

Supporting Statement A
Stem Cell Therapeutic Outcomes Database
OMB Control No. 0915-0310
Revision

Terms of Clearance: None.

A. BACKGROUND

The Stem Cell Therapeutic and Research Act of 2005 (Public Law 109-129) as amended and codified in Section 379 of the Public Health Service Act (42 U.S.C. 274k) requires “The Secretary, acting through the Administrator of the Health Resources and Services Administration, shall by one or more contracts establish and maintain a C.W. Bill Young Cell Transplantation Program...that has the purpose of increasing the number of transplants for recipients suitably matched to biologically unrelated donors of bone marrow and cord blood, and that meets the requirements of this section.”¹ On behalf of the Secretary of Health and Human Services (“the Secretary”), the Health Resources and Services Administration (HRSA) provides oversight and management of the C.W. Bill Young Cell Transplantation Program (CWBYCTP).²

The CWBYCTP was reauthorized by the Stem Cell Therapeutic and Research Reauthorization Act of 2015 (Public Law 114-104) and the Transplant Act of 2021 (Public Law 117-15). These pieces of legislation also reauthorized other related programs, including the National Cord Blood Inventory (NCBI) and the Advisory Council on Blood Stem Cell Transplantation (ACBSCT).

1. C.W. Bill Young Cell Transplantation Program (CWBYCTP)

CWBYCTP provides an infrastructure for identifying, matching, and facilitating the distribution of bone marrow and cord blood from unrelated donors to individuals in need of hematopoietic stem cell transplants (HCT).³ The transplantation of these blood-forming cells from unrelated donors can improve patient-centered outcomes for individuals who have life-threatening diseases such as leukemia, lymphoma, sickle cell anemia, or other metabolic or immune system disorders.

The CWBYCTP includes the following functions: Bone Marrow Coordinating Center, Cord Blood Coordinating Center, Single Point of Access, Office of Patient Advocacy, and Stem Cell Therapeutic Outcomes Database. In 2017, HRSA re-organized these five functions into three major contracts as described below:

¹ The Stem Cell Therapeutic and Research Act of 2005 also requires that the Secretary, by contract, “establish and maintain a scientific database of information relating to patients who have been recipients of a stem cell therapeutics product (including bone marrow, cord blood, or other such product) from a donor.” 42 U.S.C. 274l(a).

² Specifically, HRSA’s Health Systems Bureau, Division of Transplantation oversight.

³ Various acronyms refer to hematopoietic stem cell transplantation, including HPSC, HSCT, or the current usage of HCT. Unless quoting statute, regulations, or other official documents, HCT is used throughout this statement.

- **Single Point of Access-Coordinating Center (SPA-CC).** This contract coordinates a network of organizations to recruit potential donors with an emphasis on the recruitment of individuals from diverse, underrepresented racial and ethnic populations. This network collectively provides access to bone marrow transplants, provides tissue typing to match patients and donors, and engages in public and professional educational activities. The SPA-CC also contains a network of cord blood banks (CBBs) that lists its cord blood units (CBUs) and makes them available for transplantation. The SPA-CC maintains a single, searchable electronic system for health care professionals and physicians searching on behalf of patients for cells derived from adult bone marrow donors and CBUs through a single point of access.
- **Office of Patient Advocacy (OPA).** This contract supports patient advocacy and case management specific to bone marrow and blood stem cell transplantation, histocompatibility/search expertise, and guidance for patients and physicians. The OPA provides public and professional education, information, resources, and support for bone marrow transplant patients and families from diagnosis through survivorship.
- **Stem Cell Therapeutic Outcomes Database (SCTOD).** This contract provides a repository of donor and patient samples for research and supports an electronic database of blood stem cell transplantation products, processes, and outcomes for use by researchers, health care professionals, and the public. The SCTOD produces data on clinical outcomes (e.g., by HCT facility and treatment method) that supports patient decision-making and fosters continuous quality improvement efforts among health care professionals and HCT facilities.

As part of its oversight responsibilities, HRSA submits an annual Report to Congress on the performance and activities of these contractors in supporting the CWBYCTP.⁴

2. National Cord Blood Inventory (NCBI)

The NCBI Program contracts with cord blood banks (CBBs) to meet the statutory goal of building a public inventory of at least 150,000 new, high quality, and genetically diverse cord blood units (CBUs). These CBUs are available for transplantation through the CWBYCTP.

