2014: MDS/MPN Pre-HCT

The Myelodysplasia/Myeloproliferative Neoplasms Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures MDS/MPN-specific pre-HCT data such as: disease assessment at diagnosis, laboratory studies at diagnosis, pre-HCT therapy, disease transformation, most recent disease assessments, laboratory studies, and disease status prior to the preparative regimen.

This form must be completed for all recipients who are randomized to the Comprehensive Report Form (CRF) track and whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as “Myelodysplastic (MDS)/myeloproliferative (MPN) diseases (50) (Please classify all preleukemias)” and recipients with AML whose disease progressed from MDS/MPN.

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 MDS/MPN), begin 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**, select “yes” and continue with question 123.

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

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

Date	Manual Section	Add/ Remove/ Modify	Description
8/ 10/ 18	2014: MDS/MPN Pre-HCT	Added	Added an instructional blue box for question 123: Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. The CIBMTR forms capture disease subtype using the WHO classification of myeloid neoplasms and acute leukemia. Secondary myelofibrosis is not included as a separate category per the WHO classification. Therefore, when reporting the disease subtype **at the time of transplant** for recipients with secondary myelofibrosis, report "Primary Myelofibrosis (PMF)" to accurately capture these cases on the CIBMTR Forms.
9/7/ 17	2014: MDS/MPN Pre-HCT	Modify	Replaced note box regarding transformation of essential thrombocytopenia and polycythemia vera to myelofibrosis located below instructions for question 123 with Transformation to Myelofibrosis notebox. New text is highlighted red below while old text is struck out. *Recipients transplanted for post-essential thrombocythemia myelofibrosis (post-ET MF) or post-polycythemia vera myelofibrosis (post-PV MF) will be reported as ET or PV at diagnosis (Q2). Question 123: 'Did the recipient progress or transform to a different MDS/MPN subtype between diagnosis and the start of the preparative regimen?' must be answered "Yes".* ~~*Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. Do not report this as a transformation; when a patient with ET or PV develops fibrosis, do not report primary myelofibrosis as the primary indication for transplant.*~~
8/1/ 17	2014: MDS/MPN Pre-HCT	Modify	Added text (in red below) and removed text (struck out below) from instructions for question 121. *Refer to the MDS / MPN Response Criteria section when determining the recipient's disease status. Indicate if the disease relapsed from CR or progressed from hematologic improvement. If the disease relapsed or progressed, answer "Yes" and go to question 122. If "No," go to question 123.* *Progression or relapse should be reported even if it was reported in the previous set of questions regarding response to therapy (questions 118-120).* ~~*Relapse is the recurrence of disease after CR. MDS/MPN relapse requires one of the following:*~~ • ~~*Return to pre-treatment bone marrow blast percentage.*~~ • ~~*Decrease of ≥ 50% from maximum response levels in granulocytes or platelets*~~ • ~~*Transfusion dependence, or hemoglobin level ≥ 1.5 g/dL lower than prior to therapy.*~~ ~~*Progression is the worsening of the disease following hematologic improvement or stable disease. Progression requires at least one of the following in the absence of another explanation (e.g.,*~~

			~~*infection, bleeding, ongoing chemotherapy, etc.):*~~ • ~~*≥ 50% reduction from maximum response levels in granulocytes or platelets*~~ • ~~*Reduction in hemoglobin by ≥ 1.5 g/dL*~~ • ~~*Transfusion dependence*~~ • ~~*Progression to AML: ≥ 20% blasts in the blood or bone marrow*~~
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)
6/24/16	2014: MDS/MPN Pre-HCT	Add	Added information box to Q157: "Never Treated" is not an option choice on revision three of the Myelodysplasia / Myeloproliferative Disorders Pre-HSCT Data (MDS) Form. When completing revision three of this form, centers should report "No Response (NR) / Stable Disease (SD)" for recipients who have only received supportive care prior to transplant.
3/31/16	2014: MDS/MPN Pre-HCT	Add	Added an information box about transformation of polycythemia vera and essential thrombocythemia to question 123 : Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. Do not report this as a transformation; when a patient with ET or PV develops fibrosis, do not report primary myelofibrosis as the primary indication for transplant.
9/27/15	2014: MDS/MPN Pre-HCT	Modify	Modified MDS transformation table to include RA, 5q- syndrome, MDS-U, and chronic eosinophilia transformations
6/26/15	2014: MDS/MPN Pre-HCT	Modify	Modified text of Questions 121 and 123 to include the following concept: Progression to AML: ≥ 20% blasts in the **blood or** bone marrow

Last modified: 2018/08/10

Q1-18: Disease Assessment at Diagnosis

Question 1: What was the date of diagnosis?

