



## Instructions for Aplastic Anemia Pre-HSCT Data (Form 2028)

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

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: [CIBMTRFormsManualComments@nmdp.org](mailto: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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## Aplastic Anemia Pre-HSCT Data

Aplastic Anemia is a disease in which the bone marrow does not produce enough red blood cells, white blood cells, or platelets for the body. The disease can be idiopathic, or can be caused by environmental exposure, pharmaceutical or drug exposure, or exposure to viral hepatitis. Symptoms of aplastic anemia include, but are not limited to pallor, weakness, frequent infection, and/or easy bruising.

The Aplastic Anemia Pre-HSCT Data Form is one of the Comprehensive Report Forms. This form captures aplastic anemia-specific pre-HSCT data such as: disease assessment at diagnosis, laboratory studies at diagnosis, transfusion status prior to the start of the preparative regimen, and laboratory studies prior to the start of the preparative regimen.

This form must be completed for all recipients whose primary disease, as reported on Form 2000 question 9, is severe aplastic anemia, paroxysmal

National Marrow Donor Program<sup>®</sup> and The Medical College of Wisconsin

nocturnal hemoglobinuria, or one of the following inherited abnormalities of erythrocyte differentiation or function: Shwachman-Diamond syndrome, Diamond-Blackfan anemia (pure red cell aplasia), or other constitutional anemia. Fanconi Anemia and Sickle Cell Anemia each have their own forms to complete (Forms 2029 and 2030, respectively).

**NOTE: 2<sup>nd</sup> Transplant**

If this is a report of a second or subsequent transplant, please check the box located on page 1 of the form 2028 and continue with question 26.

## 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™2 application.

## Disease Assessment at Diagnosis

### Question 1: What was the date of diagnosis of Aplastic Anemia?

Report the date of first pathological evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear) that determined the diagnosis. 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 the recipient's bone marrow examined at diagnosis?**

Indicate whether a bone marrow examination was performed at diagnosis. If "yes," continue with question 3. If "no," continue with question 4.

**Question 3: Is a copy of the biopsy report attached?**

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

**Question 4: Were the recipient's cells tested for sensitivity to cross-linking agents (e.g., diepoxybutane [DEB], mitomycin C [MMC])?**

Studies that measure the sensitivity of a recipient's cells to cross-linking agents (i.e., chromosome breakage studies) are often performed for patients with anemia. If the recipient's cells were tested for sensitivity to these agents, select "yes" and continue with question 5.

If no tests for sensitivity to cross-linking agents were performed, continue with question 7.

If it is unknown if cross-linking sensitivity testing was performed, select "unknown" and continue with question 7.

**Question 5: Specify the test results:**

Indicate if the recipient's sensitivity test results were normal, revealed increased chromosome breaks, or were unknown.

**Question 6: Is a copy of the test report attached?**

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

**Questions 7-10: What was the disease etiology?**

Indicate the disease etiology of aplastic anemia.

If the etiology of aplastic anemia is Diamond-Blackfan anemia, check the box for "Diamond-Blackfan anemia." Diamond-Blackfan anemia (DBA) is a hematologic disease in which the body does not create enough red blood cells. There are associated birth abnormalities and diagnosis is usually made early in life. If the etiology of aplastic anemia is drug induced, check the box for "drug induced." If the specific drug causing the aplastic anemia is known, report it in question 8. If the specific drug is not known, select "drug unknown." Drugs that have been associated with aplastic anemia include, but are not limited to antibiotics (e.g., sulfonamides, chloramphenicol), diabetes medications (e.g., tolbutamide, carbutamide, chlorpropamide), anti-seizure medications, and phenothiazines (Thorazine, Compazine).

Source: American Cancer Society. *What are the Risk Factors for Aplastic Anemia?* January 23, 2012. <http://www.cancer.org/Cancer/AplasticAnemia/DetailedGuide/aplastic-anemia-risk-factors> (accessed July 10, 2012)

If the etiology of aplastic anemia is from viral hepatitis, check the box for “viral hepatitis.” Use question 9 to report the specific type of hepatitis or select “type unknown” if the specific type causing aplastic anemia is not known. Idiopathic aplastic anemia has no known cause. If the origin of aplastic anemia is unknown, check the box for “idiopathic.”

