the bone marrow is "known" or "not known" at diagnosis.

If "known," report the percentage documented on the laboratory report at diagnosis. If "not known," continue with question 156.

NOTE:
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 states >90% blasts, packed marrow, or sheets of blasts, enter 91% on the form.

If the report states <5% blasts, enter 4% on the form.

Question 155: Date of marrow examination
Enter the date of the bone marrow examination, just prior to the start of the preparative regimen, from which the percentage of blasts is reported. 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.

Disease Status at the Last Assessment Prior to the Preparative Regimen

Question 156: What was the disease status based on hematological test results at the last evaluation prior to the preparative regimen?
Indicate the disease status of AML at the last evaluation prior to the start of the preparative regimen.

If "1st complete remission (no previous marrow or extramedullary relapse)," "2nd complete remission," or "≥3rd complete remission" is indicated, continue with question 157.

If "primary induction failure," "1st relapse," "2nd relapse," or "≥3rd relapse" is indicated, continue with question 159.

If "no treatment" is indicated, continue with question 166.

Disease Status	Definition
No Treatment	The recipient was diagnosed with acute leukemia and never treated. For example, this disease status may be appropriate if MDS was initially diagnosed and treated, the MDS then transformed into AML, and a decision was made to proceed immediately to transplant instead of treating the AML with therapy.
Primary Induction Failure (PIF)	The recipient was treated for acute leukemia, **but never achieved complete remission (CR)** with any therapy. PIF is not limited to the number of treatments used unsuccessfully. This status only applies to recipients who have **never** been in CR.
Complete Remission (CR)*	A treatment response where **all** of the following criteria are met for at least four weeks:** • <5% blasts in the bone marrow • Normal maturation of all cellular components in the bone marrow • No blasts with Auer rods • No extramedullary disease (e.g., central nervous system or soft tissue involvement) • ANC of >1,000/µL • Platelets ≥100,000/µL • Transfusion independent **In some cases, there may not be a four-week interval between the completion of treatment for disease and the disease assessment immediately prior to the HSCT. If this is the case, CR should still be reported as the status at transplant. Although this is an exception to the general condition that CR is "durable" beyond four weeks, the status of CR represents the "best assessment" prior to HSCT. **The pre-HSCT disease status should not be changed based on early relapse or disease assessment post-HSCT.** Report that the recipient is in CR at the time of transplant no matter how many courses of therapy it may have taken to achieve that CR. Include recipients with persistent cytogenetic or molecular abnormalities who otherwise meet all the criteria of CR. The cytogenetic abnormality should be reported in the appropriate section (see question 25).

Disease Status	Definition
Complete Remission (CR)* (cont.)	Do not include recipients with extramedullary disease. They should be considered to have persistent disease or to be in relapse. **NOTE: Recipients with MDS that transformed to AML** If the recipient has residual MDS following treatment for AML, report the AML disease status as either PIF or relapse (i.e., the recipient cannot be in an AML CR if there is evidence of MDS at the time of assessment). **For hematologic CR** Hematologic CR includes all the criteria listed for CR above. For recipients who achieve a hematologic CR, indicate in questions 157-158 if the response also qualified as a cytogenetic or molecular remission.
Relapse	Recurrence of disease after CR. Relapse is defined as one or more of the following: • >5% blasts in the marrow or peripheral blood • Extramedullary disease • Reappearance of cytogenetic abnormalities and/or molecular markers associated with the diagnosis that, in the judgment of a physician, are at a level representing relapse **Relapse Number** The number of this relapse can be determined using the following guidelines: • **1st relapse:** one prior complete remission • **2nd relapse:** two prior complete remissions • **3rd or higher:** three or more complete remissions followed by relapse **Do not include a partial response (PR) when calculating the number of relapses.** Recipients who achieve a PR to treatment should be reported as either PIF (if never in CR previously) or relapse. PR in AML is generally of short duration and unlikely to predict clinical benefit.

*Sources of disease response definitions:
1) www.uptodate.com
2) http://www.cancer.gov/
3) www.jco.ascopubs.org Cheson vol. 21 number 24 pp4642-4649

Question 157: Was the recipient in cytogenetic remission?
Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

Cytogenetic remission is a treatment response where **all** of the following criteria are met:

- The karyotype reverts to normal
- There are no clonal chromosomal abnormalities detected in the blood and/or marrow

If chromosomal abnormalities associated with the recipient's disease were identified previously and the criteria above were met at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If chromosomal abnormalities associated with the recipient's disease were identified at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies

- If chromosomal abnormalities associated with the recipient's disease were not identified previously and no chromosomal abnormalities were identified at the last evaluation prior to the start of the preparative regimen, indicate "unknown."
- If chromosomal abnormalities associated with the recipient's disease were identified previously, but no cytogenetic assessment was performed prior to the start of the preparative regimen, indicate "unknown."
- If no cytogenetic assessments were performed, indicate "unknown."

Question 158: Was the recipient in molecular remission?
Molecular assessment involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection, and can indicate known genetic abnormalities. RFLP testing (with PCR amplification) is an example of a molecular test method.

Molecular remission is a treatment response in which no minimal residual disease in the blood and/or marrow can be detected by molecular testing methods (e.g., PCR).

If a molecular marker associated with the recipient's disease was identified previously, but cannot be detected by molecular testing methods at the last evaluation prior to the start of the preparative regimen, indicate "yes."

If a molecular marker associated with the recipient's disease was identified by molecular testing methods at the last evaluation prior to the start of the preparative regimen, indicate "no."

Indicate "unknown" if one of the following applies:

- If a molecular marker associated with the recipient's disease was not identified previously and no disease-related molecular markers were identified at the last evaluation prior to the start of the preparative regimen.
- If a molecular marker associated with the recipient's disease was identified previously, but no molecular assessment was performed prior to the start of the preparative regimen.
- If no molecular assessments were performed.

Continue with question 166.

Questions 159-165: Specify site(s) of active leukemia immediately prior to the preparative regimen

NOTE: Flow Cytometry
Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data can be reported in Q161.

Indicate "yes" or "no" for each site. Do not leave any responses blank. If "yes" is indicated for "other site," specify the site.

Question 166: Date of most recent assessment for disease status prior to the preparative regimen
Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. Report the date of the pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for examination for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments. If no pathological, radiographic, or laboratory assessment was performed within one month prior to transplant, report the most recent office visit in which the physician assessed the recipient's disease status.

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

Question 167: Signed
The person completing the form must sign the form; print his/her name, and provide a phone number, fax number, and e-mail address where he/she can be reached.