Report the date of the first pathological diagnosis (i.e., bone marrow biopsy) of MDS/MPN. 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 as described in General Instructions, Guidelines for Completing Forms.

Question 2: What was the MDS/MPN subtype?

Please indicate the MDS/MPN subtype at diagnosis. For a list of MDS/MPN subtypes and their diagnostic criteria, see Appendix H.

Question 3: Was the disease (MDS/MPN) therapy related?

Agents such as the radiation or systemic chemotherapy 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 MDS/MPN. If the diagnosis of MDS/MPN is therapy-related, select "yes" and continue with question 4. If the diagnosis of MDS/MPN is not therapy-related, select "no" and continue with question 12. If it is unknown if the MDS/MPN is therapy-related, select "unknown" and continue with question 12.

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

Questions 4-5: Specify prior disease:

Indicate the recipient's primary disease prior to the diagnosis of MDS/MPN.

If the recipient's prior disease is not listed, select "other" and specify the disease using question 5.

Questions 6-7: Date of diagnosis of prior disease:

Specify if the date of diagnosis of the prior disease is "known" or "unknown." If the date is "known," continue with question 7 and 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 MDS/MPN diagnosis date entered in question 1.

If the date is “unknown,” continue with question 8.

Questions 8-11: Specify therapy for prior disease:

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. Systemic therapy in the setting of malignancy generally refers to chemotherapy or cytotoxic therapy.

Intrathecal therapy is administered via injection into the lumbar cerebral spinal fluid and acts on the central nervous system.

Radiation therapy uses high-energy, ionizing radiation to kill malignant cells. It is typically referred to as radiation therapy, x-ray therapy (XRT), or radiotherapy.

For each listed treatment, indicate “yes,” “no,” or “unknown.” If the treatment administered was “other treatment,” specify the type of treatment given using question 11. Select all that apply; do not leave any responses blank.

Question 12: Did the recipient have a predisposing condition prior to diagnosis of MDS/MPN?

A predisposing condition is a condition that contributes to the susceptibility of developing MDS/MPN. If the recipient has a documented history of a predisposing condition, select “yes” and continue with question 13. If there is no history of a predisposing condition or if predisposition is unknown, indicate “no” or “unknown” and continue with question 15.

Questions 13-14 Specify condition:

Aplastic anemia may progress to MDS and/or AML. Aplastic anemia is a broad classification referring to bone marrow failure characterized by pancytopenia and marrow hypoplasia. *Also complete a CIBMTR Form 2028 – Aplastic Anemia Pre-HCT Data*. If selected, continue with question 15.

Bloom syndrome is an autosomal recessive genetic disorder characterized by excessive chromosome breakage and corresponding 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. If selected, continue with question 15.

Down syndrome is also a chromosomal disorder (trisomy 21). It is characterized by an additional chromosome 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. If selected, continue with question 15.

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. *Also complete CIMBTR Form 2029 – Fanconi Anemia Pre-HCT Data*. If selected, continue with question 15.

If the recipient had a predisposing condition not listed above, select “other condition” and specify the condition in question 14.

Question 15: Did the recipient receive any RBC transfusions at the time of diagnosis and/or during the first year post diagnosis?

Indicate if the recipient received any RBC transfusions in the first year after MDS/MPN was diagnosed. If the recipient required even one RBC transfusion as supportive care for the disease, select “yes.” Some discretion is required for this question; if the recipient required a RBC transfusion as part of a normal surgical procedure or for a reason other than their disease, indicate “no.” If it is unknown if the recipient received RBC transfusions during their first year after diagnosis, select “unknown.”

