

**Health Resources and Services Administration (HRSA)
Advisory Committee on Blood Stem Cell Transplantation (ACBSCT)**

U.S. Department of Health and Human Services (HHS)
Virtual Meeting, September 10, 2019

ACBSCT Members

Voting Members

Staci Arnold, MD; Michael Bishop, MD, FACP; Arthur W. Bracey, MD; Colleen Delaney, MD, MSc; Manish Gandhi, MD; Sergio Giralt, MD, FACP; Mary Laughlin, MD; Amanda Salazar

Non-voting (Ex Officio) Members

Frank Holloman, Acting Division Director, HRSA/Division of Transplantation; Nancy L. DiFronzo, PhD, Program Director, National Institutes of Health (NIH); Robert Hartzman, MD, Captain, Medical Corps, U.S. Navy (Ret.) Director; Sridhar Basavaraju, MD, Director, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention (CDC); Safa Karandish, Consumer Safety Officer, Food and Drug Administration (FDA)

Executive Secretary

Robert Walsh

General Counsel Staff

Rina Hakimian, JD, MPH, Senior Attorney; Mark McGinnis, JD, Senior Attorney

Welcome and Opening Remarks

Robert Walsh, ACBSCT Executive Secretary

Introduction of All Members and Roll Call

Mr. Walsh opened the meeting at 10 a.m. and asked council members to introduce themselves. Mr. Walsh is serving as acting chair since the proposed chair is still in the clearance process.

HRSA Division of Transplantation Blood Stem Cell Transplantation Program Update

Frank Holloman, Acting Director, Health Resources and Services Administration, Division of Transplantation

Mr. Holloman welcomed the public and discussed the statutory framework for the Stem Cell Therapeutic and Research Act, provided background for the HRSA Division of Transplantation, and highlighted some activities in fiscal year 2019. Statutory framework of the Act of 2005 is based on Public Law 109-129, amended by Public Law 111-264 and Public Law 114-104. The Stem Cell Therapeutic Research and Re-Authorization Act of 2015 authorizes the C.W. Bill Young Cell Transplantation Program (CWBYCTP) as well as the National Cord Blood Inventory (NCBI). HHS's ACBSCT advises the Secretary of HHS and the Administrator of HRSA on the activities of the CWBYCTP and NCBI Programs. The CWBYCTP goal is to increase the

number of bone marrow and cord blood transplants for recipients suitably matched to biologically unrelated donors. NCBI contracts with cord blood banks to build a public inventory of at least 150,000 new cord blood units (CBUs).

The CWBYCTP was authorized with the goal of increasing the number of blood marrow transplants as well as the national cord blood inventory of NCBI. The CWBYCTP contracts with blood banks to meet the goal of building CBUs. The bill also authorizes the Advisory Council on ACBSCT to make recommendations on both the CWBYCTP program and the NCBI program.

HRSA background: The Division of Transplantation within the Healthcare Systems Bureau is the primary Federal entity responsible for oversight of organ and blood cell transplantation in the United States and for initiatives to increase the level of organ and tissue donation in the country. The three-pronged oversight consists of statutory requirements, Federal regulations, and Federal contracts. HRSA staff serve as ex officio non-voting members for [National Marrow Donor Program \(NMDP\)](#) and the [Organ Procurement and Transplantation Network \(OPTN\)](#) and sit on committees and working groups of NMDP and OPTN.

Highlighted activities for fiscal 2019: the search for a permanent director; working with the National Institutes of Health (NIH) and U.S. Food and Drug Administration (FDA) to report to Congress on appropriate blood stem cells and birthing tissues for potential inclusion in the CWBYCTP; and an overview of the report to Congress. Feel free to review the HRSA website: <https://bloodcell.transplant.hrsa.gov>.

Update on Report to Congress on Appropriateness of Blood Stem Cells and Birthing Tissues or Potential Inclusion in the C.W. Bill Young Cell Transplantation Program

Dr. Amy Patterson, National Heart, Lung, and Blood Institute, National Institutes of Health

Dr. Peter Marks, Director, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration

Shelley Grant, Chief, Blood Stem Cell Transplantation Branch, Health Resources and Services Administration

Dr. Patterson thanked advisors. Team advisors were cleared by HHS and submitted to Congress. The collaborative effort included HRSA, FDA, and NIH.

