

# **Summary of Advisory Council on Blood Stem Cell Transplantation: Recommendations and Status**

---

**Shelley Grant**

**Branch Chief, Blood Stem Cell Transplantation Program**

**September 11, 2015**

# Overview

- December 20, 2005 - HRSA began the process of establishing the Advisory Council (Advisory Council) on Blood Stem Cell Transplantation
- January 2008 – 1<sup>st</sup> Advisory Council meeting held
- To date - 14 subsequent meetings have been held; resulting in 26 recommendations made and submitted to the Secretary of Health and Human Services (HHS)

# Recommendation 1

## Summary

- That the Food and Drug Administration (FDA) finalize its draft guidance for Industry on Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution in Patients with Hematological Malignancies.

## Status

- October 20, 2009 - the FDA issued its guidance and issued a draft guidance advising entities on filing an investigational new drug (IND) application to access unlicensed cord blood units (CBUs) when a suitable human leukocyte antigen (HLA) matched cord blood transplant is needed for treatment of a patient with a serious or life-threatening disease or condition and there is no satisfactory alternative treatment available.
- March 2014 – The FDA published revised guidance.

# Recommendation 2

## Summary

- That the Secretary restore full funding of the Center for International Blood and Marrow Transplant Research (CIBMTR) research focused cooperative agreement with the National Cancer Institute (NCI).

## Status

- The National Institutes of Health (NIH) provided additional funding to support the CIBMTR's research focused cooperative agreement, which was renewed on March 1, 2013, and will run through February 28, 2018.

# Recommendation 3

## Summary

- That the Secretary direct Center for Medicare and Medicaid Services (CMS) to develop an appropriate strategy for a National Coverage Determination (NCD) on allogeneic stem cell transplantation as therapy for Myelodysplastic Syndrome (MDS) based on the recent evidence-based review of the literature.

## Status

- August 4, 2010 - CMS issued a national coverage decision allowing Medicare coverage of allogeneic HSCT for the treatment of MDS when provided to Medicare beneficiaries enrolled in an approved clinical study.
- December 15, 2010 - CMS approved a study, which was submitted by the CIBMTR for Medicare patients with MDS as eligible for coverage with evidence development (CED).

# Recommendation 4

## Summary

- That the C.W. Bill Young Cell Transplantation Program (Program) implement policies that conform to a number of specific principles to protect the privacy and confidentiality of cord blood donors donating umbilical cord blood units to the Program.

## Status

- FY 2010 - HRSA reviewed and determined that its contracts' privacy and confidentiality requirements are aligned with the principles that Advisory Council identified.

# Recommendation 5

## Summary

- That the Secretary recognize both the AABB and Foundation for the Accreditation of Cellular Therapy (FACT) as accreditation organizations for the National Cord Blood Inventory (NCBI) Program. The Advisory Council will review HRSA's experience with the accreditation organizations with regard to meeting HRSA's specifications, 3 years from the time of the recognition decision by the Secretary.

## Status

- FY 2012 - HRSA signed an Memorandum of Understanding (MOU) with AABB and FACT allowing the organizations to conduct cord blood bank assessments against HRSA-specific criteria.

# Recommendation 6

## Summary

- Recommended informed consent principles and standards for public cord blood banking.

## Status

- August 2009 - HRSA reviewed and determined that its existing contract language complied with the Advisory Council's recommendation.

# Recommendation 7

## Summary

- That an expert panel be convened to review and recommend clinical indications for which stem cell transplantation is covered by insurance plans.

## Status

- At its May 5, 2010, meeting, one Advisory Council workgroup was charged to develop potential options. The blood stem cell community leveraged the work of the National Marrow Donor Program (NMDP) and participated in its Advisory Group on Financial Barriers to Transplantation (AGFBT) to address inadequate transplant coverage. HRSA is actively involved in these efforts.

# Recommendation 8

## Summary

- That the Secretary mandate that Medicare and Medicaid cover patient participation in clinical trials involving hematopoietic transplantation.

## Status

- HRSA and its contractor, the NMDP, continue to work with CMS on a case-by-case basis to provide model benefits language for clinical trials involving hematopoietic transplantation.

# Recommendation 9

## Summary

- Recommended several ways in which cord blood collections could be improved and increased.

## Status

- HRSA reviewed this recommendation with public cord blood banks participating through the NCBI Program and it has been adopted where applicable. Also, HRSA and NMDP have worked with the public cord blood bank community to identify ways to increase and improve cord blood collection.