> ! Questions 16-18 refer to MPN subtypes only; if the diagnosis was other than MPN, continue with question 19.

Question 16: Were systemic symptoms (B symptoms) present (unexplained fever > 38°C; or night sweats; unexplained weight loss > 10% body weight in six months before diagnosis)?

Indicate if systemic symptoms were present at the time of diagnosis. Systemic 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 previous to diagnosis. Indicate “yes” if any systemic symptoms were present at diagnosis (or in the case of unexplained weight loss, within the six months previous to diagnosis). Indicate “no” if systemic symptoms were not present at diagnosis. Indicate “unknown” if it is not possible to determine the presence or absence of systemic symptoms at diagnosis.

Question 17: Did the recipient have splenomegaly (spleen palpable > 3 cm below left costal margin)?

Indicate if the spleen was palpable greater than 3 centimeters below the left costal margin at the time of diagnosis. Splenomegaly is often documented during the physician’s physical assessment of the patient and represents an abnormal finding. Indicate “yes” if splenomegaly was present at the time of diagnosis.

Indicate “no” if splenomegaly was not present at diagnosis. Indicate “unknown” if it is not possible to determine the presence or absence of splenomegaly at diagnosis.

Question 18: Did the recipient have hepatomegaly (liver edge palpable > 3 cm below right costal margin)?

Indicate if the edge of the liver was palpable greater than 3 centimeters below the right costal margin at the time of diagnosis. Hepatomegaly is often documented during the physician’s physical assessment of the patient and represents an abnormal finding. Indicate “yes” if hepatomegaly was present at the time of diagnosis. Indicate “no” if hepatomegaly was not present at diagnosis. Indicate “unknown” if it is not possible to determine the presence or absence of hepatomegaly at diagnosis.

Last modified: 2017/06/30

Q19-39: Laboratory Studies at Diagnosis

Report findings laboratory results from prior to the start of first treatment of the primary disease for which the HCT is being performed. If the recipient's MDS/MPS transformed, report the studies from the original diagnosis.

Questions 19-21: Monocytes:

Indicate whether the monocyte percentage in the blood was "known" or "unknown" at the time of MDS/MPN diagnosis. If "known," report the percentage documented on the laboratory report in question 20 and the date of sample collection in question 21. If "unknown," continue with question 22.

Questions 22-24: Blasts in blood:

Indicate whether the percentage of blasts in the blood was "known" or "unknown" at the time of MDS/MPN diagnosis. If "known," report the percentage documented on the laboratory report in question 23 and the date of sample collection in question 24. If "unknown," continue with question 25.

> ✻ 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.

Questions 25-26: Was a bone marrow examination performed?

Indicate if a bone marrow examination was performed at the time of MDS/MPN diagnosis. If "yes," indicate the date the sample was collected in question 26. If "no" or "unknown," continue with question 29.

Question 27: Cellularity:

Cellularity describes the percentage of bone marrow occupied by hematopoietic cells compared to other tissues, such as adipose (fat) cells. In MDS/MPN, the percentage of hematopoietic cells is likely increased (hypercellular) due to proliferation of immature cells. In other cases, the cellularity may be normal (normocellular) or decreased (hypocellular). This distinction is made on the pathology report of a bone marrow examination.

Indicate whether the bone marrow examination revealed "decreased (hypocellular)," "normal (normocellular)," or "increased (hypercellular)" cellularity at diagnosis or prior to the first treatment. If a biopsy was not obtained or if the degree of cellularity is not addressed in the report, select "unknown."

Question 28: Fibrosis:

Fibrosis describes the replacement of bone marrow by fibrous (scar) tissue. This is evident in MDS/MPN diseases such as chronic idiopathic myelofibrosis. This distinction is made on the pathology report of a bone marrow examination.

Indicate if fibrosis in the bone marrow was “present” or “absent.” If the degree of fibrosis is not addressed in the report, select “unknown.”

Question 29: 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 MDS/MPN or prior to the start of treatment.

If molecular studies were obtained, select “yes” and continue with question 30.

If no molecular studies were obtained or it is unknown if molecular studies were performed, indicate “no” or “unknown” and continue with question 40.