3. Advisory Council on Blood Stem Cell Transplantation (ACBSCT)

The role of the ACBSCT is to advise, assist, consult with, and make recommendations to the Secretary of Health and Human Services (HHS) and the Administrator of HRSA on matters conducted by both the CWBYCTP and the NCBI Program.⁵

⁴ <https://bloodstemcell.hrsa.gov/about/legislation/reports-congress>

⁵ <https://bloodstemcell.hrsa.gov/about/advisory-council>

B. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

The Stem Cell Therapeutic and Research Act of 2005 requires that the Secretary, by contract, “establish and maintain a scientific database of information relating to patients who have been recipients of a stem cell therapeutics product (including bone marrow, cord blood, or other such product) from a donor.” 42 U.S.C. 274l(a). [see attachments] Based on this authority, HRSA requests that the Office of Management and Budget (OMB) continue approval of the collection of information for the Stem Cell Therapeutic Outcomes Database (SCTOD), a component of the C.W. Bill Young Cell Transplantation Program (CWBYCTP). The collection of these data fulfills the statutory requirements at 42 U.S.C. 274l.

2. Purpose and Use of Information

The overall purpose of the data collection is to improve the survival, treatment, and quality of life for patients who may benefit from cellular therapies. It does so by fulfilling the legislative requirement at 42 U.S.C. 274l(a) to establish and maintain a scientific database of information relating to donors and recipients of a stem cell therapeutics product. Per 42 U.S.C. 274l(b), the outcomes database shall include information regarding “diagnosis, transplant procedures, results, long-term follow-up, and such other information as the Secretary determines to be appropriate” to conduct an ongoing evaluation of the scientific and clinical status of HCT transplantation. HRSA, through its SCTOD contractor, maintains the scientific database and fulfills the statutory requirements to provide information for two primary purposes:

- The submission of an annual report to the Secretary “concerning patient outcomes with respect to each transplant center” under 42 U.S.C. 274l(c) and
- The provision of relevant and de-identified scientific information to the public in the form of summaries and data sets under 42 U.S.C. 274l(d).

To meet these requirements, the SCTOD contractor supports HRSA’s production of annual reports, including a U.S. Patient Survival Report, U.S. Transplant Data by Center Report, U.S. Transplant Data by Disease Report, and a Transplant Activity Report.^{6,7} These reports and their datasets contain center-specific transplant patient-, disease-, and procedure-related characteristics and outcomes for nearly all allogeneic and a majority of autologous HCTs performed in the U.S.

Much like Medicare’s CareCompare website for hospitals,⁸ these reports include transplant center-specific data that provide potential HCT recipients, their families, and the general public with a comparison of survival rates among the centers in the CWBYCTP network. Also, like Medicare’s CareCompare website, some of the transplant center-specific data (e.g., survival rates) are based on transparent statistical models that adjust for several risk factors. And finally,

⁶ <https://bloodstemcell.hrsa.gov/data>

⁷ <https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics/transplant-activity-report#summary>

⁸ <https://www.medicare.gov/care-compare/>

like Medicare's CareCompare website, the SCTOD contractor intends to continually improve the value of its models and public reporting. Thus, in consultation with stakeholders, it may update some of its models and their required data on a basis more frequently than every 3 years in order to reflect the most up-to-date evidence on clinical care and statistical modelling.⁹

In addition to the HRSA reports and related datasets, the SCTOD contractor also provides two major annual reports and four quarterly newsletters to the public each year:

- *Facts and Figures* is issued midyear and provides a summary of the accomplishments in each research program, key publications, and high priority initiatives;¹⁰
- *Annual Report* is issued each February and provides information on organizational goals and achievements as well as operational details on contractor operation;¹¹ and
- Quarterly newsletters are distributed via email and feature updates on working committees, data management and collection, as well as newsworthy events in the hematopoietic cell transplantation (HCT) community.¹²

To help meet the second statutory requirement, the SCTOD contractor also produces study summaries for patients, de-identified data for original and secondary analysis, and a highly detailed report on survival statistics that describes the use and outcome of autologous and allogeneic HCT in more than 500 centers that have participated in the program.^{13,14,15,16} These reports, summaries, and data are made available to assist with program operation; to encourage medical research; and to provide relevant, timely, and actionable information to transplant programs, physicians, patients, certain donor registries,¹⁷ and cord blood banks.