Drs. Marks and Patterson along with Mrs. Grant reviewed the Stem Cell Therapeutic and Research Reauthorization Act of 2015 and provided an overview of the report and a discussion of findings and recommendations.

The HHS Secretary consulted the NIH Director, FDA Commissioner, HRSA Administrator, and ACBSCT regarding a review of the state of the science of using adult stem cells and birthing tissues to develop new therapies for patients, with the purpose of considering the potential inclusion of such new types of therapies in CWBYCTP. The Report to Congress was due June

30, 2019, and was submitted to 1) the Senate Committee on Health, Education, Labor, and Pensions, and 2) the House Committee on Energy and Commerce. The report included:

Statutory Mandate:

The purpose of CWBYCTP is to 1) increase the number of bone marrow and cord blood transplants for recipients suitably matched to biologically unrelated donors; and 2) provide a structure to facilitate blood stem cell transplantation with blood-forming cells from unrelated donors for individuals with leukemia and other life-threatening blood disorders with five key functions:

- Facilitate and coordinate bone marrow transplantation
- Facilitate and coordinate cord blood transplantation
- Office of Patient Advocacy
- Single Point of Access Coordinating Center
- Stem Cell Therapeutic Outcomes Database

Background on Stem Cell Therapies:

- Hematopoietic stem cells and birthing tissues for Hematologic or Immunologic Reconstitution
- Applications include use of bone marrow-derived stem cells, peripheral blood-derived stem cells, and cord blood-derived stem cells

Adult Stem Cells and Birthing Tissues for Other Uses (hematologic and immunologic reconstitution) generally require study. This occurs under Investigational New Drug applications (INDs) and approval of Biologic Licensing Applications (BLAs) prior to marketing (section 351 of the Public Health Service Act) are being investigated for use in rheumatologic diseases, neurologic diseases, and cardiovascular diseases. Currently there are no FDA-approved adult stem cell products or birthing tissues products for use outside of hematologic or immunologic reconstitution.

- Regulatory Framework for Stem Cell Therapies
- Efforts to Expedite Progress Developing Adult Stem Cell and Birthing Tissue Treatments: Regenerative Medicine Advanced Therapy Designation (RMAT)

Proposed Criteria for Inclusion of New Cellular Therapies in the CWBYCTP:

To help patients who need a potentially life-saving bone marrow transplant or umbilical cord blood transplant from an unrelated marrow donor or CBU, new cellular therapies should include only those adult stem cell and birthing tissue products—including those with new uses outside of hematologic or immunologic reconstitution—that:

- Are utilized as treatments for serious or life-threatening conditions
- Require donor matching, if appropriate
- Have been demonstrated to be safe and effective as evidenced by FDA approval or, if FDA approval is not required, through adoption as a standard of care

Key Findings Regarding Inclusion of Adult Stem Cells and Birthing Tissue Products in the CWBYCTP were:

- Bone marrow and cord blood transplants are widely accepted by clinicians; adult stem cells and birthing tissues for other investigational applications inherently do not represent a standard of care
- Access and transparency regarding clinical trials are desirable
- Intermingling of proven and unproven/unapproved therapies in the CWBYCTP are undesirable

Recommendations for criteria for inclusion of new cellular therapies in the CWBYCTP are that:

- The CWBYCTP should include only those adult stem cell and birthing tissue products that are used as treatments for serious or life-threatening conditions; require donor matching, if appropriate; and have FDA approval, through adoption as a standard of care. 1) The inclusion of adult stem cells and birthing tissues for uses other than hematologic and immunologic reconstitution is not recommended at this time. 2) In the future, it may be appropriate to include such products as new classes of cell-based products are developed that meet regulatory approval standards for safety and effectiveness. Therefore, re-evaluation by HRSA, NIH, and FDA is recommended every 2-3 years, or as needed, with issuance of a report on the outcomes of these evaluations when relevant.

ACBSCT Report Feedback: Council members agreed with the report's premise and recommendations and acknowledged the potential risks posed by unproven therapies, and focused primarily on the three key elements of the proposed criteria for inclusion of new cellular therapies in the CWBYCTP.

