

2011: ALL Pre-HCT

The Acute Lymphoblastic Leukemia Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures ALL-specific pre-HCT 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-HCT treatments administered, and disease status prior to the preparative regimen.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track and whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as Acute Lymphoblastic Leukemia (ALL). Recipients with precursor B-cell or precursor T-cell Lymphoblastic Lymphoma should be reported as precursor B-cell or precursor T-cell Acute Lymphoblastic Leukemia.

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype and **this baseline disease insert was not completed for the previous transplant** (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1.

If this is a report of a second or subsequent transplant for a **different disease** (e.g., patient was previously transplanted for a disease other than Acute Lymphoblastic Leukemia), begin the form at question 1.

If this is a report of a second or subsequent transplant for the **same disease and this baseline disease insert has previously been completed**, check the indicator box and continue with question 98.

[Q1-10: Disease Assessment at Diagnosis](#)

[Q11-57: Laboratory Studies at Diagnosis](#)

[Q58-97: Pre-HCT Therapy](#)

[Q98-149: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen](#)

[Q150-157: Disease Status at the Last Evaluation Prior to the Start of the Preparative Regimen](#)

Manual Updates:

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

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

| Date | Manual Section | Add/ Remove/ Modify | Description |
|-----------------|--|---------------------------|--|
| 2/ 24/ 17 | Comprehensive Disease- Specific Manuals | Modify | Updated explanations of triggers for disease inserts to refer to the primary disease reported on the Pre-TED Disease Classification Form (Form 2402) instead of the Pre-TED Form (Form 2400) |

Q1-10: Disease Assessment at Diagnosis

Question 1: What was the date of diagnosis?

Report the date of the first pathological diagnosis (e.g., bone marrow biopsy, CSF evaluation) of ALL. 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 HCT is often a significant indicator for the recipient's prognosis post-HCT.

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

Question 2: Did the recipient have a predisposing condition prior to the diagnosis of ALL?

A predisposing condition is a condition that makes the patient more susceptible to developing leukemia. The diagnosis of this kind of condition indicates an increased likelihood that the recipient will develop leukemia. If the recipient has a documented history of a predisposing condition, check "yes" and continue with question 3. If there is no history of a predisposing condition or predisposition is unknown, indicate "no" or "unknown" and continue with question 5.

Questions 3-4: Specify condition

Aplastic anemia is an acquired or inherited disorder of the bone marrow characterized by pancytopenia, where the body does not produce a sufficient number of new blood cells. Inherited aplastic anemias include Fanconi anemia (specified separately on this form), Shwachman-Diamond anemia, Diamond-Blackfan anemia, and dyskeratosis congenita. Acquired aplastic anemia may develop after exposures to toxins, radiation, and/or chemotherapy, or may result from an autoimmune condition such as systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA). The majority of presenting signs and symptoms in aplastic anemia patients are directly related to their low blood counts and include fatigue, dizziness, shortness of breath, abnormal bleeding or bruising, and frequent infections.

Bloom syndrome is an autosomal recessive genetic disorder characterized by excessive chromosome breakage and corresponding chromosomal rearrangements. It is characterized by proportional dwarfism and sun sensitivity. The chromosomal instability seen in Bloom syndrome is generally assumed to be responsible for these individuals' predisposition to malignancy.

Down syndrome, a chromosomal disorder often referred to as trisomy 21, is characterized by an additional chromosome 21. Down syndrome patients exhibit characteristic facial features, 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 in which the body does not produce enough 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 leukemia.

Neurofibromatosis type 1, also known as von Recklinghausen disease, is an autosomal dominant genetic disorder characterized by the mutation of chromosome 17 resulting in the inactivation of the NF1 gene. This results in abnormal growth and proliferation of neural crest cells. Patients with neurofibromatosis type 1 often have multiple neurofibromas (benign neural tumors), skeletal abnormalities, café au lait spots, Lisch nodules, freckling in the axilla or groin, and/or optic nerve glioma. Patients with biallelic inactivation of NF1 may have an increased risk of developing malignant neoplasms, including rhabdomyosarcoma, pheochromocytoma, and, in children, myelodysplastic syndrome and acute leukemia.