As part of its ongoing efforts to provide transparency, demonstrate value, and welcome research, the SCTOD contractor maintains a Working Committee Research Portfolio that lists recently published and current studies for each Working Committee, and it provides information regarding the committee structure and contact information for those who may wish to participate in or lead studies.¹⁸ The data, resources, and support provided by the entity currently serving as the SCTOD contractor have resulted in over 1,500 peer-reviewed publications, including more than 100 journal articles in 2021.^{19,20,21}

9 Transplant center-specific survival rates are based on one-year overall survival and estimated using a censored data logistic regression model that adjusts for several risk factors: https://www.cibmtr.org/ReferenceCenter/SlidesReports/USStats/Documents/CIBMTR_HCT_Center_Survival_Report_Methodology.pdf

10 <https://www.cibmtr.org/About/AdminReports/Pages/index.aspx>

11 <https://www.cibmtr.org/About/AdminReports/Pages/index.aspx>

12 <https://www.cibmtr.org/ReferenceCenter/Newsletters/Pages/index.aspx>

13 <https://www.cibmtr.org/ReferenceCenter/Patient/PatientSummaries/pages/index.aspx>

14 https://www.cibmtr.org/Data/Available/Pages/index.aspx#data_request

15 <https://www.cibmtr.org/ReferenceCenter/PubList/PubDsDownload/Pages/default.aspx>

16 <https://www.cibmtr.org/ReferenceCenter/SlidesReports/StatReport/Pages/index.aspx>

17 Donor registries awarded a contract under section 379 of the Public Health Service Act (42 U.S.C. 274k).

18 Study lists are available at: <https://www.cibmtr.org/Studies/Observational/StudyLists/Pages/index.aspx>

19 The publication list is available at: <https://www.cibmtr.org/ReferenceCenter/PubList/Pages/index.aspx>

20 All disclosures by the SCTOD contractor are governed by Privacy Act System of Records Notice #09-15-0068 (notification of an altered system of records was published on February 14, 2018, at 83 FR 6591).

21 Though the collection of data for the SCTOD is not a research project, the SCTOD contractor submitted for ethical review to the NMDP Institutional Review Board (IRB) and was approved. The NMDP IRB is registered with the HHS Office of Human Research Protections (Registration IRB00001253) and has an approved Federalwide

The SCTOD contractor also supports decision-making for other parts of the Government. For example, the SCTOD contractor currently sponsors five separate clinical studies to support the Centers for Medicare and Medicaid Services (CMS) and its coverage with evidence development (CED) process. These five clinical studies aim to develop evidence to support coverage decisions regarding stem cell transplantation as a treatment for Myelodysplastic Syndrome (MDS), Sickle Cell Disease, Myelofibrosis, and Multiple Myeloma.^{22,23,24,25,26,27}

3. Use of Improved Information Technology

The Stem Cell Therapeutic Outcomes Database (SCTOD) has ingested electronic records and data that are submitted to the database through one of two primary methods: a secure Web-based application known as FormsNet and an open-source messaging system specifically designed to exchange HCT data using a secure, standards-based system, known as AGNIS® (A Growable Network Information System). The SCTOD contractor also implemented an application that uses an HHS-approved application programming interface (API) known as the HL7 Fast Healthcare Interoperability Resources® (FHIR®) standard that enables automated acquisition of data from EMR and other real world evidence source systems deployed within reporting centers.^{28,29}

The SCTOD contractor's current default method for data collection is FormsNet, which is a single Web-based application for data entry, viewing, and auditing of electronic data and allows remote data entry of all transplant baseline and follow-up data by transplant centers.³⁰ Important features included in the current version of FormsNet application (v3) are:

- 24/7 accessibility;
- create/edit data collection instruments and inserts;
- create/edit all contractor-specific inserts;
- create/edit confirmation of Human Leukocyte Antigen (HLA) typing and product data;
- audit trail and user interface;
- data entry and data reconciliation; and
- tools for monitoring accuracy and processes.

FormsNet also includes: automated validation checks within and between data collection instruments; automatically generated error reports; field-level saving and field-level audit trails;

Assurance (FWA00000441) [<https://ohrp.cit.nih.gov/search/IrbDtl.aspx>]. All HCT facilities must obtain IRB-approved informed consent from recipients to allow SCTOD data to be used for research studies.

