HRSA
Health Resources & Services Administration
5600 Fishers Lane
Rockville, MD 20857

DATE: July 26, 2024

TO: Daniel Cline, OMB Desk Officer

FROM: Joella Roland, 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 (SCTOD) Collection (OMB 0915-0310 expiration date 08/31/2025).

Purpose: The purpose of this request is to request minor revisions to the pre-transplant data collection to maintain current and effective data collection. This memo explains the changes and supporting rationale.

Changes: HRSA is requesting OMB approval to make minor changes to the pre-transplant data collection. The request is to revise seven pre-transplant variables to include updates to the classifications of diseases found in response options as suggested by the World Health Organization (or similar international consensus organizations) and reflect the feedback from experts in the transplant community. These changes include new response options, and updated disease nomenclature for existing response options. While we are adding some response options, the number and content of questions are not increasing. Individual respondents will only answer one or two of these questions with updated response options. The revised response options will lead to more accurate information. See the "Change Summary" tab of Attachment 1, rows 2-8, for more details.

"Specify Myelodysplastic syndrome, unclassifiable (MDS-U)" was asked twice during pre-transplant information collection; the first time it was asked in reference to the initial diagnosis of MDS, and the second time it was asked in reference to potentially transformed MDS. Both questions will be removed from the form entirely. Per recommendations from the World Health Organization (or similar international consensus organizations), this disease categorization is obsolete. See the "Change Summary" tab of Attachment 1, rows 9-10 for more details.

Time Sensitivity: The SCTOD data collection changes must be completed in a timely manner to fulfill C.W. Bill Young Cell Transplantation Program requirements. These changes are considered non-substantive. Approval of

these changes is needed by August 15, 2024, to implement the changes in the data collection system during the scheduled Fall 2024 release. If this timeline is not met, the next release of data collection forms is scheduled approximately three months later.

Burden: The changes requested to update disease classifications/nomenclature only affect response options for seven questions without the addition of new questions. Although response options were updated for seven separate questions, individual respondents will only complete one or two of these questions depending upon the recipient's disease. These changes may improve response accuracy and clarify the choices for respondents. They will reduce the need to provide write-in responses and will not affect the response burden. Therefore, the changes are non-substantive and do not substantially change the estimated reporting burden for patients with these indications.

The removal of two questions is expected to reduce the burden slightly, but not significantly enough to adjust the burden hours.

SUMMARY OF PROPOSED NON-SUBSTANTIVE CHANGES FOR STEM CELL THERAPEUTIC OUTCOMES DATABASE VARIBLES.

Details can be found in Attachment 1 (complete spreadsheet of data collection to support the SCTOD). Table 1 below shows the change in red.

Item ID	Information Collection Domain Sub-Type	Information Collection update:	Proposed Information Collection Data Element (if applicable)	Proposed Information Collection Data Element Response Option(s)	Rationale for Information Collection Update
PRE044	Disease Classification	Change/Clarification of Response Options	Did AML transform from MDS or MPN?	no, ~~yes~~ yes, MDS-Also complete MDS Disease Classification questions yes, MPN- MPN Disease Classification questions	Capture data accurately
PRE047	Disease Classification	Change/Clarification of Response Options	Specify condition	~~Bloom syndrome~~, Biallelic germline BLM variant (Bloom syndrome) ~~Dyskeratosis congenita,~~ Telomere biology disorders (Dyskeratosis congenita and others) Down Syndrome, Fanconi anemia, Germline CEBPA variant (CEBPA-associated familial AML) Germline DDX41 variant Germline TP53 variant (Li-Fraumeni Syndrome) Germline RUNX1 variant (familial platelet disorder with associated myeloid malignancy, FPD-MM) Germline ANKRD26 variant (Thrombocytopenia 2) Germline ETV6 variant (Thrombocytopenia 5) Germline GATA2 variant (GATA2-deficiency) Germline SAMD9 variant (MIRAGE Syndrome)	Be consistent with the current clinical landscape and improve transplant outcome data.