Indicate the recipient's predisposing condition prior to the diagnosis of leukemia. If ALL arose from aplastic anemia or Fanconi anemia, also complete the associated baseline disease inserts (CIBMTR forms 2028 or 2029, respectively). If the condition was "other," specify the condition in question 4.

Question 5: Was extramedullary disease present?

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 ALL patients include nodal, testicular, or CNS involvement, or lymphoblastic mass. If there is evidence of extramedullary disease at the time of diagnosis or at any time prior to initiation of treatment, indicate "yes" and continue with question 6. If there is no evidence of extramedullary disease at the time of diagnosis, indicate "no" and continue with question 11. If the status of extramedullary sites at the time of diagnosis is unknown, indicate "unknown" and continue with question 11.

Questions 6-10: Specify site(s) of disease

Indicate all sites of extramedullary disease. If question 5 was answered "yes," then every question 6-9 must be answered as "yes" or "no." Do not leave any response blank. If "other" site of extramedullary disease was present, specify in question 10.

Q11-57: Laboratory Studies at Diagnosis

Report findings at the time of diagnosis. If multiple studies were performed prior to beginning therapy, report the latest values prior to the start of treatment.

Questions 11-13: WBC

Indicate whether the white blood count (WBC) was “known” or “unknown” at the time of ALL diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 12; indicate the date the sample was collected in question 13. If “unknown,” continue with question 14.

Questions 14-16: Blasts in blood

Indicate whether the percentage of blasts in the peripheral blood was “known” or “unknown” at the time of ALL diagnosis. If “known,” report the percentage documented on the laboratory report in question 15; indicate the date the sample was collected in question 16. If “unknown,” continue with question 17.

✿ 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.

! Blast counts obtained by flow cytometry should be reflected under the flow cytometry data fields; only report percentage blasts as determined by peripheral blood differential.

Questions 17-19: Blasts in bone marrow

Indicate whether the percentage of blasts in the bone marrow was “known” or “unknown” at the time of ALL diagnosis. If “known,” report the percentage documented on the laboratory report in question 18; indicate the date the sample was collected in question 19. If “unknown,” continue with question 20.

✿ 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%.

Question 20: Were cytogenetics tested (conventional or FISH)?

Cytogenetic analysis 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 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 time the recipient was diagnosed with ALL or prior to the start of treatment.

If cytogenetic studies were obtained, check "yes" and continue with question 21.

If cytogenetic studies were not obtained or it is unknown if chromosome studies were performed, indicate "no" or "unknown" and continue with question 51.

Question 21: Date sample collected

Report the date the sample was collected for cytogenetic or FISH testing. If multiple studies were performed prior to the start of therapy, report the last assessment before the start of treatment.

Question 22: Results of test

If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), indicate "abnormalities identified" and continued with question 23.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 51.

Questions 23-49: Specify abnormalities

If question 22 indicates that abnormalities were identified, every question 23-48 must be answered as "yes" or "no." Do not leave any response blank. Indicate "yes" for each cytogenetic abnormality identified at diagnosis or prior to the start of first therapy; indicate "no" for all options not identified on cytogenetic assessment at diagnosis or prior to the start of first therapy. If one or more abnormalities are best classified as "other abnormality," specify in question 49.

If ≥ 3 cytogenetic abnormalities are identified at the time of ALL diagnosis or prior to the start of first therapy, select "yes" for question 47 (complex, ≥ 3 distinct abnormalities) and specify the corresponding abnormalities in questions 23-46. If any of these abnormalities are not listed in questions 23-46, report "other abnormality," and specify in question 49. For example, if the karyotype included 7, +8, and 13, report

“yes” for questions 23, 25, 47, and 48/49. Answer the remaining questions “no,” and do not leave any response blank.

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

| Favorable | Intermediate | Poor | Very Poor |
|--|--|--|---|
| High hyperdiploidy (51-65 chromosomes) | Normal 11a abnormalities del(6q) del(17p) del(9p) del(12p) -13/del(13q) t(14q32) t(10;4) Low hyperdiploidy (47-50 chromosomes) Tetraploidy (>80 chromosomes) | -7/del(7p) +8 11q23 abnormalities/ MLL t(1;19) t(17;19) t(5;14) t(9;22) | ≥ 5 abnormalities t(4;11) t(8;14) |

¹ Pullarkat V, Slovak ML, Kopecky KJ, Forman SJ, and Appelbaum FR. (2008). Impact of cytogenetics on the outcome of adult acute lymphoblastic leukemia: results of Southwest Oncology Group 9400 study. *Blood*, 111(5), 2563-2572.

