Advisory Council on Blood Stem Cell Transplantation (ACBSCT) Subcommittee on Cord Blood

August 22, 2024

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Purpose of Subcommittee: During the last ACBSCT meeting on December 6, 2022, members requested that HRSA form a subcommittee to further discuss cord blood (with an emphasis on increasing utilization in transplantation). HRSA would also like the subcommittee to discuss and define a high-quality cord blood unit for banking specifications.

Subcommittee Representatives:

ACBSCT Members: Dr. Navneet Majhail, Dr. Juliet Barker, Marcie Finney, Dr. Filippo Milano

Subcommittee consultants:

- Dr. EJ Shpall, transplant physician and cord blood banker – lead for subcommittee
- Dr. Suzanne Pontow – cord blood banker
- Lisa Maxon- cord blood transplant recipient
- Dr. Alexes Harris- cord blood transplant recipient
- Dr. Eneida Nemecek – transplant physician
- Dr. Stella Davies – transplant physician

ACBSCT Subcommittee on Cord Blood

Summary of Activities:

1. Defining a high-quality cord blood unit;
2. Sharing the need for more cord blood transplant – focused research
3. Examining ways to increase cord blood utilization
4. Informing the subcommittee about the National Cord Blood Network
5. Exploring ideas for potential cord blood demonstration projects aimed to increase health equity and patient access to lifesaving transplants, while also increasing cord blood utilization
6. Developing proposed recommendations for the full ACBSCT to consider

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OBJECTIVE ONE: Recommend the Definition a high-quality cord blood unit for banking specifications

National Cord Blood Inventory (NCBI)

- Contracts with cord blood banks (CBBs) to continue to build the National Cord Blood Inventory (NCBI) by adding new, high-quality, genetically diverse cord blood units (CBUs).
- NCBI supports HRSA's mission to improve access to quality healthcare and services by contracting services to achieve the statutory goal of adding at least 150,000 new, high-quality, genetically diverse CBUs to the NCBI and making these CBUs available through the CWBYCTP.

4.3.1 Operate a Cord Blood Bank

Have and maintain its CBB in compliance with:

- U.S. FDA BLA, Section 351 of the Public Health Service Act, for the biological product, Hematopoietic Progenitor Cell (HPC), Cord Blood, for use in unrelated donor hematopoietic progenitor cell transplantation procedures.

- Accreditation Standards for all NCBI accrediting organizations that it has achieved accreditation.

Proposed Recommendation:

Advisory Council on Blood Stem Cell Transplantation (ACBSCT) Subcommittee on Cord Blood recommends that a high-quality cord blood unit is appropriately defined in the FDA Guidance for Industry for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood

Guidance for Industry

Biologics License Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System

B. HPC, Cord Blood Description and Characterization

Table A provides the description and characteristics of the cord blood and HPC, Cord Blood (i.e., tests performed and the results) used to obtain the clinical data submitted to FDA in docket number FDA-1997-N-0010 (Legacy Docket number 97N-0497). These clinical data demonstrate the safety, purity, and potency of HPC, Cord Blood. You would be expected to obtain similar test results using the recommended or other appropriate tests in order to rely on these clinical data in support of your BLA. In addition, release specifications as described in section VII.B.14.a. of this guidance should be included in this section.

Table A. Required and Recommended Tests and Test Results[1]

Product Characteristics[2]	Testing	Sample (Type and Timing)	Results of Product Testing
Safety	Infectious diseases – Testing required. (21 CFR 1271.45 through 1271.90)	Maternal peripheral blood obtained within 7 days of cord blood collection – Type and Timing Required. (21 CFR 1271.80(a) and (b))	All tests negative; except, non-treponemal test for syphilis when specific treponemal confirmatory test is negative. (Cytomegalovirus (CMV) results are recorded).
			CMV – Report
	Sterility - Bacterial and fungal cultures – Testing required. (21 CFR 211.165(b), and 21 CFR 610.12)	HPC, Cord Blood (pre-cryopreservation)*	No growth
	Hemoglobin	Cord blood** or appropriate donor sample obtained at time of cord blood recovery	No homozygous hemoglobinopathy
Purity and Potency[3]	Total nucleated cells (TNC)	HPC, Cord Blood (pre-cryopreservation)	$\geq 5.0 \times 10^8$ TNC***/ unit HPC, Cord Blood
	Viable nucleated cells	HPC, Cord Blood (pre-cryopreservation)	≥ 85% viable nucleated cells
	Viable CD34+ cells (flow cytometry)	HPC, Cord Blood (pre-cryopreservation)	$\geq 1.25 \times 10^6$ viable CD34+ cells****/unit HPC, Cord Blood
Identity	Human leukocyte antigen (HLA) typing	Cord blood	Report
	Confirmatory HLA typing	Attached segment of HPC, Cord Blood	Confirms initial typing
	Blood Group and Rh Type	Cord blood	Report

[1] Testing, Sample (Type and Timing), and Results are recommended unless specifically noted as required.
[2] The PHS Act requires a demonstration that the product is safe, pure, and potent.
[3] Other purity and potency assays may be considered under the BLA.
* Sample may be obtained before or after addition of the cryoprotectant.
** Cord blood = a sample of unmanipulated cord blood. A red cell sample or other cord blood aliquot obtained after volume reduction may be used for testing with appropriately validated reagents or test systems.
*** Based on 20 kg recipient, a target dose of $\geq 2.5 \times 10^7$ nucleated cells/kg and ≥ 70% post-thaw recovery = 1.7×10^7 nucleated cells/kg.
**** Based on CD34+ cells ≥ 0.25% of TNC prior to freezing.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/bla-minimally-manipulated-unrelated-allogeneic-placentalumbilical-cord-blood-intended-hematopoietic