22 <https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCID=366&DocID=110.23>

23 <https://clinicaltrials.gov/ct2/show/NCT01166009>

24 <https://clinicaltrials.gov/ct2/show/NCT02766465>

25 <https://clinicaltrials.gov/ct2/show/NCT02934477>

26 <https://clinicaltrials.gov/ct2/show/NCT01166009>

27 <https://clinicaltrials.gov/ct2/show/NCT03127761>

28 <https://fhir.nmdp.org/ig/cibmtr-reporting/>

29 The Office of the National Coordinator for Health Information Technology adopted a new standardized Application Programming Interface (API) certification criterion for patient and population services that requires the use of the FHIR® standard and references several standards and implementation specifications adopted in 45 CFR §170.213 and 45 CFR §170.215 to support interoperability (85 FR 25642)

30 <https://www.cibmtr.org/DataManagement/SystemApplications/FormsNet3/Pages/default.aspx>

review functions for center supervisors; forms due reporting; and the flexibility to add additional features. And finally, FormsNet provides additional functionality that can reduce burden and increase data quality (e.g., modifying response options in drop down boxes to align with current medical evidence and modifying question paths to align with respondent workflow).

FormsNet is fully compliant with Federal database security requirements as established by HRSA's Office of Information Technology (OIT) and the Food and Drug Administration (FDA) *21 CFR Part 11; Electronic Records; Electronic Signatures Maintenance of Electronic Records and Computerized Systems Used in Clinical Trials*.

In an effort to continually improve its data collection process, the SCTOD contractor performed an analysis to identify the gaps between the current state and desired future state for collecting data that (1) reduces burden and (2) results in data that are timely, meaningful, and actionable. Based on this analysis, the SCTOD contractor implemented its Data Transformation Initiative (DTI), whose vision is "to optimize the acquisition and utilization of entrusted data assets to accelerate breakthroughs that transform patient experiences."³¹ To support the Initiative, the SCTOD contractor took two simultaneous paths to improving data quality and reducing burden:

- Development and implementation of an Epic®-based CIBMTR Reporting Application (CRA) that auto-populates fields in the FormsNet application using data from the HCT facility's electronic health record and
- Development and release of tools, performance of voluntary pilots, and enrollment of interested facilities into a program to submit data using the HL7 Fast Healthcare Interoperability Resources® (FHIR®) standard.^{32,33,34,35}

With the increased use of these interoperability tools, HRSA and its contractor intend to continually refine and improve their data collection so that it reflects the most up-to-date medical evidence while simultaneously reducing HCT facility burden.

4. Efforts to Identify Duplication

The SCTOD data system is the only nationwide data collection effort specific to donors and recipients of a stem cell therapeutics product (including bone marrow, cord blood, or other such product). The system's unique and robust data collection efforts using internationally recognized instruments makes it helpful for research, education, and policy development purposes. No other entity is authorized by the Federal government to gather similar data related to HCT.

³¹ <https://www.cibmtr.org/DataManagement/DataTransformation/Pages/default.aspx>

³² <https://apporchar.d.epic.com/Gallery?id=754>

³³ <https://www.cibmtr.org/DataManagement/DataTransformation/Pages/default.aspx>

³⁴ In October 2020, the SCTOD contractor began testing a proof-of-concept pilot for use of the HL7® FHIR® standard. In six months, four diverse transplant centers successfully completed the pilot. As of March 2022, eighteen HCT facilities are submitting data via the HL7® FHIR® standard, ten are in the implementation process and another sixty have expressed interest.

³⁵ As described by the Office of the National Coordinator for Health Information Technology, "The HL7® FHIR® standard defines how healthcare information can be exchanged between different computer systems regardless of how it is stored in those systems. It allows healthcare information, including clinical and administrative data, to be available securely to those who have a need to access it, and to those who have the right to do so for the benefit of a patient receiving care." See: <https://www.healthit.gov/sites/default/files/2019-08/ONCFHIRFSWhatIsFHIR.pdf>

5. Impact on Small Businesses or Other Small Entities

This project will not be collecting any data from small businesses as defined by OMB. The data collected will not have any significant impact on small business or other small entities.

6. Consequences if Information Collected Less Frequently

The information collection activity outlined in this request is required under the Stem Cell Therapeutic and Research Act of 2005, as amended and codified in Section 379 of the Public Health Service Act (42 U.S.C. 274k et seq.). These data, and their data collection periods, represent a consensus-based solution to balancing reporting burden with statutory requirements. Additionally, facilities who submit data to the SCTOD are regularly consulted regarding any improvements and changes in data collection [See Section B.3. Use of Improved Information Technology]. For example, the SCTOD contractor holds an annual Clinical Research Professionals / Data Management conference and a bi-annual Center Outcomes Forum. At these conferences, transplant physicians and center directors, the American Society for Transplantation and Cellular Therapy (ASTCT), governmental funding agencies, patients, private payers, and statisticians are consulted regarding data collection and outcomes reporting.³⁶

The requirements for data collection include numbers of transplants facilitated by the CWBYCTP, numbers of transplants performed annually in the United States, outcomes of those transplant procedures, long-term outcomes of blood stem cell transplantation, effective use of cord blood units for transplantation, and alternative uses of cells derived from bone marrow, peripheral blood, and cord blood. Additionally, these requirements include annual Transplant Center-Specific Survival Reports that are made available to patients, physicians, and the public.