Question 30: Date sample collected:

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

Questions 31-38: Specify abnormalities at diagnosis:

If question 29 indicates that tests for molecular markers were performed, then each of questions 31-38 must be answered as “positive,” “negative,” or “not done.” Do not leave any response blank. If question 37 is answered “positive,” specify the identified molecular marker.

Note that the *JAK2* mutation question only needs to be completed for recipients with MPN.

Questions 37-38 should be copied to report more than one other molecular marker.

Question 39: 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.

Last modified: 2015/02/24

Q40-122: Pre-HCT Therapy

Complete a “Pre-HCT Therapy” section for each line of therapy administered prior to the start of the preparative regimen. If multiple lines of therapy were administered, copy and complete questions 41-122 for each line of therapy.

Question 40: Was therapy given?

Indicate if the recipient received treatment for MDS/MPN after the time of diagnosis and before the start of the preparative regimen. If “yes,” continue with question 41. If “no,” continue with question 123.

Questions 41-43: WBC

Indicate whether the white blood cell (WBC) count was “known” or “unknown” prior to the start of this line of therapy. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 88 and the date of sample collection in question 89. If “unknown,” continue with question 90.

Questions 44-46: Hemoglobin

Indicate whether the hemoglobin was “known” or “unknown” prior to the start of this line of therapy. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 45 and the date of sample collection in question 46. If “unknown,” continue with question 48.

Question 47: Were RBC transfused ≤ 30 days before the date of test?

✻ Currently there is an issue on the 2014 form regarding RBC transfusion dates. The question should read: “Were RBCs transfused ≤ 30 days before the date of test?”

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who received these cells from a transfusion.

Indicate if red blood cells were transfused less than or equal to 30 days prior to the testing.

Questions 48-50: Platelets:

Indicate whether the platelet count was “known” or “unknown” prior to the start of this line of therapy. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 49 and the date of sample collection in question 50. If “unknown,” continue with question 52.

Question 51: Were platelets transfused ≤ 7 days before date of test?

> ✻ Currently there is an issue on the 2014 form regarding platelet transfusion dates. The question should read: "Were platelets transfused ≤ 7 days before the date of test?"

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who received these cells from a transfusion.

Indicate if platelets were transfused less than or equal to 7 days prior to the testing.

Questions 52-54: Neutrophils:

Indicate whether the neutrophil percentage in the blood was "known" or "unknown" prior to the start of this line of therapy. If "known," report the value documented on the laboratory report in question 53 and the date of sample collection in question 54. If "unknown," continue with question 55.

Questions 55-57: Blasts in bone marrow:

Indicate whether the percentage of blasts in the bone marrow was "known" or "unknown" prior to the start of this line of therapy. If "known," report the percentage documented on the laboratory report in question 56 and the date of sample collection in question 57. If "unknown," continue with question 58.

Question 58: Were cytogenetics tested (conventional or FISH)?

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 prior to the start of this line of therapy. If cytogenetic studies were obtained, select "yes" and continue with question 59.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select "no" or "unknown" and continue with question 87.

Question 59: 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 prior to the start of treatment.

Question 60: Results of test:

If cytogenetic studies identified abnormalities, indicate “abnormalities identified” and continue with question 61.
If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 87.

Question 61: Specify the number of distinct cytogenetic abnormalities:

Indicate the total number of abnormalities identified prior to this line of therapy.

Questions 62-86: Specify abnormalities identified prior to this line of therapy:

Report all abnormalities identified by all methods of cytogenetic assessment prior to the start of this line of therapy by selecting “yes” or “no” for each question. Do not leave any responses blank. If one or more abnormalities are best classified as “other abnormality” select “yes” for question 85 and specify the abnormality in question 86.

Question 87: Systemic Therapy:

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously to the whole body. These drugs enter the bloodstream and are distributed throughout the body.

Also report therapies for supportive care. These therapies include chelation therapy (for iron overload from chronic RBC transfusions) and treatment with growth factors (EPO, G-CSF, GM-CSF, etc.).

Indicate “yes” if the patient received systemic therapy and continue with question 88. If the patient did not receive systemic therapy, indicate “no” and continue with question 113.