There is much promise for products, but more must be learned before they can go to market, so that it becomes necessary to think about the key characteristics of a registry:

- Single (or a few) similar well-defined products included
- Use of similar outcome measures for the products
- Ability to analyze data across comparable products
- Characteristics of Hematopoietic Stem Cell Transplantation Registry
- Inclusion of blood- and bone marrow-derived cells, cord blood units
- Inclusion of GvHD rates, relapse rates, and survival rates for similar clinical indications (hematologic and immunologic reconstitution)
- Comparison of different product categories
- Products derived from adult stem cells and birthing tissues for clinical purposes other than hematologic and immunologic reconstitution are highly diverse and do not meet the criteria for inclusion in such a registry

Discussion

With respect to limited cord blood resources, *Dr. Bracey* asked if there is any information on whether or not the many entrepreneurs in this area are beginning to divert potential products and resources from known effective areas. *Dr. Patterson* was aware of many of these entrepreneurs in areas including cancer and various forms of anemia and asked *Dr. Marks* for his opinion. *Dr. Marks* was aware of some groups taking a unit and splitting it into multiple units, but he was not

clear if these units would have found their way into the banking system to begin with and was not aware of any major diversion efforts.

Dr. Bracey has seen plasma centers developing parallel collection sites and paying donors, with the effect that the number of actual volunteers is diminishing. A possible conclusion to be gathered from various reports is that there are resulting financial challenges for some of the cord blood centers. *Mrs. Grant* explained that at HRSA, part of the statutory framework allow for cord blood banks to distribute units that are not clinically appropriate for transplantation, so the banks report out to HRSA the number of units they are releasing for research purposes. In addition, some contractors may be using cord blood for other things that may be permissible but HRSA does not want the outcome data submitted to and merged with the C.W. Bill Young Cell Transplantation Program's outcomes database. There are other NIH mechanisms available to report that data. HRSA looks at the potential of cord blood and what could benefit patients. The RAND study also spoke to the importance of using cord blood for other cellular therapy purposes to help sustain the field. For now, however, those data will not be reported to the Stem Cell Therapy Outcomes Database. *Dr. Kurtzberg* opined that the data on how frequently cord blood is being used should be reported to NIH for research purposes. *Dr. Delaney* stated that a lot of cord blood that is not obtained via the 13 banks is being used for research. For example, we have local institutional review board-approved cord blood for a local hospital. There is a lot of local collection going on with us but I don't know how you'd capture all that data. We use 1,200 to 1,300 units per year through our local partnership. *Dr. Machia Scaradavou* noted that, working at the National Cord Blood Program in New York, they collect and select units for banking and also units for research that do not meet the banking for transplantation criteria. We report this to HRSA. *Dr. Delaney* stated that is a very good resource and that researchers may not know about how to work with public banks and many researchers would like to know about it.

Cord Blood Products in the Era of Zika Infection

Update on the Current Status of Zika Virus Epidemiology

Dr. Carolyn Gould, Medical Epidemiologist, Centers for Disease Control and Prevention (CDC), Division of Healthcare Quality Promotion

Surveillance uses standardized case definitions, which are reported to CDC's ArboNET system. In the United States, cases among U.S. travelers increased and there were outbreaks in three U.S. Territories and two States. From 2016-2019, there were over 41,680 cases; just over 1,118 in 2017, with 222 in 2018 and 41 in 2019. For confirmed disease cases in the Americas reporting to Pan American Health Organization (PAHO), there were 651,346 cases in 2016; 56,085 in 2017; 31,576 in 2018; and 12,076 in 2019. The majority of cases (2,650) occurred in Brazil. Incidence and disease risk among U.S. travelers have followed the epidemiology of outbreaks in the Americas.

Screening of Cord Blood Donors for Zika Virus Infection

Dr. Brychan Clark, Medical Officer, U.S. Food and Drug Administration, Center for Biologics Evaluation and Research, Office of Tissues and Advanced Therapies

HCT/Ps are defined as human cells, tissues, and cellular and tissue-based products such as cardiovascular tissue, skin, and ocular tissue intended for implantation, transplantation, infusion, or transfer into a human recipient (§1271.3(d)). These include cellular-derived therapeutic products (e.g., pancreatic islets, mesenchymal stem/stromal cells, fibroblasts) as well as hematopoietic stem/progenitor cells (HPCs) derived from peripheral or cord blood.