				Germline SAMD9L variant (SAMD9L-related Ataxia Pancytopenia Syndrome) RASopathies (Neurofibromatosis type 1, CBL syndrome, Noonan syndrome, Noonan syndrome-like disorders) Severe congenital neutropenia (SCN) Other condition	
PRE137	Disease Classification	Change/Clarification of Response Options	Specify condition	Aplastic anemia ~~Bloom syndrome,~~ Biallelic germline BLM variant (Bloom syndrome) , Down Syndrome, Fanconi anemia, Germline DDX41 variant Germline TP53 variant (Li-Fraumeni Syndrome) Germline RUNX1 variant (familial platelet disorder with associated myeloid malignancy, FPD-MM) Germline ANKRD26 variant (Thrombocytopenia 2) Germline ETV6 variant (Thrombocytopenia 5) Germline PAX5 mutation Germline IKZF1 mutation Other condition	Be consistent with the current clinical landscape and improve transplant outcome data.
PRE222	Disease Classification	Change/Clarification of Information Requested and Response Option	Specify condition	Aplastic anemia, Germline CEBPA variant (CEBPA-associated familial AML), ~~DDX41-associated familial MDS,~~ Germline DDX41 variant Fanconi anemia, ~~GATA2 deficiency (including Emberger syndrome, MonoMac syndrome, DCML deficiency),~~Germline GATA2 variant (GATA2-deficiency) ~~Li-Fraumeni Syndrome,~~Germline TP53 variant (Li-Fraumeni Syndrome) Other condition, Paroxysmal nocturnal hemoglobinuria, Diamond-Blackfan Anemia, ~~RUNX1 deficiency (previously "familial platelet disorder with propensity to myeloid malignancies"),~~Germline RUNX1 variant ~~SAMD9- or SAMD9L-associated familial MDS,~~ Shwachman-Diamond Syndrome, Telomere biology disorder (including dyskeratosis congenita) Germline ANKRD26 variant (Thrombocytopenia 2) Germline ETV6 variant (Thrombocytopenia 5) SAMD9 variant (MIRAGE Syndrome) SAMD9L variant (SAMD9L-related Ataxia Pancytopenia Syndrome) Severe congenital neutropenia (SCN)	Be consistent with the current clinical landscape and improve transplant outcome data.
PRE365	Disease Classification	Change/Clarification of Information Requested and Response Option	Specify the lymphoma histology	**Hodgkin Lymphoma** Classic Hodgkin lymphoma (150), Lymphocyte depleted (154), Lymphocyte-rich (151), Mixed cellularity (153), Nodular lymphocyte predominant Hodgkin lymphoma (155), Nodular sclerosis (152) **Burkitt lymphoma** Burkitt lymphoma (111) **Large B-cell lymphomas** Diffuse large B-cell lymphoma, NOS (107), Diffuse, large B-cell lymphoma, Germinal center B-cell subtype (1820), Diffuse large B-cell lymphoma, Activated B-cell subtype (1821), T-cell / ~~histiocytic-rich~~ histiocyte-rich large B-cell lymphoma (120), Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with MYC and BCL2 rearrangements (1831), Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with MYC and BCL6 rearrangements, Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with MYC, BCL2, and BCL6 rearrangements, ALK-positive large B-cell lymphoma	Be consistent with the current clinical landscape and improve transplant outcome data.