Questions 88-89: Date therapy started:

Indicate “known” if the therapy start date is documented and use question 89 to specify the first date of systemic therapy administration. If the date is unknown, indicate “unknown” and continue with question 90.

Questions 90-91: Date therapy stopped:

Indicate “known” if the therapy completion date is documented and use question 91 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 “unknown” and continue with question 92.

Questions 92-112: Specify systemic therapy:

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 drug or multiple drugs. Additionally, drugs may be administered on a single day, over consecutive days, or continuously.

Indicate “yes” or “no” for each therapy listed. Do not leave any responses blank. If the recipient received a chemotherapy agent that is not listed, select “yes” for “other systemic therapy” and specify the treatment.

Question 113: Other therapy:

Indicate if the recipient received therapy other than the systemic therapy listed above, including radiation and splenectomy. If the recipient received other therapy, select “yes” and continue with question 114. If the recipient did not receive other therapy, select “no” and continue with question 118.

Questions 114-117: Specify other therapy:

Indicate “yes” or “no” for each therapy listed. Do not leave any responses blank. If the recipient received therapy that is not listed, select “yes” for “other therapy” and specify the therapy in question 117.

Question 118: Best response to line of therapy:

Indicate the disease response of MDS/MPN to each line of therapy using the definitions found in the text on FormsNet. These definitions are also located in the MDS/MPN Response Criteria.

If the recipient’s disease status was “Complete remission (CR),” “No response (NR)/stable disease (SD),” “Progression from hematologic improvement (Prog from HI),” “Relapse from complete remission (Rel from CR),” or “Progression to AML (AML),” continue with question 120.

If the recipient’s disease status was “Hematologic improvement (HI),” continue with question 119.

If the disease status was “unknown” or “not assessed,” continue with question 123.

Question 119: Specify the cell line examined to determine HI status:

Indicate the cell line examined to determine hematologic improvement. Review the Hematologic Improvement criteria on the MDS/MPN Response Criteria section to determine the cell line.

Question 120: 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 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 as described in General Instructions, Guidelines for Completing Forms.

Question 121: Did disease relapse/progress following this line of therapy?

Refer to the MDS / MPN Response Criteria section when determining the recipient's disease status. Indicate if the disease relapsed from CR or progressed from hematologic improvement. If the disease relapsed or progressed, answer "Yes" and go to question 122. If "No," go to question 123.

Progression or relapse should be reported even if it was reported in the previous set of questions regarding response to therapy (questions 118-120).

> **Transformation to AML & Lines of Therapy**
> If the recipient's disease transforms from MDS/MPN following this line of therapy, complete the form until question 126 and then skip to the signature lines. Any additional lines of therapy intended to treat the newly transformed AML should be reported on the Acute Myelogenous Leukemia (AML) Pre-HCT Form (F2010).

Indicate if the disease relapsed from CR or progressed from hematologic improvement or stable disease. If the disease relapsed or progressed, answer "yes" and continue with question 122. If "no," continue with question 123.

Progression or relapse should be reported even if it was reported in the previous set of questions regarding response to transplant (questions 118-120).

Question 122: Date of relapse/progression:

Enter the date of the assessment that established relapse 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 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 examination 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, Guidelines for Completing Forms.

Last modified: 2018/06/25

Q123-126: Transformation

Question 123: Did the recipient progress or transform to a different MDS/MPN subtype between diagnosis and the start of the preparative regimen?

Indicate if the recipient's disease progressed to AML or transformed into a different MDS/MPN subtype between initial diagnosis and the start of the preparative regimen. Approximately one-third of MDS cases transform into AML, which is usually associated with a poorer prognosis. Progression to AML is defined by an increase in blood or bone marrow blasts equal to or greater than 20%.

