DATE: July 17, 2020

TO: Elizabeth Ashley, OMB Desk Officer

Quinn Hirsch, OMB Desk Officer

FROM: Lisa Wright-Solomon, HRSA Information Collection Clearance Officer

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Request: The Health Resources and Services Administration (HRSA) Division of Transplantation requests approval for non-substantive changes to the Stem Cell Therapeutic Outcomes Database Collection (OMB #0915-0310, expires 10/31/2022).

Purpose: The purpose of this request is to make changes to the Disease Classification Form 2402 to maintain current and effective data collection. This memo explains the changes and supporting rationale.

The **Disease Classification Form 2402** is being modified to update and re-format relevant classifications of aplastic anemia, inherited bone marrow failure syndromes, and hemoglobinopathies.

The "inherited abnormalities of erythrocyte differentiation or function" section has been split into two sections for "inherited bone marrow failure syndromes" and "hemoglobinopathies." The "aplastic anemia" section has been updated to ensure accurate capture of relevant subtypes. This includes removing the "severe" language from all "severe aplastic anemia" text. Severity is now captured in a new question. Two new subtypes have also been added. Under "Hemoglobinopathies," two subtypes have been added including "transfusion dependent thalassemia" and "other transfusion dependent thalassemia."

These updates will be helpful to more accurately classify aplastic anemia, inherited bone failure syndromes, and hemoglobinopathies. It will simplify reporting for clinical research professionals who complete the forms. This will also save time for having to write in an "other" disease classification when a specific disease is not available on the form. The information requested should be routinely available.

Lastly, the form is also being modified to remove minimal, irrelevant questions from the Myelodysplastic Syndrome (MDS) and Multiple Myeloma / Plasma Cell Disorder (PCD) sections.

Time Sensitivity: The SCTOD data collection changes must be completed in a timely manner to fulfill Program requirements. To collect data on this form by late-October, approval of these changes is needed by September 15, 2020. The next release for data collection forms is scheduled approximately three months later.

Burden: The revisions included herein do not substantially change the estimated reporting burden for patients with these indications.

PROPOSED CLARIFICATIONS AND REVISIONS FOR STEM CELL THERAPEUTIC OUTCOMES DATABASE FORMS:

Form 2402

a. Question 2 Dropdown – Update

i. Updated "severe aplastic anemia" to "aplastic anemia."
ii. Updated "inherited abnormalities of erythrocyte differentiation or function" and split into "inherited bone marrow failure syndromes" and "hemoglobinopathies."
iii. Added "paroxysmal nocturnal hemoglobinuria (PNH)" (this was moved from the previous "inherited abnormalities of erythrocyte differentiation or function" section).

Rationale:

i. In prior years, only patients who met the definition for true severe aplastic anemia would proceed to transplant. More recently, transplants are performed more frequently and with many different regimens. Updating the nomenclature allows CIBMTR to clearly capture recipients with aplastic anemia who do not meet the definition of SAA and still proceed to transplant.
ii. "Inherited bone marrow failure syndromes" and "hemoglobinopathies" are accurate classifications (prior classification incorrect).
iii. PNH is correctly a singular primary disease.

b. Question 257 Dropdown – Removal

Removed option for "high transfusion burden (HTB)."
Rationale: This option would never be selected for a recipient with disease status "Hematologic improvement (HI)" at time of transplant.

c. Question 258 (F2402 R5) – Removal

Removed question to specify a major or minor response achieved.
Rationale: Recipients will never have high transfusion burden at transplant, therefore the major / minor response is not clinically relevant.

d. Question 422 (F2402 R5) – Removal

Removed question to capture plasma cells in blood by flow cytometry.

Rationale: Absolute number of plasma cells in blood by flow cytometry cannot be obtained and should be removed.

e. Question 446 (text and dropdown)– Update

i. Added floating text to clarify if the recipient developed MDS or AML, MDS or AML should be indicated as the primary disease.
ii. Removed "severe" language from question text and all "SAA" categories.
iii. Added floating text "(any form of hepatitis)" to the option "acquired AA secondary to hepatitis."
iv. Moved "dyskeratosis congenita" option under "inherited bone marrow failure syndromes" section.
v. Added options for "acquired AA secondary to chemotherapy" and "acquired AA secondary to immunotherapy or immune effector cell therapy."

Rationale:

i. Floating text adds further clarification.
ii. Severity will be captured in new Q447.
iii. Floating text adds further clarification.
iv. "Dyskeratosis congenita" most accurately falls under "inherited bone marrow failure syndromes" category.
v. These are relevant subtypes to capture.

f. Question 447– Addition

Added question to capture the aplastic anemia severity.

Rationale: Allows CIBMTR to capture recipients who do not meet the criteria for severe aplastic anemia.

g. Question 449 (text and dropdown) – Update

i. Added floating text to clarify if the recipient developed MDS or AML, MDS or AML should be indicated as the primary disease.
ii. Added "dyskeratosis congenita" option (moved from prior "severe aplastic anemia" section).
iii. Moved "Kostmann agranulocytosis (congenital neutropenia)" option from "Disorders of the Immune System" section and updated nomenclature to "Severe congenital neutropenia (including Kostmann syndrome)."
iv. Removed "other constitutional anemia."

Rationale:

i. Floating text adds further clarification.
ii. "Dyskeratosis congenita" most accurately falls under the "inherited bone marrow failure syndromes" section.

iii. This is the most accurate category and option text based on published literature.
iv. "Other constitutional anemia" is not relevant.

h. Question 451 Dropdown – Update / Addition

i. Removed "sickle thalassemia" and kept "sickle cell disease"
ii. Added option for "transfusion dependent thalassemia."

Rationale:

i. "Sickle thalassemia" falls under "sickle cell disease."
ii. "Transfusion dependent thalassemia" option allows capture of all genotypes that indicate thalassemia severity and could be treated by transplant.

i. Question 452 – Update / Addition

New question that includes:

i. Subtype "beta thalassemia major" updated to "transfusion dependent beta thalassemia."
ii. Added option for "other transfusion dependent thalassemia."

Rationale:

i. These are equivalent, however updated terminology is most accurate.
ii. Important to capture "other" subtypes which do not fall under the "transfusion dependent beta thalassemia" category.

j. Questions 455-460 – Update

Now only to be answered for "transfusion dependent thalassemia" recipients.
Rationale: Questions only relevant for these recipients, not sickle cell disease recipients.

k. Question 461 – Update

Updated hemoglobin measurement to maintain 9-10 g/dL (rather than 7 g/dL).
Rationale: This is more accurate measurement.

l. Question 474-477 – Update / Addition

Updated text to ask "if there was evidence of" and updated the options to "Yes", "No", and "Unknown." Will also capture the type of the fibrosis.
Rationale: More clear question text and intent.

m. Question 488 Dropdown – Update

Moved "Kostmann agranulocytosis (congenital neutropenia)" to section "Inherited Bone Marrow Failure Syndromes" (Question 449) and updated nomenclature to "Severe congenital neutropenia (including Kostmann syndrome)."
Rationale: This is the most accurate category and option text based on published literature.

Attachments:

1. Disease Classification F2402 R5. Current, approved form.
2. Disease Classification F2402 R6. All changes highlighted in yellow are updates, and all items highlighted in blue are additions.