HCT/P donor eligibility based on donor screening and testing for relevant communicable disease agents or diseases (RCDADs; including HIV-1 and -2, hepatitis B virus, hepatitis C virus, syphilis, TSE, sepsis, vaccinia, WNV, Zika virus (ZIKV), HTLV-1 and CMV, chlamydia trachomatis, and Neisseria gonorrhoea) is required for any implant, transplant, infusion, or transfer except as provided in §§1271.60(d), 1271.65(b), and 1271.90. Donor testing results for relevant communicable disease agents (described in §1271.80 and §1271.85) must be negative or nonreactive, except as provided in §1271.80(d)(1). The donor must be free from: risk factors for, and clinical evidence of, infection due to relevant communicable disease agents and diseases; and communicable disease risks associated with xenotransplantation.

Use of HCT/Ps from an ineligible donor (§1271.65(b)) are permitted in the case of urgent medical need (UMN (§1271.3(u)), in which case there are special labeling and notification requirements (§1271.65(b)(2)-(3)). Under the regulatory framework for HCT/Ps, minimally manipulated umbilical cord blood products for unrelated allogeneic use are regulated as biological products under Section 351 of the Public Health Service Act and the Food, Drug, and Cosmetic Act, and are subject to premarket review requirements.

Unlicensed CBUs may be used under an IND because FDA recognized the importance of patients having continued access to the best matched available CBU that may not meet all the licensure requirements but may be otherwise suitable for transplantation. Similarly, cord blood from ineligible donors may be used for hematopoietic stem cell transplantation under an IND (exception in §1271.65(b)(1)(iii)).

ZIKV GUIDANCE AND RISK COMMUNICATION

ZIKV was identified as an RCDAD for all donors of HCT/Ps on March 1, 2016. An updated guidance document providing more recent epidemiological findings; ZIKV transmission data; ZIKV test availability; sexual contact risk factors; areas of transmission risk; and scientific references was published May 2018. The May document also supports recommendations to screen living donors of HCT/Ps for risk of ZIKV infection (based on geographic areas with risk).

HCT/P living donors are ineligible if they were: diagnosed with ZIKV infection, residents of or traveled to a ZIKV area of transmission risk, or had sex with a person with risk factor 1 or 2 (above) in the past 6 months. Additionally, donors of umbilical cord blood, placenta, or other gestational tissues are ineligible if the birth mother who seeks to donate gestational tissues has

experienced medical diagnosis of ZIKV infection; residence in, or travel to, an increased ZIKV transmission risk area with an increased risk for ZIKV transmission within the past 6 months; or had sex at any point during that pregnancy with a person who is known to have either of the risk factors listed in items 1 or 2, above.

In addition, non-heart-beating (cadaveric) donors should be considered ineligible if the cadaveric donor had a medical diagnosis of ZIKV infection in the past 6 months.

ZIKV is readily detected in HCT/Ps, such as semen and umbilical cord blood or other gestational tissues, after viral RNA is no longer detectable in plasma. Currently, appropriate testing measures to prevent the transmission of ZIKV through HCT/Ps are not available. At this time, nucleic acid tests (NATs) are designed to detect ZIKV RNA in plasma isolated from a donor blood specimen; however, blood plasma NAT alone is not sufficient to determine whether a donor's HCT/Ps may be infected with ZIKV.

The FDA does not provide recommendations on testing HCT/P donors. Currently, two ZIKV-NATs with high sensitivity and high specificity, but potential false positives, are available that have been licensed by the FDA to detect ZIKV RNA in plasma specimens. As disease incidence decreases, positive predictive value decreases and false positives increase despite high specificity. Tests package inserts explain that ZIKV RNA may persist in certain organs and tissues, as well as other body fluids, longer than it is detectable in plasma and serum.

A donor with a reactive or positive test must be determined ineligible (§1271.75(a)&(d)). The FDA continues to recommend screening HCT/P donors for ZIKV risk as stated in the current Zika guidance updated in May 2018, and to not rely on test results. Because ZIKV can be detected in some HCT/Ps after RNA is no longer in plasma, a nonreactive plasma NAT does not assure that recovered cells or tissues are not infected with ZIKV and a nonreactive test does not override any identified risk factors for ZIKV. Test results become part of donor's relevant medical records. The FDA is committed to working with manufacturers interested in developing tests for HCT/P donors and will consider appropriate recommendations for use of such tests upon their availability.

An area is considered to have an increased risk for ZIKV transmission when locally transmitted, mosquito-borne ZIKV has been reported or the potential is suspected based on epidemiological evidence. The CDC World Map indicates four categories of risk for areas outside the United States: country or territory with current Zika outbreak (red), country or territory with any prior or current reports of mosquito-borne Zika transmission (purple), country or territory with the vector and no reported mosquito-borne Zika transmission (yellow), and country or territory with no mosquitoes that spread Zika (green). As of February 28, 2019, there are currently no areas at increased Zika virus transmission through blood or tissue donation in the United States.