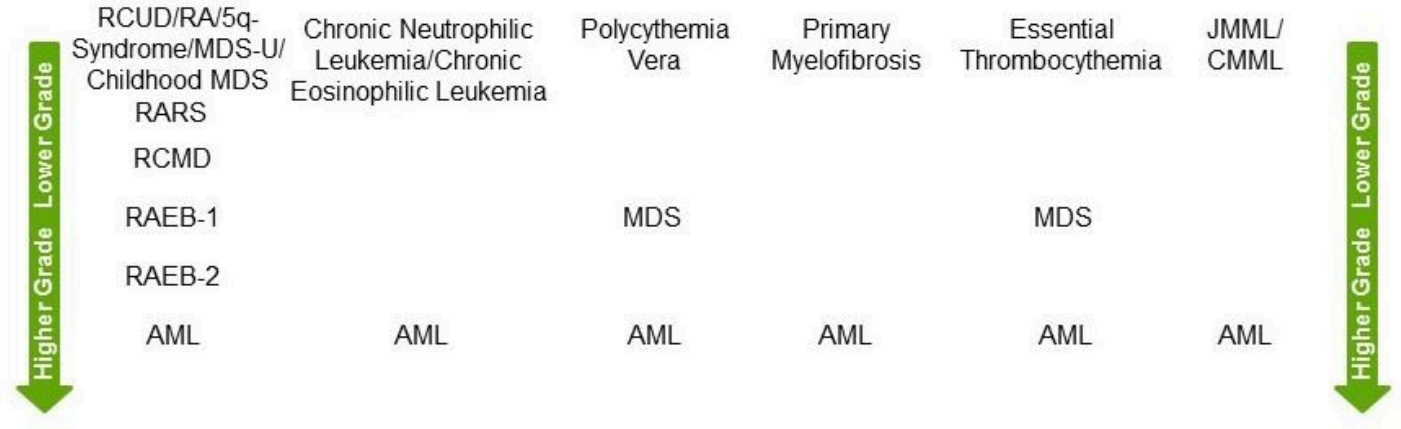
MDS/MPN subtypes may also transform from one into another. A progression from one subtype of MDS to another indicates that the number of cytopenias, number of blasts, and/or morphology of marrow sufficiently qualified them for a higher grade (i.e., more severe) MDS. For example, an MDS classified as RCUD at diagnosis whose blast count rises to 8% as documented on bone marrow aspirate would have progressed to RAEB-1.

Conversely, 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). For example, a recipient who is diagnosed with RAEB-2, but whose assessments show that they meet the criteria for RAEB-1 as a response to treatment, would **not** qualify as a 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 a progression/ transformation. See the table below for guidance in determining the severity of MDS/MPN progressions and transformations.

Transformation to Myelofibrosis
Recipients transplanted for post-essential thrombocythemia myelofibrosis (post-ET MF) or post-polycythemia vera myelofibrosis (post-PV MF) will be reported as ET or PV at diagnosis (Q2). Question 123: 'Did the recipient progress or transform to a different MDS/MPN subtype between diagnosis and the start of the preparative regimen?' must be answered "Yes".

Transformation to Myelofibrosis
Myelofibrosis that develops in patients with essential thrombocythemia (ET) or polycythemia vera (PV) is considered secondary myelofibrosis. The CIBMTR forms capture disease subtype using the WHO classification of myeloid neoplasms and acute leukemia. Secondary myelofibrosis is not included as a separate category per the WHO classification. Therefore, when reporting the disease subtype **at the time of transplant** for recipients with secondary

myelofibrosis, report “Primary Myelofibrosis (PMF)” to accurately capture these cases on the CIBMTR Forms.



Indicate if the recipient’s disease progressed to AML or transformed from one MDS/MPN subtype to another. If the recipient’s disease did transform or progress, select “yes” and continue with question 124. If there was no documented transformation or progression, select “no” and continue with question 127.

Question 124: Was a subsequent complete remission achieved?