# Recommendation 10

## Summary

- That the Secretary recognize hematopoietic transplantation for generally accepted indications as a covered benefit for all federal programs for which the Secretary has appropriate responsibility and oversight.

## Status

- HRSA and NMDP are working with the American Society for Blood and Marrow Transplantation (ASBMT) to complete a list of indications for transplant, which represent the current standard of care. This list of proposed transplant indications will inform future discussions on potential changes to coverage by federal programs.
- The NMDP, through its AGFBT, has developed model benefits language to share with public and private insurers and benefits managers. HRSA is actively involved in these efforts.

# Recommendation 11

## Summary

- That Medicare reimburse for the acquisition of blood, marrow, and cord blood products for hematopoietic transplantation on a cost basis similar to how reimbursement is made for graft acquisition in solid organ transplantation.

## Status

- Discussions between HRSA and CMS are ongoing on this issue.

# Recommendation 12

## Summary

- That the Secretary clarify that the expiration date can be placed on an attached label provided with the unit at the time of release to a transplant center for cord blood units incapable of bearing a full label.

## Status

- Through the FDA licensure process, which has resulted in 5 HRSA-funded NCBI banks obtaining licenses to date (starting November 2011), the FDA has clarified guidance on labeling to permit attachment of a tag disclosing expiration date and other information as acceptable.

# Recommendation 13

## Summary

- That the Secretary work with the FDA to review requirements for licensure in light of concerns over the potential for licensure requirements to result in increased cost and decreased availability of public cord blood units, with the goal that the FDA urgently meet with the cohort of applicant cord blood banks and representatives of transplant centers to share and resolve specific concerns regarding licensure.

## Status

- The FDA has engaged in a number of ongoing outreach efforts to educate public cord blood banks about understanding the licensure process, meeting licensure requirements and submitting a biological license application.
- The IND pathway - Guidance for Industry and the FDA Staff: IND Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System.” (March 2014 )

# Recommendation 14

## Summary

- That models for remote collection of CBUs be allowed with only limited, scientifically-justified safety precautions. Also, that the Secretary allow for cord blood unit collection from routine deliveries without temperature or humidity monitoring of delivery rooms in hospitals approved by the appropriate bodies for hospital accreditation.

## Status

- Pilot program implemented to test whether remote cord blood collections can be performed in a safe and efficient manner. The pilot's results showed (1) increased opportunities to expectant mothers who would not otherwise be able to donate their umbilical cord blood because there was no collection hospital in their area; (2) remote CBU collections can be conducted safely and efficiently; and (3) increased awareness from racial and ethnically diverse populations.

# Recommendation 15

## Summary

- That the Secretary recognize public cord blood bank oversight of the collection process as a sufficient means to ensure safe manufacturing practices and oppose the requirement for hospitals to register with the FDA as the establishment responsible for recovery.

## Status

- December 2011 - the FDA communicated that, in general, recovery establishments are required to register and list with the FDA (21 CFR Part 1271) unless an exception applies.
- Section 1271.15(f) - an individual under contract agreement or other arrangement with a registered establishment, who is engaged in solely recovering cells or tissues for the registered establishment, may be exempt from requirements to register and list with the FDA, but must comply with all other applicable requirements in 21 CFR Part 1271.

# Recommendation 16

## Summary

- That the Secretary support the collection of cord blood from uncomplicated deliveries in accredited hospitals without environmental monitoring of delivery rooms.

## Status

- December 2011 - the FDA published its “Guidance for Industry: Current Good Tissue Practice and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps).”
- This guidance provided information about what environmental control and monitoring issues should be considered for recovery of HCT/Ps.

# Recommendation 17

## Summary

- That the FDA recognize and accept laboratory-developed testing (LDT) performed in Clinical Laboratory Improvement Act (CLIA)-certified, high complexity histocompatibility laboratories.

## Status

- September 30, 2014 - “Proposed LDT Regulatory Oversight Framework” published by the FDA.
- The framework is available for review and public comment. The FDA is specifically seeking feedback on LDTs used for rare diseases and traditional LDTs interpreted by laboratory professionals who are appropriately qualified and trained as required by the CLIA regulations, among other issues.

# Recommendation 18

## Summary

- That the FDA broaden the IND and biologics license application (BLA) clinical indications for unrelated donor cord blood transplantation to include use for hematopoietic and/or immune reconstitution or enzyme replacement in any situation where HSCT is the appropriate approach to treatment.