Although other information such as post-donation follow-up on donor's health status may be helpful, it is unknown whether such measures would be adequate for preventing the transmission of ZIKV through HCT/Ps. Potential challenges include method of follow-up; adequate timeframe; and feasibility of uniform implementation for all donors of gestational tissues, including cord blood.

Cord Blood Advisory Group – Challenges Operationalizing the FDA’s Donor Screening Requirements

Challenges Resulting from Implementing Donor Screening Recommendations to Reduce Risk of Zika Transmission: Background

Dr. Beth Shaz, Executive Vice President, Chief Medical and Scientific Officer, New York Blood Center

Zika Virus Background: Flavivirus is related to dengue, yellow fever, and West Nile Virus from non-human primates, which was reported in Uganda in monkeys (1947) and in humans (*Zika Forest*; 1952). The virus is found in semen, urine, and breast milk. ZIKV is transmitted via mosquito bite, sex, or blood transfusion. ZIKV infection during pregnancy (particularly the first trimester) may cause severe brain defects and microcephaly. Fetal abnormalities detected by ultrasonography are presented in 29 percent of women with ZIKV infection during pregnancy.

There is risk of CBUs being infected and risk of Zika transmission because Zika infects placental macrophages, cytotrophoblasts, and umbilical cord mesenchymal stromal cells. The five features of congenital Zika syndrome are severe microcephaly, decreased brain tissue, eye damage, congenital contractures, and hypertonía. Neurologic risks include Guillain-Barre syndrome.

Blood safety: There is a possibility that ZIKV can be spread through blood transfusions. FDA Recommendations for Blood and Blood Components, February 2016: 1) Areas without active transmission: Donor history deferral-infection, travel, or sexual history; 2) Areas without active transmission: Pathogen reduction or testing. August 2016 Recommendations: 1) NAT or pathogen reduction on all blood components (implementation roll-out based on State risk): 2) Donor questions removed. July 2018 recommendations: MP-NAT allowed (ID-NAT in active areas).

Important Information for HCT/P Establishments Regarding ZIKV Transmission Risk in the World: When screening living donors of HCT/Ps, access the CDC webpage for Blood and Tissue Safety (<https://www.cdc.gov/zika/areasatrisk.html>). *To evaluate domestic travel*, the “Areas at increased risk for Zika virus transmission through blood or tissue donation in United States” is listed first and continues to be defined at the county level within a State. *For evaluating travel to areas outside of the United States*, use the link to the world map and consider countries and territories categorized as “red” or “purple” as areas with increased risk of ZIKV transmission. (When an area outside the United States becomes shaded as red or purple for the first time on the world map, that area and the date of the change will be posted on the Blood and Tissue Safety webpage [<https://www.cdc.gov/zika/areasatrisk.html>]). Note: The CDC webpage for Blood and Tissue Safety should be monitored frequently for any updates.

Donor ineligibility due to Zika risk makes the unit ineligible for licensure; however, the unit is still able to be stored and used with documented urgent medical need.

Approximately 10 percent of cord blood inventory through NMDP/BTM has a yes answer to any Zika question. Cord blood banks are tracking donations that are ineligible for licensure. Some are testing mothers using the blood donor screening licensed NAT assay and some are following up with mothers regarding infant's health at 1-year post donation.

Investigational testing for ZIKV done among U.S. blood donors and reported to ArboNET showed that 74 ZIKV disease cases were reported in the United States and 148 disease cases were reported in the U.S. Territories. Donor screening recommendation guidance for the industry came out in March 2016 and was updated in May 2018.

Dr. Shaz Request:

“We respectfully request that the ACBSCT work with the Food and Drug Administration, the Centers for Disease Control and Prevention, the Health Resources and Services Administration, other organizations, and infectious disease experts to get a more accurate estimate of the risk of ZIKV transmission in the various countries, identify research or data needed to support policy changes, and identify potential ways to test HCT/P donors (in blood or tissue) or possibly clear donors retrospectively by following up on their health status, and therefore continue to ensure the safety and availability of cord blood units.”