Indicate if a subsequent complete remission was achieved. For recipients whose disease transformed from one MDS/MPN to another, complete remission is a treatment response that *requires all of the following maintained for a minimum of four weeks*:

Bone marrow evaluation:

- < 5% myeloblasts with normal maturation of all cell lines

Peripheral blood evaluation:

- Hemoglobin ≥ 11 g/dL untransfused without erythropoietic support
- ANC ≥ 1000/mm3 without myeloid growth factor support
- Platelets ≥ 100,000/mm3 without thrombopoietic support
- 0% blasts in blood

Alternative CR criteria are accepted in the setting of **pediatric** MDS and are as follows:

- Complete donor chimerism (≥ 95% donor chimerism without recipient cells detected)
- Hemoglobin ≥ 11 g/dL untransfused without erythropoietic support
- ANC ≥ 1000/mm3 without myeloid growth factor support
- Platelets ≥ 100,000/mm3 without thrombopoietic support

For recipients whose MDS/MPN transformed to AML, complete remission is a treatment response that *requires all of the following maintained for a minimum of 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 independence

Question 125: Specify the date of the most recent transformation:

Enter the date of the assessment that determined the most recent disease transformation (i.e., if there were multiple transformations, report the date of the most recent). 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 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 126: Specify the MDS/MPN subtype after transformation:

Indicate the recipient's current MDS/MPN subtype after transformation. If the recipient experiences more than one transformation after diagnosis, report the most recent subtype in this question. For MDS/MPN subtype characteristics, see Appendix H. Continue with question 127, unless the recipient transformed to AML.

If the disease transformed to AML, continue to the signature line. *Also complete a CIBMTR Form 2010 – AML Pre-HCT Data*.

Last modified: 2018/08/10

Q127-153: Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen

Questions 127-129: Monocytes:

Indicate whether the monocyte percentage in the blood was “known” or “unknown” prior to the start of the preparative regimen. If “known,” report the percentage documented on the laboratory report in question 128 and the date of sample collection in question 129. If “unknown,” continue with question 130.

Questions 130-132: Blasts in blood:

Indicate whether the percentage of blasts in the peripheral blood was “known” or “unknown” prior to the start of the preparative regimen. If “known,” report the percentage documented on the laboratory report in question 131 and the date of sample collection in question 132. If “unknown,” continue with question 133.

> ✻ 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.

Questions 133-134: Was a bone marrow examination performed?

Indicate if a bone marrow examination was performed prior to the start of the preparative regimen. If “yes,” indicate the date sample was collected in question 134. If “no,” continue with question 137.

Question 135: Cellularity:

Cellularity describes the percentage of bone marrow occupied by hematopoietic cells compared to other tissues, such as adipose (fat) cells. In MDS/MPN, the percentage of hematopoietic cells is likely increased (hypercellular) due to proliferation of immature cells. In other cases, the cellularity may be normal (normocellular) or decreased (hypocellular). This distinction is made on the pathology report of a bone marrow examination.

Indicate whether the bone marrow examination revealed “decreased (hypocellular),” “normal (normocellular),” or “increased (hypercellular)” cellularity prior to the start of the preparative regimen. If a biopsy was not obtained or if the degree of cellularity is not addressed in the report, select “unknown.”

Question 136: Fibrosis:

Fibrosis describes the replacement of bone marrow by fibrous (scar) tissue. This is evident in MDS/MPN diseases such as chronic idiopathic myelofibrosis. This distinction is made on the pathology report of a bone marrow examination.

Indicate if fibrosis in the bone marrow was “present” or “absent” prior to the start of the preparative regimen. If the degree of fibrosis was not addressed in the report, select “unknown.”

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 prior to the start of the preparative regimen.

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

If no molecular studies were obtained or it is unknown if molecular studies were performed, indicate “no” or “unknown” and continue with question 147.

Question 138: Date sample collected:

Report the date the sample was collected for molecular testing. If multiple studies were performed prior to the start of the preparative regimen, report the last assessment prior to the start of treatment.

Questions 139-146: Specify abnormalities at last evaluation prior to the start of the preparative regimen:

If question 137 indicates that tests for molecular markers were performed, then each of the questions 139-145 must be answered as “positive,” “negative,” or “not done.” Do not leave any response blank. If question 145 is answered “positive,” specify the identified molecular marker in question 146.

Note that the JAK2 mutation question only needs to be completed for recipients with MPN.

Questions 145-146 should be copied to report more than one other molecular marker.

Question 147: 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 MDS, MPN, and 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.

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, select “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 154.

Questions 148-149: 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, select “yes” and report the date the sample was collected in question 149.

If flow cytometry was not performed on peripheral blood, indicate “no” and continue with question 151.