## Status

- November 2011 - the FDA granted the first license for a cord blood product. The product was licensed for use in patients with disorders affecting the hematopoietic system. Subsequently licensed cord blood products have had similar indications.

# Recommendation 19

## Summary

- That all cord blood products have the same IND and BLA clinical indications; this is scientifically and medically sound.

## Status

- March 2014 - the FDA revised its language for covered indications. The titles of both the FDA guidance documents now correspond to each other: (“...intended for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system”), and thus they are “the same” per the recommendation.

# Recommendation 20

## Summary

- Recommended implementation of a transition plan, initially stated as on or before October 20, 2011, to allow time for the FDA to review recommendations 17 and 18 and to allow for implementation of any changes by transplant centers that will be needed to put these changes through their institutional review boards.

## Status

- The NMDP has developed an IND protocol under which non-licensed cord blood units may be accessed and distributed.
- The FDA continues to work with other sponsors to address the availability of cord blood products.

# Recommendation 21

## Summary

- That CBUs collected, through distribution of kits sent to motivated maternal donors or obstetrical units by an obstetric provider, which meet all NCBI Program/the FDA qualifications, be eligible for listing on the NCBI Program and for the FDA licensure.

## Status

- May 2011 - the FDA confirmed that public cord blood banks, including those that hold NCBI Program contracts with HRSA, may apply for a BLA that covers remote kit collections.
- May 2012 - the first NCBI cord blood bank submitted an application with cord blood being collected through the distribution of kits. The FDA approved the collection model and those units are eligible for NCBI Program funding and listing.

# Recommendation 22

## Summary

That the Secretary take and support all reasonable efforts to ensure that compensation for marrow, peripheral blood stem cells, and similar products continues to be prohibited.

## Status

- October 2, 2013 - HRSA published a Notice of Public Rule-making in the *Federal Register*. Responses are still under internal HRSA review.

# Recommendation 23

## Summary

- That the Secretary consider appropriate mechanisms to assure that the revised NHLBI publication entitled "Management and Therapy of Sickle Cell Disease" includes expert opinion about the curative option of hematopoietic cell transplantation for this disorder.

## Status

- The Advisory Council's recommendation was shared with NHLBI by the NIH's ex-officio Advisory Council member. Some changes were made to the final publication that was released in 2014.

# Recommendation 24

## Summary

- That HRSA undertake educational/outreach efforts to the sickle cell disease (SCD) patient and provider community to educate them about the progressive nature of SCD, increasing morbidity and mortality in early adulthood (ages 16-35 years), and the role of HSCT and its complications.

## Status

- HRSA is engaging in public and professional outreach at national and regional SCD conferences, as well as working to ensure that the appropriate audiences, including primary care physicians and hematologists, are reached.

# Recommendation 25

## Summary

- That the Secretary recognize hematopoietic transplantation for SCD as a covered benefit for all federal programs for which the Secretary has appropriate responsibility and oversight.

## Status

- At the end of FY 2014, the recommendation was under internal review at HRSA.

# Recommendation 26

## Summary

- That the Secretary direct HRSA and other HHS agencies to collaborate with CIBMTR to review research level data collection on allotransplants performed for SCD and consider appropriate reimbursement to optimize research data collection.
- This review should include SCD-specific data elements collected, the completeness of data collection, and mechanisms for reimbursement.

## Status

- The recommendation under internal review at HRSA and with its contractor.

# References

- ACBSCT - <http://bloodcell.transplant.hrsa.gov>
- “Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution for Specified Indications.” October 20, 2009.
- “Guidance for Industry and the FDA Staff: IND Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System.” March 2014. <http://www.theFDA.gov/biologicsbloodvaccines/guidancecomplianceinformation/guidances/cellularandgenetherapy/ucm388218.htm>
- “Guidance for Industry: Current Good Tissue Practice and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps).” December 2011. <http://www.theFDA.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM285223.pdf>.
- “Proposed LDT Regulatory Oversight Framework.” September 30, 2014. <http://www.theFDA.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm407296.htm>

# Contact Information

Shelley (Tims) Grant, MHSA

Branch Chief, Blood Stem Cell Transplantation Program

Division of Transplantation

5600 Fishers Lane Room 08W67

Rockville, MD 20857

Health Resources and Services Administration

301-443-8036

Fax: 301-594-6095

[sgrant@hrsa.gov](mailto:sgrant@hrsa.gov)