				(1833, Large B-cell lymphoma with IRF4 rearrangement (1832), High-grade B-cell lymphoma with 11q aberrations (1834), Lymphomatoid granulomatosis (1835), EBV-positive diffuse large B-cell lymphoma (1823), Diffuse, large B-cell lymphoma associated with chronic inflammation (1825), Fibrin-associated large B-cell lymphoma (1839), Fluid overload-associated large B-cell lymphoma (1840), Plasmablastic lymphoma (1836), Primary cutaneous diffuse, large B-cell lymphoma, leg type (1822), Intravascular large B-cell lymphoma (136), Primary mediastinal large B-cell lymphoma (125), Mediastinal grey zone lymphoma (149), High-grade B-cell lymphoma, NOS (1830) **Primary large B-cell lymphoma of immune-privileged sites** Primary large B-cell lymphoma of the CNS (118), Primary large B-cell lymphoma of the vitreoretina (1882), Primary large B-cell lymphoma of the testis (1881) **KSHV/HHV8-associated B-cell lymphoid proliferations and lymphomas** Primary effusion lymphoma (138), KSHV/HHV8-positive diffuse large B-cell lymphoma (1826) **Lymphoplasmacytic lymphoma** Lymphoplasmacytic lymphoma (173), IgM-LPL/Waldenstrom macroglobulinemia (1883), Non-IgM-LPL/Waldenstrom macroglobulinemia (1884) **Marginal zone lymphoma** Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (122), Primary cutaneous marginal zone lymphoma (1813), Nodal marginal zone lymphoma (123), Pediatric marginal zone lymphoma (1813) **Splenic B-cell lymphomas** Splenic B-cell lymphoma/leukemia, with prominent nucleoli (1811), Splenic diffuse red pulp small B-cell lymphoma (1812), Splenic marginal zone lymphoma (124) **Follicular lymphoma** Duodenal-type follicular lymphoma (1815), Follicular, mixed, small cleaved and large cell (Grade II follicle center lymphoma) (103), Follicular, predominantly large cell (Grade IIIA follicle center lymphoma) (162),Follicular, predominantly large cell (Grade IIIB follicle center lymphoma) (163), Follicular, predominantly large cell (Grade IIIA vs IIIB not specified) (1814), Follicular, predominantly small cleaved cell (Grade I follicle center lymphoma) (102), Follicular (grade unknown) (164), Pediatric-type follicular lymphoma (1816) **Cutaneous follicle center lymphoma** Primary cutaneous follicle center lymphoma (1817) **Mantle cell lymphoma** Mantle cell lymphoma (115), Leukemic non-nodal mantle cell lymphoma (1886) **Transformations of indolent B-cell lymphomas** Transformations of indolent B-cell lymphomas (1887) **Lymphomas associated with immune deficiency and dysregulation** Classical Hodgkin lymphoma PTLD (1876), Infectious mononucleosis PTLD (1872), EBV-positive mucocutaneous ulcer (1824), Monomorphic PTLD (B- and T-/NK-cell types) (1875), Hyperplasia arising in immune deficiencies (e.g. PTLD) (1871), Polymorphic	

				lymphoproliferative disorders arising in immune deficiency/dysregulation (1874) **Mature T-cell and NK-cell leukemias** T-large granular lymphocytic leukemia (126), NK-large granular lymphocytic leukemia (1856), Adult T-cell lymphoma / leukemia (134), Sézary syndrome (142), Aggressive NK-cell leukemia (27) **Primary cutaneous T-cell lymphomas** Primary cutaneous acral CD8-positive T-cell lymphoproliferative disorder(1853), Primary cutaneous CD4-positive small or medium T-cell lymphoproliferative disorder (1854), Mycosis fungoides (141), Primary cutaneous CD30-positive T-cell lymphoproliferative disorder: Lymphomatoid papulosis (147), Primary cutaneous CD30-positive T-cell lymphoproliferative disorder: Primary cutaneous anaplastic large cell lymphoma, Subcutaneous panniculitis-like T-cell lymphoma (146), Primary cutaneous gamma/delta T-cell lymphoma (1851), Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma (1852), Primary cutaneous peripheral T-cell lymphoma, NOS (1889) **Intestinal T-cell and NK-cell lymphoid proliferations and lymphomas** Indolent T-cell -lymphoma of the gastrointestinal tract (1858), Indolent NK-cell lymphoproliferative disorder of the gastrointestinal tract , Enteropathy-associated T-cell lymphoma (133), Monomorphic epitheliotropic intestinal T-cell lymphoma (1857) Intestinal T-cell lymphoma, NOS **Hepatosplenic T-cell lymphoma** Hepatosplenic T-cell lymphoma (145) **Anaplastic large cell lymphoma** ALK-positive anaplastic large cell lymphoma (143), ALK-negative anaplastic large cell lymphoma (144), Breast implant-associated anaplastic large cell lymphoma (1861) **Nodal T-follicular helper (TFH) cell lymphoma** Nodal TFH cell lymphoma, angioimmunoblastic-type (131), Nodal TFH cell lymphoma, follicular-type (1859), Nodal TFH cell lymphoma, NOS (1860) **Other peripheral T-cell lymphomas** Peripheral T-cell lymphoma NOS (130) **EBV-positive NK/T-cell lymphomas** EBV-positive nodal T- and NK-cell lymphoma (1892), Extranodal NK / T-cell lymphoma (137) **EBV-positive T- and NK-cell lymphoid proliferations and lymphomas of childhood** Systemic EBV-positive T-cell lymphoma of childhood (1855), Other B-cell lymphoma (129), Other T-cell / NK-cell lymphoma (139)	
PRE477	Disease Classification	Change/Clarification of Information Requested and Response Option	Specify histiocytic disorder classification	**Diseases of immune dysregulation, Familial Hemophagocytic Lymphohistiocytosis (FHL)** Familial Hemophagocytic Lymphohistiocytosis, Perforin deficiency (FHL2) Familial Hemophagocytic Lymphohistiocytosis, UNC13D (FHL3) Familial Hemophagocytic Lymphohistiocytosis, STX11 (FHL4) Familial Hemophagocytic Lymphohistiocytosis, STXBP2 (FHL5) Familial Hemophagocytic Lymphohistiocytosis, no mutation identified. Familial Hemophagocytic Lymphohistiocytosis, other mutations	Be consistent with the current clinical landscape and improve transplant outcome data.