If the origin of aplastic anemia is from some other cause, check the box for “other.” Specify the other disease etiology using question 10, or select “etiology unknown” if the cause of aplastic anemia is not known.

**Question 11: Was testing for paroxysmal nocturnal hemoglobinuria (PNH) performed?**

Paroxysmal nocturnal hemoglobinuria (PNH) is a disease in which the red blood cells break down too quickly. The disease is characterized by anemia, red urine, and thrombosis. Indicate if the recipient had testing for paroxysmal nocturnal hemoglobinuria. If “yes,” continue with question 12. If “no,” continue with question 19.

If it is not known if the recipient received testing for paroxysmal nocturnal hemoglobinuria, select “unknown” and continue with question 19.

**Questions 12-18: Specify PNH test and results:**

Indicate which test(s) were performed for PNH. If a test was performed that is not listed, select “yes” for “other test” and specify the test using question 18. Do not leave any question blank.

Flow cytometry is a technique that counts and differentiates cell surface markers. CD55, CD16, and CD59 surface markers are associated with PNH. Ham’s acid hemolysis test is performed to determine if red blood cells are more likely to break when placed in a mild acid.\*

Hemosiderinuria testing measures the amount of hemosiderin in the urine. Hemosiderin is found within cells and acts as an iron storage device. Hemosiderin in the urine often causes the urine to appear brown.

PIGA GPI anchor protein defects are associated with PNH. PIGA is an enzyme that is required to synthesize the GPI anchor. The GPI anchor allows proteins (such as CD55, CD16, and CD59) to become attached to the surface of the cell. Defects in the PIGA enzyme, and subsequently the GPI anchor, prevent these surface marker proteins from becoming attached. Due to the lack of these

proteins on the surface of red blood cells, the immune system may not recognize the cells causing them to be destroyed. Report assessments (such as molecular PCR testing) to detect defects in the PIGA gene or GPI anchor using this option.

Sugar water/sucrose lysis tests are performed to detect how fragile red blood cells become when placed in a high-sugar/low-salt environment.\* This environment causes the red blood cells to swell; fragile cells are more prone to break down.

\*Definitions of these tests were found at the A.D.A.M. Medical Encyclopedia at <http://www.nlm.nih.gov/medlineplus/encyclopedia.html>

## Laboratory Studies at Diagnosis

Report findings prior to any first treatment for aplastic anemia.

### Question 19: WBC:

Indicate whether the white blood count (WBC) is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “not known,” continue with question 20.

### Question 20: Hemoglobin:

Indicate whether the hemoglobin is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the laboratory value and unit of measure documented on the laboratory report. If “not known,” continue with question 21.

### NOTE: RBC and Platelet Transfusions

Currently, there is an error on the Form 2028 regarding transfusion history. The form should state: “Was RBC transfused less than **or equal to** [≤] 30 days before the date of test?” and “Were platelets transfused less than **or equal to** [≤] 7 days before the test?”

### Question 21: Was RBC transfused < 30 days before 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 requires transfusions to support the counts.

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

### Question 22: Platelets:

Indicate whether the platelet count is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the laboratory value and unit of

measure documented on the laboratory report. If “not known,” continue with question 23.

**Question 23: Were platelets transfused < 7 days before 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 requires transfusions to support the counts.

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

**Question 24: Neutrophils:**

Indicate whether the neutrophil count in the blood is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the value documented on the laboratory report. If “not known,” continue with question 25.

**Question 25: Reticulocytes (uncorrected):**

Indicate whether the uncorrected reticulocyte count in the blood is “known” or “not known” at the time of aplastic anemia diagnosis. If “known,” report the value documented on the laboratory report. If “not known,” continue with question 26.

Report the absolute value of reticulocytes in  $\_\_ \times 10^9/L$ . Do not report a percentage, the corrected reticulocyte count, or the reticulocyte production index.