Question 50: Was documentation submitted to the CIBMTR (e.g., cytogenetic or FISH report)?

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 51: Were tests for molecular markers performed (e.g., PCR)?

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

Indicate if molecular studies were obtained at the time the recipient was diagnosed with ALL or prior to the start of treatment.

If molecular studies were obtained, check “yes” and continue with question 52.

If molecular studies were not obtained or it is unknown if molecular studies were performed, indicate “no” or “unknown” and continue with question 58.

Question 52: Date sample collected

Report the date the sample was collected for molecular testing.

Questions 53-56: Specify abnormalities

If question 51 indicates that molecular markers were identified, then every question 53-55 must be answered as “positive,” “negative,” or “not done.” Do not leave any response blank. If question 55 is answered “positive,” use question 56 to specify the molecular marker identified. Duplicate questions 55-56 if more than one “other molecular marker” is identified.

Table 2. Common Molecular Markers Associated With ALL

| Molecular Abnormality | Characteristics |
|----------------------------|---|
| BCR-ABL | BCR-ABL, <i>aka</i> Philadelphia chromosome, refers to the tyrosine kinase gene fusion resulting from the translocation of material from chromosome 9 (ABL) onto chromosome 22 (BCR). Molecular weight varies depending on exact location of the translocation; isoform p190 is typically seen in ALL. Tyrosine kinase inhibitor therapies such as imatinib mesylate (GLEEVEC) target and block ABL from fusing with BCR. Presence of the BCR-ABL gene fusion is associated with poorer outcomes. ² |
| TEL-AML/.AML1 ³ | TEL-AML1, <i>aka</i> ETV6-RUNX1, is a fusion gene resulting from translocation of chromosomes 12 and 21. It is the most common fusion gene seen in childhood precursor B-cell ALL. Research in murine models shows that cell lines expressing TEL-AML1 proliferate more slowly than the non-expressing cell lines, but evade inhibition of proliferation typically regulated by tissue growth factor β (TGF- β), ultimately leading to the growth of the leukemic cell population. TEL-AML1 is considered a favorable prognostic indicator. ⁴ |
| Other Molecular Marker | Assessments for other molecular markers known or believed to be associated with ALL may be performed. If these studies are performed, indicate “yes” and specify in question 56. |

² Wassmann B, Pfeifer H, Scheuring UJ, et al. (2004). Early prediction of response in patients with relapsed or refractory Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL) treated with imatinib. *Blood*, 103(4), 1495-1498.

³ Ford AM, Palmi C, Bueno C, et al. (2009). The TEL-AML1 leukemia fusion gene dysregulates the TGF- β pathway in early B lineage progenitor cells. *Journal of Clinical Investigation*, 119(4), 826-836.

⁴ Jamil A, Kahwash S, Ruymann FB, Klopfenstein KJ. (2000). TEL/AML-1 fusion gene: its frequency and prognostic significance in childhood acute lymphoblastic leukemia. *Cancer Genetics and Cytogenetics*, 122(2), 73-78.

Question 57: Was documentation submitted to the CIBMTR?

Indicate if a copy of the molecular report(s) is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the molecular report. Attaching a copy of the report may prevent additional queries.

Q58-97: Pre-HCT Therapy

Question 58: Was central nervous system prophylaxis given?

CNS therapy may be administered prophylactically to prevent the spread of leukemia into the central nervous system. This therapy often includes brain and spinal cord irradiation and/or intrathecal chemotherapy and is given prior to any evidence of leukemic infiltrate into the central nervous system. If the recipient received CNS prophylaxis to prevent the spread of leukemia into the central nervous system prior to HCT, indicate “yes” and continue with question 59. If “no,” or “unknown” continue with question 65. Therapy given as treatment for CNS disease should be specified in questions 65-96.

Questions 59-64: Specify CNS prophylaxis

Indicate which CNS therapies were used to prevent the spread of leukemia into the central nervous system. These treatments must have occurred prior to the start of the preparative regimen. Indicate “yes” or “no” for each therapy listed. Do not leave any response blank. High dose methotrexate is defined as $\geq 500 \text{ mg/m}^2$, typically administered over 4 to 36 hours and followed by leucovorin rescue. If the patient received a therapy that is not listed, check “yes” for “other prophylaxis” and use question 64 to specify the treatment given.