We suggest the following paths forward:

- Validation of current assays for cord blood, birthing tissues, and other stem cell products
- Understanding the process and challenges/limitations for updating the CDC risk map
- Understanding the risk of Zika infection for the increased travel risk areas
- Determining the cord blood or other stem cell sources ability to transmit ZIKV
- Determining the length of time infective virus is in these cells

The Impact of Current Policies for Zika Virus Screening on Accrual to the Carolinas Cord Blood Bank

Dr. Joanne Kurtzberg, Director, Carolinas Cord Blood Bank (CCBB), Duke University Medical Center

CCBB was established in 1997 and has a current inventory ~38,000 + ~6,000 CBUs with a median TNCC of 1.5×10^9 and 10 collection sites.

Innovations include:

- Formal collection training program
- Flexible staffing models
- Grady Hospital collection site
- All Collect Model (EPIC consent for collection)

Challenges include:

- Licensure
- Delayed cord clamping
- Zika travel risk exclusions

Recommendations:

- Obtain detailed travel histories for baby's mother and father.
- Test all mothers with Zika NAT as part of DS/DT
- Confirm normal PE (lack of microcephaly) on newborn physical examination
- For donors with travel risks: Obtain follow-up 1-year post donation and confirm that baby is healthy, has normal development, and has had no significant illnesses in the first year of life that would raise suspicion of Zika infection.
- If confirmed, the donor is eligible and the unit is licensed and NCBI eligible

Impact of ZIKA Virus Risk on Public Cord Blood Banking

Dr. Machi Scaradavou, Medical Director, National Cord Blood Program New York Blood Center

There is a two-part informed consent at collection including: 1) permission to review maternal record and collecting of CB, and 2) donation informed consent including detailed review of medical records. Questions include: 1) travel history (MOB alone or with FOB); 2) contact with person at risk; and 3) domestic travel, one parent or both.

CBUs considered for evaluation are from asymptomatic mothers and newborns with no findings associated with ZIKV. CBUs from ineligible donors cannot be licensed and cannot be included in the NCBI, but can be used for transplantation under urgent medical need.

Dr. Scaradavou displayed the CDC map showing geographic areas at increased risk for ZIKV transmission through blood or tissue donation-banked CBUs from March 2016-June 2019. Ineligible CBUs were at 28.1 percent and ZIKV-ineligible CBUs were 19.7 percent. Fifty-seven CBUs were released, with 49 eligible/licensed CBUs, 9 ineligible, and 5 ineligible for ZIKV risk.

Out of the 4,500 units banked during the period of evaluation, 57 have been released for transplant, 5 with Zika risk. One patient was engrafted but died from other causes, and another double unit graft was okay after 4 months with full recovery of counts.

Zika-risk infants were all reported healthy with two mailer questionnaires. Now, 3.5 years later, there are no outbreaks, but we need to draw attention to current policies. Zika risk has a negative effect by placing a red flag on a big proportion of minority donors, which helps detract from the growth of the program and adds to the cost of banks. Dr. Scaradavou respectfully requested to reevaluate the current policies to address Zika risk.

There has been a dramatic drop in the numbers of Zika risk identified. The overall ineligible donors were 70 percent because of Zika but what is interesting is that 94 percent were ineligible for white Hispanics but lower for other races. The variability seems to depend on the collection site. Rates in three New York areas and Virginia were high, but Georgia donors have much lower percentage of risk. Different sites serve different populations and therefore have different risks.

Certain ethnic groups have been reported for risk since 2016. When can they get off the purple map? We need a better understanding of the risk of transmission to newborns.

It may be time to reconsider the regulatory framework in regard to the following considerations:

1. What is the risk of exposure now? Countries at risk per CDC data are those that had outbreaks at any time.
2. How can we evaluate accurately the risk of transmission to the newborn? By using other testing options, for example to test with assays under IND? By instituting infant donor follow-up? By “retrospective clearance” of the infant donor?
3. How do the changes in the overall incidence/prevalence of ZIKV and experience from blood donors help evaluate the risks?

Discussion

Dr. Hartzman: I heard there is no clinical evidence for risk from Zika currently. Would it be reasonable to reevaluate the path developed several years ago, since it is causing a large problem? *Dr. Bracey:* We need to develop certain eligibility criteria and the knowledge of how to have safety on both sides, but clearly we’re overly restrictive at this point. *Dr. Delaney:* I would agree with all of that. *Moderator:* Dr. Gould, or Dr. Shaz, can you let us know if there are any ongoing activities looking to reevaluate those countries? *Dr. Gould:* Because of the wide variation of surveillance capability internationally, we don’t have data to look sufficiently at areas of risk in these countries, but I do ask if there’s a timeline for reevaluation.