To meet these requirements, HRSA requests continuation of the current data collection schedule:

Pre-transplant Data (within 30 days of transplant)

- Baseline recipient data including patient demographics, pertinent medical history, disease characteristics and status, and co-morbidities;
- Procedure characteristics, including preparative regimen; and
- Donor data.

Transplant Data (within 60 days of transplant)

- Graft-vs-Host Disease (GVHD) prophylaxis, graft source, donor type and degree of HLA matching and graft manipulation;
- Graft characteristic data for cord blood units, including infused cell dose; and
- Product information.

Post-Transplant Data (100 days after transplant, 6 months after transplant, 1 year after transplant, annually for 6 years after transplant and then biennially thereafter)³⁷

³⁶ <https://www.cibmtr.org/Meetings/Materials/Pages/index.aspx>

³⁷ In the circumstance that a patient dies, cause of death data will be collected as soon as possible after death.

- Hematopoietic recovery and engraftment,³⁸ serious complications including GVHD and second cancers, disease status, survival status, and cause of death; and
- Subsequent procedures.

These expectations and timelines for data submission are the result of ongoing input from the transplant community and the facilities who provide the data. In order to meet statutory requirements under 42 U.S.C. 274l, the SCTOD contractor will continue to work with stakeholders in order to improve the quality of data used for clinical research and outcomes reporting (e.g., disease classification, risk factors, and risk adjustments).

Collecting data at the proposed time points is not only essential to understand outcomes at various time points in the transplant process but it also represents standard time points of assessment for allogeneic transplant recipients. These time points are also meant to reinforce the importance of follow-up assessments by transplant centers to avoid losing contact with transplant recipients in a system where recipients gradually become more remote from the tertiary care centers where allogeneic transplantation is performed.

If the information required by statute is not collected at the desired timepoints, HRSA will not be in compliance with the authorizing legislation. Additionally, collecting less information at each timepoint than that which is proposed would also be contrary to statutory direction and community consensus.³⁹ These data are also required by the Secretary to report the following:

- Whether program funds for the SCTOD are fulfilling the mission of the CWBYCTP;
- The indications for and outcomes from various types of transplants performed in U.S.; and
- Facility-specific HCT outcomes.

The legal obstacles to reducing burden are the authorizing statutes at 42 U.S.C. 274k and 274l.

7. Special Circumstances Relating to the Guidelines at 5 CFR 1320.5(d)(2)

As described above, HCT facilities may report data to HRSA's contractor more often than quarterly. The HCT data reporting schedule is patient-based as opposed to facility-based and follows a standardized schedule: baseline (within 30 days of HCT), 100 days after HCT, 6 months after HCT, 1 year after HCT, annually for 6 years after HCT and biennially thereafter, and, if the patient dies, cause of death data. The reason for this scheduling is that the timeliness of pre- and post-transplant data collection is essential to improving patient outcomes and advancing organ transplantation policy and science.

Other than this special circumstance described above regarding 5 CFR 1320.5(d)(2)(i), there are no other special circumstances that would require an information collection to be conducted in a manner that requires respondents to:

- Prepare a written response to a collection of information in less than 30 days after receipt;

³⁸ The process in which transplanted hematopoietic cells begin to grow in the bone marrow of the host and to produce new white blood cells, red blood cells and platelets.

³⁹ For example, the Foundation for Accreditation of Cellular Therapy (FACT), which accredits HCT facilities, coordinates with the SCTOD contractor on data quality and announced on March 1, 2017, that it will no longer include verification of clinical data against source data as FACT clinical inspectors have access to CIBMTR data audit results.