Question 65: Was therapy given?

Indicate if the recipient received treatment for ALL after the time of diagnosis and before the start of the preparative regimen. If “yes,” continue with question 66. If “no,” continue with question 97.

Question 66: Purpose of therapy

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

The first phase of chemotherapy, induction therapy, is 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.⁵

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 chemotherapy may follow consolidation therapy. Maintenance chemotherapy is given in lower doses and is intended to prolong remission. Maintenance therapy is used less commonly for the treatment of ALL than other malignancies and has not been shown to improve outcomes.

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 at that point 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.

⁵ Gaynon PS, Desai AA, Bostrom BC, et al. (1997). Early response to therapy and outcome in childhood acute lymphoblastic leukemia: a review. *Cancer*, 80(9), 1717-1726.

Question 67: Systemic therapy

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body.

Intrathecal therapy, administered via injection into the spinal subarachnoid space, reaches the cerebral spinal fluid and acts on the central nervous system.

Indicate “yes” if the patient received systemic or intrathecal therapy and continue with question 68. If the patient did not receive systemic or intrathecal therapy, indicate “no” and continue with question 85.

Questions 68-69: Date therapy started

Indicate “known” if the therapy start date is documented and use question 69 to specify the first date of systemic therapy administration. If the date is unknown, indicate this and continue with question 70.

Questions 70-71: Date therapy stopped

Indicate if the date therapy stopped is “known” or “unknown.” If the date of therapy completion is documented, mark “known” and use question 71 to specify the date therapy stopped. If the patient is receiving systemic therapy in cycles, specify the first day of the last cycle of systemic therapy. If the patient is receiving a single line or single administration, indicate the last day systemic therapy was administered.

If the date is unknown, indicate this and continue with question 72.

Questions 72-73: Number of cycles

Indicate if the number of cycles is “known” or “unknown.” If the number of cycles is known, continue with question 73 and specify the number of cycles of chemotherapy administered. If the patient received a single administration or one line of chemotherapy, indicate a single cycle. If the patient received long-term maintenance therapy consisting of a single agent, such as imatinib mesylate (GLEEVEC) therapy, indicate “unknown” for question 72; the number of cycles is not applicable in this situation.

If the number of cycles is unknown, continue with question 74.

Questions 74-84: Specify systemic or intrathecal therapy agents

Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Drugs may be administered in an inpatient or outpatient setting, and treatment may consist of one or multiple drugs. Additionally, drugs may be administered on a single day, over consecutive days, or continuously.

Indicate “yes” or “no” for each systemic therapy agent administered for the line of therapy being reported. Do not leave any response blank. If the recipient received a cytotoxic or chemotherapeutic agent, indicate “yes” for question 76. If the patient received a systemic therapeutic agent that is not listed, check “yes” for “other systemic therapy” and specify the treatment in question 84.

 Any intrathecal therapy administered as part of a pre-HCT line of therapy should be reported only in the “intrathecal therapy” category (question 80) and not in its corresponding drug category (generally “chemotherapy,” question 76). For example, if intrathecal methotrexate is administered as part of a pre-HCT line of therapy and the patient does not receive systemic cytotoxic agents, question 76 is answered “no,” and question 80 is answered “yes.” It is not necessary to specify the intrathecal agent in question 84.

Question 85: Radiation therapy

Radiation therapy uses high-energy ionizing radiation to “kill” malignant cells; however, much like non-targeted systemic therapy, radiation therapy does not specifically target malignant cells and does have significant side effects. For that reason, high-dose radiation often targets a limited field. Radiation therapy may be used in the treatment of ALL. It is generally reserved for the treatment of brain, spinal fluid, or testicular involvement.

Indicate if the recipient received radiation treatment for ALL after the time of diagnosis and before the start of the preparative regimen. If “yes,” continue with question 86. If “no,” continue with question 93.

Questions 86-87: Date therapy started

Indicate “known” if the radiation therapy start date is documented and continue with question 87 to specify the first date of radiation administration. If the date is unknown, indicate this and continue with question 88.