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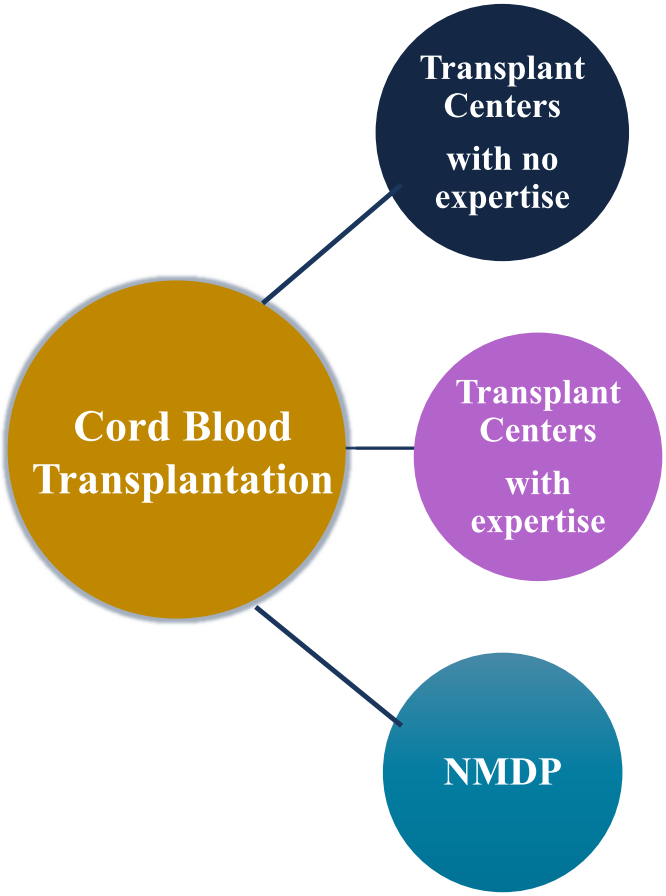
OBJECTIVE TWO: How to Increase Utilization of Cord Blood in Transplantation

CBT Landscape/Stakeholders: Opportunities for Improvement



1. No interest in CBT given increased MMURD transplants
2. Ignoring clinical data for patients with high-risk disease
3. No experience in searches, graft selection or early post-transplant management of CBT patients.

1. Internal challenges limiting physician bandwidth prohibiting external collaborations including data sharing & time for research
2. Lack of internal support limiting research

1. Initiatives have not translated to effective support
2. Prioritization of MMURD despite major problems with donor availability
3. Minimal social media leading to conflicting

How to increase cord blood utilization

Enhance Expertise/ Education

- Disseminate ASTCT guidelines
- Meet with experts to:
  - Present clinical data
  - Share opinions, indications (high-risk disease, second transplant) & expertise

Collaborations/ Publications/ Communications

- Create CB Network to:
  - Optimize collaborations & national practices
  - Create research infrastructure
  - Fund innovative proposals
  - Share data & samples
- Harmonization of NMDP, ASTCT, CBA, CB Network & CIBMTR activities.
- Social Media (CBT stories & community outreach)

Innovation/ Research

- Funding from NIH or other sources:
  - To study mechanism of protection from relapse
  - Evaluate novel approaches (eg granulocytes, non-matched products)
  - Support novel technologies for specific indications (UM171)

National Cord Blood Network

Consortium of collaborating new & existing CBT centers to increase transplant access

NATIONAL CORD BLOOD NETWORK

https://www.cordbloodnetwork.org

Steering Committee

J. Barker (WCM), A. Scaradavou (MSKCC) & M. Finney (CCBC)

Administration:
Infrastructure, IT & oversight

10 Participating Centers/ Programs:
Distributed nationally

Collaborations with stakeholders

HRSA, CBA, NMDP, CIBMTR, Anthony Nolan, CB banks, patient advocates & media.
Future: ASTCT, FACT, WMDA, ISCT.

Current focus: Formalize & increase activities.
Create optimized guidelines, protocols, webinars & disseminate.
Create search coordinator consortium & health equity initiatives.
Engage stakeholders & pursue funding.
Create infrastructure to advance the field

Weill Cornell Medicine | NewYork-Presbyterian
University Hospitals Cleveland Medical Center
University of Colorado Cancer Center
Children's Healthcare of Atlanta
Fred Hutch Cancer Center
Memorial Sloan Kettering Cancer Center
The James — The Ohio State University Comprehensive Cancer Center
Hackensack Meridian Health

ACBSCT Subcommittee on Cord Blood Recommendations:

For the purposes of the National Cord Blood Inventory, HHS should define a high-quality cord blood unit as one meeting the specifications outlined in the FDA Guidance for Industry for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood.

HHS should strongly encourage the National Cancer Institute (NCI) to support research specifically focused on cord blood transplantation and cord blood-derived cellular therapy including the necessary associated infrastructure. The aim of this funding is to increase the utilization of HRSA-funded high quality cord blood units for the treatment of patients with life-threatening cancers.

HHS should support additional demonstration projects that have the potential to increase cord blood utilization and thereby extend access to allogeneic transplantation, especially for minority patient groups.