Question 150: 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, select “no.”

Questions 151-152: 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, select “yes” and report the date the sample was collected in question 152.

If flow cytometry was not performed, indicate “no” and continue with question 154.

Question 153: 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, select “no.”

Last modified: 2015/02/16

Q154-161: Disease Assessment at the Last Evaluation Prior to the Preparative Regimen

! Questions 154-156 refer to MPN subtypes only; if the diagnosis is other than MPN, continue with question 157.

Questions 154: Were systemic symptoms (B symptoms) present (unexplained fever > 38°C; or night sweats; unexplained weight loss > 10% body weight in six months before last evaluation prior to the start of the preparative regimen)?

Indicate if systemic symptoms were present at the last evaluation prior to the preparative regimen. Systemic 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 “yes” if any systemic symptoms were present at the last evaluation before the preparative regimen. Indicate “no” if systemic symptoms were not present at the last evaluation prior to the preparative regimen. Indicate “unknown” if it is not possible to determine the presence or absence of systemic symptoms at the last evaluation prior to the start of the preparative regimen.

Question 155: Did the recipient have splenomegaly (spleen palpable > 3 cm below left costal margin)?

Indicate if the spleen was palpable greater than 3 centimeters below the left costal margin at the last evaluation prior to the preparative regimen,. Splenomegaly is often documented during the physician’s physical assessment of the patient and represents an abnormal finding. Indicate “yes” if splenomegaly was present at the last evaluation prior to the preparative regimen. Indicate “no” if splenomegaly was not present at the last evaluation prior to the preparative regimen. Indicate “unknown” if it is not possible to determine the presence or absence of splenomegaly at the last evaluation prior to the preparative regimen.

Question 156: Did the recipient have hepatomegaly (liver edge palpable > 3 cm below right costal margin)?

Indicate if the edge of the liver was palpable greater than 3 centimeters below the right costal margin at the time of last evaluation prior to the preparative regimen. Hepatomegaly is often documented during the physician’s physical assessment of the patient and represents an abnormal finding. Indicate “yes” if hepatomegaly was present at the time of the last evaluation prior to the preparative regimen. Indicate “no” if hepatomegaly was not present at the last evaluation prior to the preparative regimen. Indicate “unknown” if it is not possible to determine the presence or absence of hepatomegaly at the last evaluation prior to the preparative regimen.

Question 157: What was the disease status?

> ✻ "Never Treated" is not an option choice on revision three of the Myelodysplasia / Myeloproliferative Disorders Pre-HSCT Data (MDS) Form. When completing revision three of this form, centers should report "No Response (NR) / Stable Disease (SD)" for recipients who have only received supportive care prior to transplant.

Indicate the disease status of MDS/MPN at the last evaluation prior the start of the preparative regimen using the definitions found in the text or on FormsNet. These definitions are also located in the MDS/MPN Response Criteria.

If the recipient's disease status was "Complete remission (CR)," or "No response (NR)/stable disease (SD)" prior the start of the preparative regimen, continue with question 161.

If the recipient's disease status was "Hematologic improvement (HI)" prior to the start of the preparative regimen, continue with question 158.

If the recipient's disease status was "Progression from hematologic improvement (Prog from HI)" prior the start of the preparative regimen, continue with question 159.

If the recipient's disease status was "Relapse from a complete remission (Rel from CR)" prior the start of the preparative regimen, continue with question 160.

If the disease status was "not assessed" prior the start of the preparative regimen, continue with the signature lines at the bottom of the form.

Question 158: Specify the cell line examined to determine HI status:

Indicate the cell line examined to determine hematologic improvement. Review the Hematologic Improvement criteria shown above to determine the cell line.

Question 159: Date of progression:

Enter the assessment date that progression from hematologic improvement was established prior to the start of the preparative regimen. 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 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 160: Date of relapse:

Enter the date of the assessment that established relapse from complete remission prior to the start of the preparative regimen. 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 was detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place.

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 161: 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 work-up period (approximately 30 days prior to transplant). 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 evaluations; enter the date the imaging took place for radiographic assessments.

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.

Last modified: 2016/06/24