Questions 88-89: Date therapy stopped

Indicate “known” if the radiation therapy completion date is documented and continue with question 89 to specify the last date of radiation administration. If the date is unknown, indicate this and continue with question 90.

Questions 90-92: Specify site(s) of radiation therapy

Indicate “yes” or “no” for each radiation site. Do not leave any response blank. Question 90 asks if radiation was delivered to the central nervous system, which consists of the brain and spinal cord. If the recipient received radiation to any other site, indicate “yes” for question 91 and specify the site in question 92.

Question 93: Best Response to Line of Therapy

Complete hematologic response (CR) is 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 extramedullary disease (e.g., central nervous system or soft tissue involvement)
- ANC > 1,000/ μ L
- Platelets \geq 100,000/ μ L
- Transfusion independent

Include recipients with persistent cytogenetic or molecular testing abnormalities who otherwise meet all criteria of hematologic CR. Recipients with persisting extramedullary disease are not considered to be in CR.

Indicate if the patient’s best response to this line of therapy was a complete remission or was not a complete remission.

Question 94: Date assessed

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). If no pathologic evaluation was reported, report the date of 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 for reporting partial or unknown dates described in [General Instructions, Guidelines for Completing Forms](#).

Question 95: Did the recipient relapse following this line of therapy?

Relapse is the recurrence of disease after CR. ALL relapse is demonstrated by one or more of the following findings:

- $\geq 5\%$ blasts in the marrow and/or peripheral blood
- Extramedullary disease evident upon radiographic examination
- Disease presence determined by a physician upon clinical assessment

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

Question 96: Date of relapse

Enter the date of the assessment that established relapse had occurred 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 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 a physician determines evidence of relapse 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 97: Did the recipient have central nervous system leukemia at any time prior to 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 ALL involvement at any time between the ALL diagnosis and the start of the preparative regimen. In the absence of a negative CSF assessment, lack of neurological signs and symptoms documented throughout the patient's disease course is sufficient to indicate that the recipient never had central nervous system leukemia. If the patient's CNS status was unknown prior to the start of the preparative regimen, indicate "unknown." If the patient never had a CNS evaluation (e.g., CSF) *and* it is not clear that the patient never had neurological signs and symptoms, indicate "unknown."

Q98-149: Laboratory Studies at Last Evaluation 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 pre-transplant workup period (approximately 30 days) prior to the start of 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 sample was drawn before any radiation or systemic therapy was administered.

Questions 98-100: WBC

Indicate whether the white blood count (WBC) was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 99; indicate the date the sample was collected in question 100. If “unknown,” continue with question 101.

Questions 101-103: Blasts in blood

Indicate whether the percentage of blasts in the peripheral blood was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the percentage documented on the laboratory report in question 102; indicate the date the sample was collected in question 103. If “unknown,” continue with question 104.

 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. Blasts quantified in the peripheral blood by flow cytometry are captured separately in question 144.

Questions 104-106: Blasts in bone marrow

Indicate whether the percentage of blasts in the bone marrow was “known” or “unknown” immediately prior to the start of the preparative regimen. If “known,” report the percentage documented on the laboratory report in question 105; indicate the date the sample was collected in question 106. If “unknown,” continue with question 107.

- * 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%.

Question 107: 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. Testing methods include conventional chromosome analysis (karyotyping) or fluorescence *in situ* hybridization (FISH).

Indicate if cytogenetic studies were obtained immediately prior to the start of the preparative regimen.

If cytogenetic studies were obtained, check “yes” and continue with question 108.

If cytogenetic studies were not obtained or it is unknown if chromosome studies were performed, indicate “no” or “unknown” and continue with question 136.

Question 108: Date sample collected

Report the date the sample was collected for cytogenetic or FISH testing.

Question 109: Results of test

If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), indicate “abnormalities identified” and continue with question 110.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 137.

Questions 110-136: Specify abnormalities

If question 109 indicates that abnormalities were identified, every question 110-135 must be answered as “yes” or “no.” Do not leave any response blank. In questions 110-135, indicate “yes” for each cytogenetic abnormality identified at the last evaluation prior to the start of the preparative regimen. Indicate “no” for all options not identified on cytogenetic assessment prior to the start of the preparative regimen. If one or more abnormalities are best classified as “other abnormality,” specify in question 136.