- Submit more than an original and two copies of any document;
- Retain records, other than health, medical, government contract, grant-in-aid, or tax records for more than 3 years;
- Collect data in connection with a statistical survey that is not designed to produce valid and reliable results that can be generalized to the universe of study;
- Use a statistical data classification that has not been reviewed and approved by OMB;
- Include a pledge of confidentiality that is not supported by authority established in statute or regulation that is not supported by disclosure and data security policies that are consistent with the pledge, or which unnecessarily impedes sharing of data with other agencies for compatible confidential use; or
- Submit proprietary trade secret, or other confidential information unless the agency can demonstrate that it has instituted procedures to protect the information's confidentiality to the extent permitted by law.

8. Comments in Response to the Federal Register Notice/Outside Consultation

Section 8A:

The 60-day notice required in 5 CFR 1320.8(d) was published in the *Federal Register* on March 18, 2022 (87 FR 15439). No comments were received.

The 60-day notice required in 5 CFR 1320.10(a) was published in the *Federal Register* on June 7, 2022 (87 FR 34692). No comments were received.

Section 8B:

HRSA and its SCTOD contractor regularly consult with outside persons to obtain their views on the data collected, including consideration of data availability, data frequency, instructions, data dictionaries, reporting, and disclosures. These data, and their data collection periods, represent a consensus-based solution to balancing reporting burden with statutory requirements. Facilities who submit data to the SCTOD are regularly consulted regarding any improvements and changes in data collection [See Section B.3. Use of Improved Information Technology].

The SCTOD contractor holds an annual Clinical Research Professionals / Data Management conference and a bi-annual Center Outcomes Forum. At these conferences, transplant physicians and center directors, the ASTCT, governmental funding agencies, patients, private payers, and statisticians are consulted regarding data collection and outcomes reporting.⁴⁰

Data collection instruments are reviewed on an established timeline, at least once every three years, to ensure that the most relevant data are being collected. Broad stakeholder participation in this process is accomplished through the Working Committees established by the SCTOD contractor, and include cord blood banks, other CWBYCTP contractors, HCT facilities, and other stakeholders such as Eurocord, the European Group for Blood and Marrow Transplantation (EBMT), the Worldwide Network for Blood and Marrow Transplantation (WBMT), ASTCT, and the Foundation for the Accreditation of Cellular Therapy (FACT).

⁴⁰ <https://www.cibmtr.org/Meetings/Materials/Pages/index.aspx>

HRSA and its SCTOD contractor promote international harmonization of HCT data standards by participating in the annual data standards review of the EBMT and the WBMT. Broad acceptance of these standards facilitates the acquisition of data regarding HCTs done outside the U.S. using U.S. products. The SCTOD contractor will also continue to work with ASTCT, EBMT, WBMT, the Clinical Working Group of the World Marrow Donor Association (WMDA), cord blood banks (using the Cord Blood Data Working Group), and other CWBYCTP members to achieve consensus on any revisions to the standard dataset. Finally, the SCTOD contractor will continue to coordinate with the SPA-CC contractor and NMDP Histocompatibility Advisory Group to ensure that HLA data reflect current matching algorithms.

9. Explanation of Any Payment/Gift to Respondents

Respondents will not receive any payments or gifts associated with completing these forms for the CWBYCTP.

10. Assurance of Confidentiality Provided to Respondents [respondents are facilities]

All data collected will be subject to Privacy Act protection (Privacy Act System of Records #09-15-0068). Data collected under the SCTOD contract also are well protected within the contractor's robust cybersecurity program, which is aligned to NIST 800-53, Security and Privacy Controls for Federal Information Systems and Organization, and is assessed annually by a qualified, independent third-party auditor to ensure that it meets or exceeds the requirements as prescribed by OMB Circular A-130, Appendix III, Security of Federal Automated Information Systems, and the Departments Automated Information Systems Security Program Handbook. These security features are implemented within a comprehensive System Security Plan that addresses administrative, operational and technical controls, including but not limited to:

- Annual risk assessment;
- System and component inventories;
- Annual security awareness & data privacy training;
- System and data access control and entitlement reviews;
- System event auditing and accountability;
- Configuration and change management;
- Threat and vulnerability management and remediation;
- Incident response and management;
- Contingency Planning;
- Annual privacy impact assessment;
- Physical and facilities access and security; and
- Continuous Monitoring,

The SCTOD contractor utilizes a unique identification (ID) registration system for transplant recipients to avoid redundant reporting of transplant recipients across transplant centers and across time. This unique ID registration system exists within an isolated server and uses identifying information about transplant recipients provided by the transplant center to assign a unique ID number that does not contain personal identifiers. Subsequently, this unique number

is used by the transplant center and other CWBYCTP components to exchange data regarding transplant recipients for purposes of reporting outcomes to the Government.