**Question 26: Was therapy given for treatment of aplastic anemia prior to the start of the preparative regimen?**

Indicate if the recipient received treatment for aplastic anemia between the time of diagnosis and the start of the preparative regimen. If “yes,” continue with question 27. If “no” or “unknown,” continue with question 45.

**Questions 27-44: Specify what treatment(s) were given:**

Indicate the treatment(s) given to the recipient.

**Androgens** (e.g., danazol, fluoxymesterone, oxymethalone, stanozolol, testosterone) are male hormones that can cause the bone marrow to create more red blood cells.<sup>1</sup>

**ATG (anti-thymocyte globulin), ALS (anti-lymphocyte serum), ATS (anti-thymocyte serum), and ALG (anti-lymphocyte globulin)** are immunosuppressive therapies that attack lymphocytes (T cells).<sup>2</sup>

**Chelation therapy** (e.g., deferoxamine, deferasirox, deferiprone) for iron is the removal of iron from the body. Iron overload is a complication resulting from many red blood cell transfusions.<sup>1</sup>

**Corticosteroids** (e.g., methylprednisolone) are used as an immunosuppressive therapy that causes the immune system to create fewer antibodies.<sup>2</sup>

**Cyclosporine (CsA, Neoral<sup>®</sup>, Sandimmune<sup>®</sup>)** is an immunosuppressive treatment that prevents T cells from becoming active.<sup>1</sup>

**Cytokines** are groups of proteins that signal cell growth and differentiation. These *growth factors* stimulate the growth of red blood cells (**erythropoietin**) and white blood cells (**G-CSF, GM-CSF, interleukin-3, pegfilgrastim**). If the recipient received a cytokine or growth factor that was not listed in questions 33-38, select “yes” for question 39, and specify in question 40 which cytokine or growth factor was used.

**Other immunosuppression** includes those immunosuppressive therapies not already listed above. If the recipient received immunosuppressives not listed, such as mycophenolate mofetil or monoclonal antibodies (e.g., alemtuzumab, rituximab), select “yes” for question 41 and specify in question 42 which other immunosuppressant(s) were used.

**Other treatment** includes those treatments not already listed above. If the recipient received treatments not listed, such as chemotherapy (not given as the preparative regimen for transplant), select “yes” for question 43 and specify in question 44 which other treatment(s) were used.

<sup>1</sup>Aplastic Anemia and MDS International Foundation. *Aplastic Anemia: Treatment*. May 30, 2011. <http://www.aamds.org/about/aplastic-anemia/treatment> (accessed July 10, 2012)

<sup>2</sup>Be The Match. *Immunosuppressive Therapy for Aplastic Anemia*. [http://marrow.org/Patient/Disease\\_and\\_Treatment/About\\_Your\\_Disease/Aplastic\\_Anemia/Immunosuppressive\\_Therapy.aspx](http://marrow.org/Patient/Disease_and_Treatment/About_Your_Disease/Aplastic_Anemia/Immunosuppressive_Therapy.aspx) (accessed July 10, 2012)

## Transfusion Status from Diagnosis to the Start of the Preparative Regimen

### **Question 45: Did the recipient receive red blood cell transfusions between diagnosis and the start of the preparative regimen?**

If the recipient received red blood cell transfusions after diagnosis and before the start of the preparative regimen, select “yes” and continue with question 46. If the recipient did not receive red blood cell transfusions prior to the preparative regimen, indicate “no” and continue with question 47.

**Question 46: Specify the total number of donor exposures (best estimate):**

Indicate the total number of red blood cell transfusions the recipient received after diagnosis and before the start of the preparative regimen. Using your best judgment, estimate the total number of transfusions based on progress notes and transfusion summaries since diagnosis. For example, if you have progress notes from a referring physician that state the recipient received one red blood cell transfusion a month for one year and then two transfusions monthly for six months before arriving at your center for HCT (i.e., 24 RBC transfusions prior to the preparative regimen), indicate that the recipient had 21-30 donor exposures between diagnosis and the start of the preparative regimen.