If ≥ 3 cytogenetic abnormalities are identified immediately prior to the start of the preparative regimen, select “yes” for question 134 (complex, ≥ 3 distinct abnormalities) and specify the corresponding abnormalities in questions 110-133. If any of these abnormalities are not listed in 110-133, report “other abnormality,” and specify in question 136. For example, if the karyotype included 7, +8, and 13, report “yes” for questions 110, 112, 134, and 135/136. Complete the remaining indicators as “no,” and do not leave any response blank.

Question 137: Were tests for molecular markers performed (e.g., PCR)?

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

Indicate if molecular studies were obtained immediately prior to the start of the preparative regimen.

If molecular studies were obtained, check “yes” and continue with question 138.

If molecular studies were not obtained or it is unknown if molecular studies were performed, indicate “no” or “unknown” and continue with question 143.

Question 138: Date sample collected

Report the date the sample was collected for molecular testing.

Questions 139-142: Specify abnormalities

If question 138 indicates that molecular markers were identified, then every question 139-141 must be answered as “positive,” “negative,” or “not done.” Do not leave any response blank. If question 141 is answered “positive,” use question 142 to specify the molecular marker identified. Duplicate questions 141-142 if more than one “other molecular marker” is identified.

See [Table 2](#) in this manual for additional information on common molecular markers associated with ALL.

Question 143: Was flow cytometry performed?

Flow cytometry assessment is a method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics. Its primary clinical purpose in the setting of leukemia 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.

Indicate if flow cytometry was performed on peripheral blood and/or bone marrow sample immediately prior to the start of the preparative regimen.

If flow cytometry was performed, check “yes” and continue with question 144.

If flow cytometry was not performed or it is unknown if flow cytometry was performed, indicate “no” or “unknown” and continue with question 150.

Question 144: Blood

Indicate if flow cytometry was performed on peripheral blood immediately prior to the start of the preparative regimen.

If flow cytometry was performed on a peripheral blood sample, check “yes” and continue with question 145.

If flow cytometry was not performed or it is unknown if flow cytometry was performed, indicate “no” or “unknown” and continue with question 147.

Question 145: Date sample collected

Report the date the peripheral blood sample was collected for flow cytometry analysis.

Question 146: Was disease detected?

Indicate if evidence of disease was detected in the peripheral blood sample sent for flow cytometry analysis. Evidence of disease may include the presence of blasts or an immunophenotype known to characterize the patient’s disease.

If flow cytometry results were not consistent with continued evidence of disease, check “no.”

Question 147: Bone marrow

Indicate if flow cytometry was performed on bone marrow immediately prior to the start of the preparative regimen.

If flow cytometry was performed on a bone marrow sample, check “yes” and continue with question 148.

If flow cytometry was not performed or it is unknown if flow cytometry was performed, indicate “no” or “unknown” and continue with question 150.

Question 148: Date sample collected

Report the date the bone marrow sample was collected for flow cytometry analysis.

Question 149: Was disease detected?

Indicate if evidence of disease was detected in the bone marrow sample sent for flow cytometry analysis. Evidence of disease may include the presence of blasts or an immunophenotype known to characterize the patient's disease.

If flow cytometry results were not consistent with continued evidence of disease, check "no."

Q150-157: Disease Status at the Last Evaluation Prior to the Start of the Preparative Regimen

Question 150: What was the disease status based on hematological test results?

Indicate the disease status of ALL at the last evaluation prior to the start of the preparative regimen. **See [ALL Response Criteria](#) for disease status definitions.**

If “1st complete remission,” “2nd complete remission,” “≥ 3rd complete remission,” or “no treatment” is indicated, continue with question 157.

If “primary induction failure,” “1st relapse,” “2nd relapse,” or “≥ 3rd relapse” is indicated, continue with question 151.

Questions 151-156: Specify which of the following [sites] showed active leukemia at last evaluation prior to the start of the preparative regimen

Indicate “yes,” “no,” or “unknown” for every site specified in questions 151-155. Do not leave any response blank. If “yes” is indicated for “other site,” specify the site in question 156. If the patient is not in complete remission, at least one of the questions 151-155 must be answered “yes.”

Question 157: Date assessed

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant workup period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluation; enter the date the imaging took place for radiographic assessment.

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