The ID registration system and the exchange of data between entities exists within the context of the designation of the SCTOD contractor, CIBMTR, as a public health authority for purposes of the Health Insurance Portability and Accountability Act (HIPAA) as determined by the HHS Office of General Counsel (OGC) and Office of Civil Rights (OCR) in fulfillment of the contract requirements (PHA letter attached). The OGC has determined, and OCR concurs, that the SCTOD contractor meets the Privacy Rule's definition of a public health authority and is authorized by law to collect the information necessary for the SCTOD to fulfill its statutory purpose and functions. Under this analysis, transplant centers that are covered entities may disclose to the SCTOD contractor the individually identifiable health information collected by the SCTOD to comply with its statutory purposes. Additionally, the electronic systems used to create and maintain the unique ID system exist under the auspices of HRSA's Office of Information Technology (OIT) Certification and Accreditation system.

Although the data collection instruments do not request direct identifiers, by virtue of the nature of reporting transplant outcomes required for the SCTOD contract, they request birth dates, procedure dates, complication and event dates, and death dates. These data are housed in secure electronic data systems which exist with certification and accreditation from HRSA OIT.

Data will be kept private to the extent allowed by law. This data collection is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify a patient in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless the patient has consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if the patient has consented to the disclosure, including for medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by Federal funding agencies or for information that must be disclosed in order to meet the requirements of the U.S. Food and Drug Administration (FDA).

11. Justification for Sensitive Questions

There are no questions of a possible sensitive nature, except for race and ethnicity. These data are necessary to support analysis of demographic subgroups and support efforts to improve health equity. The only patient-level identifying information is birth date, procedure and complication dates, and death dates. These are required for outcomes reporting for the SCTOD. However, as

detailed above, these data are maintained in secure and protected systems. Only aggregate data summarizing transplant activity and outcomes are included in reports published by the SCTOD.

12. Estimates of Annualized Hour and Cost Burden

The estimate of annualized respondent burden hours and costs to complete data collection instruments is shown in Tables 1 and 2. As shown in the Table 1, the SCTOD contractor collects transplant data from 177 U.S. transplant centers using these reporting instruments. Over time there is an expected increase in the number of recipients for whom data are reported as the number of transplants performed annually is increasing and survivorship after transplantation is improving. The burden of data collection and reporting will vary by transplant center, as HCT facilities exhibit a large variation in the number of allogeneic transplants performed.

12A.

Table 1. Estimated Annualized Burden Hours - Stem Cell Therapeutic Outcomes Database

Form Name ⁴¹	Number of Respondents ⁴²	Number of Responses per Respondent ⁴³	Total Responses ⁴⁴	Average Burden per Response (in hours)	Total Burden Hours
Pre-Transplant Information Collection	177	52.6	9,310 ⁴⁵	1.4 ⁴⁶	13,041
Transplant Procedure and Product Information	177	52.6	9,310 ⁴⁷	1.1 ⁴⁸	10,247
Post-Transplant Periodic Information Collection based on Predetermined Schedule	177	319.1	56,481 ⁴⁹	0.5 ⁵⁰	28,238

41 This burden estimate table refers to data collections at different time periods consistent with approved practice. The SCTOD contractor is working with respondents to reduce burden by submitting data using interoperability standards. These data collections may include OMB-approved forms.

42 The total number of transplant centers that submit data to the SCTOD is 177.

43 The Number of Responses per Respondent was calculated by dividing the Total Responses by the Number of Respondents and rounding to the nearest tenth.

44 The total number of responses is less than previous calculations because of improvements in estimation. Previous estimates assumed all years had the same number of transplants. This improved estimate includes accurate transplant counts from prior years, which are often less than the current year leading to less follow-up activity.

45 Total responses for Pre-Transplant Information Collection equals estimated number of new transplant patients in 2021.

46 Pre-transplant Data includes baseline recipient data including patient demographics, pertinent medical history, disease characteristics and status, and co-morbidities, transplant data procedure characteristics, including preparative regimen, and donor data. This number is rounded to nearest tenth. The actual burden estimate for these data is 1.4175.

47 Transplant Procedure and Product Information equals estimated number of new transplant patients in 2021.

48 Transplant Procedure and Product Information includes Graft-vs-Host Disease (GVHD) prophylaxis, graft source, donor type and degree of HLA matching and graft manipulation; graft characteristic data for cord blood units, including infused cell dose; and product information. This number is rounded to nearest tenth. The actual burden estimate for these data is 1.0616.