				Histiocytic disorder, not otherwise specified (570), Langerhans cell histiocytosis (histiocytosis-X) (572), Hemophagocytosis (reactive or viral associated) (573), Malignant histiocytosis (574),Other histiocytic disorder (579) **Diseases of immune dysregulation, hemophagocytic lymphohistiocytosis** Chediak-Higashi syndrome, Griscelli syndrome type 2, Hermansky-Pudlak syndrome type 2, Other pigmentary dilution disorder **Diseases of immune dysregulation, EBV susceptibility** SAP deficiency (XIAP-1) XIAP-2 deficiency ITK deficiency	
PRE464	Disease Classification	Change/Clarification of Information Requested and Response Option	Specify disorder of immune system classification	**Severe Combined Immunodeficiencies** SCID, T- B- NK-, Adenosine deaminase (ADA) deficiency SCID, T- B- NK-, reticular dysgenesis, SCID, T- B- NK+, RAG 1/2 deficiency SCID, T- B- NK+, DCLRE1C (Artemis) deficiency SCID, T-, normal B and NK cells, ILR alpha deficiency SCID, T- B- NK-, NOS SCID, not otherwise specified, Other SCID, **Combined Immunodeficiencies** CD40 ligand deficiency, DOCK8 Deficiency MHC Class II Deficiency (Bare lymphocyte syndrome) Omenn syndrome, ZAP-70 deficiency **Combined Immunodeficiencies with Associated or Syndromic Features** Ataxia telangiectasia, Cartilage-hair hypoplasia, DiGeorge anomaly, NEMO Deficiency Syndrome Wiskott-Aldrich syndrome, **Predominately Antibody deficiencies** Common variable immunodeficiency, Activated PI3 Kinase Delta Deficiency Syndrome (APDS1 or PIK3CD) ~~**Diseases of immune dysregulation, hemophagocytic lymphohistiocytosis**~~ ~~Chediak-Higashi syndrome,~~ ~~Griscelli syndrome type 2,~~ ~~Hermansky-Pudlak syndrome type 2,~~ ~~Other pigmentary dilution disorders,~~ ~~**Diseases of immune dysregulation, EBV susceptibility**~~ ~~SAP deficiency (XIAP-1)~~ ~~XIAP-2 deficiency~~ ~~ITK deficiency~~ **Diseases of immune dysregulation, syndromes with Autoimmunity, and Others, NOS** Autoimmune Lymphoproliferative Syndrome (ALPS) CTLA4 deficiency IPEX, Immune Dysregulation Polyendocrinopathy, enteropathy X-linked (FOXP3 deficiency) LRBA Deficiency STAT3 Gain of Function **Congenital defects of phagocyte** Chronic granulomatous disease, GATA2 deficiency Leukocyte adhesion deficiencies, Neutropenia with combined immune deficiency (MKL1 deficiency, Actin deficiency)	Be consistent with the current clinical landscape and improve transplant outcome data.

				Other Immunodeficiencies STAT1 Gain of Function Other immunodeficiencies, HIV infection, Immune deficiency, not otherwise specified.	
PRE218	Disease Classification	Deletion of Information Requested	Specify Myelodysplastic syndrome, unclassifiable (MDS-U)	~~Specify Myelodysplastic syndrome, unclassifiable (MDS-U)~~	Reduce burden: data no longer relevant
PRE246	Disease Classification	Deletion of Information Requested	Specify Myelodysplastic syndrome, unclassifiable (MDS-U)	~~Specify Myelodysplastic syndrome, unclassifiable (MDS-U)~~	Reduce burden: data no longer relevant

Attachments:

1. Current SCTOD Information Collections – Fall 2024