**Question 47: Did the recipient receive platelet transfusions between diagnosis and the start of the preparative regimen?**

Indicate “yes” if the recipient received platelet transfusions after diagnosis and before the start of the preparative regimen. Indicate “no” if the recipient did not receive any platelet transfusions prior to the preparative regimen.

## Laboratory Findings Prior to the Start of the Preparative Regimen

**Question 48: Reticulocytes (uncorrected):**

Indicate whether the uncorrected reticulocyte count in the blood is “known” or “not known” prior to the start of the preparative regimen. If “known,” report the value documented on the laboratory report. If “not known,” continue with question 49.

Report the absolute value of reticulocytes in \_\_\_ x 10<sup>9</sup>/L. Do not report a percentage, the corrected reticulocyte count, or the reticulocyte production index.

**Question 49: Date of most recent bone marrow biopsy:**

Report the date of the most recent bone marrow biopsy prior the start of the preparative regimen. Enter the date the sample was collected for examination.

**Question 50: Is a copy of the most recent bone marrow biopsy report attached?**

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

**Question 51: Were any clinically important infections present or being treated within one week prior to the preparative regimen?**

Indicate if there were any clinically important bacterial, viral, fungal, or parasitic infections present or being treated within one week prior to the start of the



preparative regimen. If “yes,” continue with question 52. If “no,” continue with question 80.

If it is unknown if the recipient had a clinically important infection or was being treated for any clinically important infections within one week prior to the start of the preparative regimen, select “unknown” and continue with question 80.

**Questions 52-79: Report each infection organism, site and date of diagnosis:**

For each infection, report the organism, site, and date of diagnosis.

**Organism:**

From the table “Codes for Commonly Reported Organisms,” select the code corresponding to the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. Report the code in the boxes provided. If the specific organism is not listed, use the “other, specify” code (198 - bacteria, 209 - *Candida*, 219 - *Aspergillus*, 259 - fungus, 329 - virus, 409 - parasite) and report the name of the organism in the space provided. If an organism is suspected, but not identified, report using codes 501-505 as applicable. If the source of the infection is not determined, use code 509.

**Bacterial infections:** *Atypical bacteria* (codes 101-119 and 501) are collected separately from other more common types of bacteria. *Typical bacteria* are codes 120-198 and 502. If more than one typical bacterial organism is found in a single site, include all the organisms in one listing; do not record each separately. Either write the code in the margin or use Report “Notes.”

**Fungal infections:** Note the inclusion of pneumocystis (formerly found under parasites). The most commonly found fungal infections are *Candida* (*C. albicans*, *C. tropicalis*, *C. glabrata* [also known as *Torulopsis glabrata*], *C. parapsilosis*, *C. krusei*), *Aspergillus* (*A. fumigatus*), *Fusarium* sp., and Zygomycetes.

**Viral infections:** These are caused by exposure to a new virus or reactivation of a dormant virus already present in the body. The most common viral infections are due to HSV (herpes simplex virus), VZV (varicella zoster virus, shingles), and CMV (cytomegalovirus).

**Parasitic infections:** Parasites are fairly rare. *Toxoplasma gondii* is often transmitted through the handling of a cat litter box. *Giardia* and *Cryptosporidium* can be found in contaminated water.

**Fever of undetermined origin:** Defined as “any fever (> 38°C) not associated with documented/suspected infection in a specific site,” data on fevers of undetermined origin are not collected by the CIBMTR, as the occurrence is too common for analysis.

**Site:**

From the table “Codes for Common Sites of Infection,” select the code corresponding to the site of the infection.

If three or more sites are infected with the same organism, enter code 2 (Disseminated - generalized, isolated at 3 or more distinct sites).

**NOTE: Disseminated Infections**

The CIBMTR acknowledges that a discrepancy exists between the CIBMTR definition (3 or more sites) and the BMT-CTN definition (2 or more sites) for disseminated infections. For the purposes of this form, please use “disseminated” when the same organism is isolated at three or more distinct sites.

**Date of Diagnosis:**

Report the collection date for the positive microbiology culture as the date of diagnosis for the infections. For suspected infections, enter the date of a radiology test or the date treatment was started as date of diagnosis. For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

**Question 80: 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.