49 The number of responses for Post-Transplant Periodic Information Collection is based on a predetermined schedule: 100 days after transplant, 6 months after transplant, 1 year after transplant, annually for 6 years after transplant and then biennially thereafter. In any given year the number of responses is a function of the number of

Total	177		75,101		51,526
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12B.

Table 2. Estimated Annualized Burden Costs

Type of Respondent	Total Burden Hours	Hourly Wage Rate (\$) ⁵¹	Total Respondent Costs (\$)
Data Manager	51,526	20.38	1,050,500
Total	51,526	20.38	1,050,500

13. Estimates of other Total Annual Cost Burden to Respondents or Recordkeepers/ Capital Costs

Other than their time, there is no cost to respondents.

14. Annualized Cost to the Federal Government

The annual estimated government cost for a contract to carry out this study is approximately \$4 million to be spent on all aspects of the contract for the operation of the Stem Cell Therapeutic Outcomes Database. The annual cost to the federal government for the SCTOD contract in FY 2020 was \$4,601,550.

Additionally, HRSA obligated \$4,730,240 to the SCTOD contract for FY2021. The information is collected as part of the SCTOD's contract requirements. The SCTOD is a firm fixed-price contract that HRSA awarded to the SCTOD contractor for five years in FY2017. The total cost of this contract is approximately \$22,478,225.

15. Explanation of Program Changes or Adjustments

This is a revised collection of information with an estimated reduction to the overall hour burden inventory to 75,101 due to improvements in burden estimation. As noted in Table 1, the total number of responses is less than previous calculations because of improvements in estimation. The number of responses in any given year is a function of three values: the number of transplants in the year of interest, the number of transplants in previous years, and expected patient survival between the time of transplant and any follow-up activity. Previous estimates assumed all years had the same number of transplants. This improved estimate includes accurate transplant counts from prior years, which are often less than the year of interest.

16. Plans for Tabulation, Publication, and Project Time Schedule

Publication: The data collected using the instruments outlined above populate a database for the SCTOD and are used for numerous analyses, reports, and publications. Data collected for the

transplants in that year, the number of transplants in previous years, and expected patient survival between the time of transplant and any follow-up activity.

50 Post-Transplant Data Collection includes hematopoietic recovery and engraftment, serious complications including GVHD and second cancers, disease status, survival status, and cause of death; and subsequent procedures. This number is rounded to nearest tenth. The actual burden estimate is 0.5247.

51 Source: Hourly Wage Rate based on the United States Department of Labor, Bureau of Labor Statistics (https://www.bls.gov/news.release/archives/ecec_06082018.htm)

SCTOD are shared with other components of the CWBYCTP in fulfillment of the goals and statutory charge of the CWBYCTP. The data collected is shared to HRSA and reports from the data are shared to umbilical cord blood banks and the transplant programs themselves. The outcomes database is also used to prepare reports about the CWBYCTP for the Secretary, the Advisory Council on Blood Stem Cell Transplantation, HRSA, and the public. One of the main reports produced under SCTOD is the Transplant Center-Specific Survival Report, which outlines the specific survival rates for all transplant centers in the U.S. This is an extremely important report for patients and physicians, both for improving quality of care at transplant centers and for helping patients and their physicians make well-informed choices about which transplant centers are most appropriate for each patient.

In addition, as required in 42 U.S.C. 2741(d), the outcomes database makes relevant scientific information that does not contain individually identifiable information available to the public. This information is provided by CIBMTR in the form of summaries and data sets to encourage medical research and to provide information to transplant programs, physicians, patients, and cord blood banks. The Transplant-Center Specific Survival Report and the U.S. Transplant Activity Report are available on the HRSA website, and the de-identified dataset is available upon request.

Analysis Plan: The report will provide tabulations at the national level, and for relevant subpopulations, including age groups, gender, racial and ethnic groups, and broad disease group. It will include an executive summary along with detailed findings about factors related to center specific survival and/or transplant activity that occurred in the United States. This information collection will not use statistical methods such as sampling, imputation, or other statistical estimation techniques.

Time Schedule: The center-specific survival analysis report is delivered to HRSA annually in the fall and made available to the public each December. The data collection is ongoing and the maximum number of years for clearance (3 years) is requested.

17. Reason(s) Display of Expiration Date is Inappropriate

The OMB number and Expiration date will be displayed on every page of every form/instrument.

18. Exceptions to Certifications for Paperwork Reduction Act Submissions

There are no exceptions to the certification.