Moderator: As far as guidelines, can we expect an update?

Dr. Clark: At the FDA, we can’t comment on any future guidance.

Dr. Bracey: Not purple, but red, perhaps in order to give those reconsidering more direct guidance. It seems that value of purple items in promoting safety is coming under question. We’ve heard two suggestions including the consideration of a time window around purple. But considering that the marked fall-off in clinical disease denoting the purple regions as regions of increased risk seems to be of minimal return, maybe we should ask those reconsidering to particularly focus on denoting purple areas as points of ineligibility.

Reducing Barriers to Transplantation National Marrow Donor Program Payor Policy Efforts

Overview of the National Marrow Donor Program's Payor Policy Efforts

Ms. Ericka Narr, Manager, Cord Blood Program, National Marrow Donor Program

Innovation Lab Improves Cord Blood Experience and Payor Policy

The purpose and task of Innovation Lab was to address critical issues impacting providers' and patients' cord blood experiences to increase utilization. The Lab was an inaugural project from the special initiative of fiscal year 2019. The focus is on patients and it provides cord blood experts an opportunity to improve and reduce barriers and highlight the value of umbilical cord blood with the underlying goal of protecting this graft source and sustaining access. The Lab is composed of six cross-functional team members.

Key observations: Supply and demand are off balance. There are highly concentrated cord blood centers, with some of them struggling. We can be the match space to assist with increasing awareness. We did a data dive, discovery with literature reviews, interviews of internal and external stakeholders, and examination of root cause. We also did a deep dive into the RAND report to look at the current state in terms of three pillars and findings:

- Sustainability: Investments in cord blood are not currently sustainable
- Evidence: Transplants are built more on preference than data; want more retrospective and prospective evidence
- Leadership: Cord blood leadership needs to come together to support patients

The emerging plan is to address the supply with related lab concerns, protect and optimize the supply, suggest recommendations with reimbursement, focus on partners with HRSA to reevaluate potential adjustment of the reimbursement threshold on NCBI contracts, protect the cord blood units, increase reimbursement threshold to meet the needs of patients, and protect highly viable CBUs from being destroyed or damaged if CBBs's financial sustainability is threatened.

To increase demand via service opportunities requires data-driven research ideas; high-resolution typing for more accurate matching; support for transplant teams; recommendations given to physicians for additional evidence for safer, less expensive engraftment; provision of instructional guidance for teams that use cord blood less frequently; provision of focused attention on the needs of transplant teams; provision to physicians with evidence for proper care; and creation of data-driven strategies for a safer, easier, and less expensive engraftment experience.

To align the matches, it is necessary to create new opportunities; raise cord blood awareness internally; restructure the Cord Blood Advisory Group (CBAG) to be action oriented; fund new cord blood treatment/alternative therapies clinical trials; have "Be the Match" raising cord blood awareness internally and taking responsibility in order to drive necessary change; restructure CBAG to be mission driven and action oriented; and fund new cord blood treatment clinical trials.

Ellie Beaver, Manager, Health Policy and Reimbursement, National Marrow Donor Program

The payor policy highlight is to ensure patient access to transplants they need, and our mission is to remove barriers through policy change.

Transplant centers lose thousands of dollars on each Medicare beneficiary they treat. Those losses threaten their ability to continue to provide these transplants. The Patient Access to Cellular Transplant (PACT) Act will require that donor search and cell acquisition costs be reimbursed separately and at a reasonable cost rate, significantly improving reimbursement.

The PACT Act will increase reimbursement by:

- Responding to Centers for Medicaid & Medicare Services (CMS) -proposed rules with data on cost and charges for cell procurement
- Working with commercial payers to ensure full coverage of search and procurement services
- Monitoring State and Federal legislation to ensure patients have access to insurance that covers transplant

PACT directs CMS to reimburse for searching and procuring therapy product separate from reimbursement payment for transplant, etc. (as in solid organ world). Members of the House of Representatives and Senators are co-sponsoring the PACT Act bill.

We are also working to respond to proposed CMS rules through our data on cost and charges for cell procurement. We are looking at hospital charges and rates to ensure they are as adequate as possible when CMS sets their rates. We are working with commercial payors to track their changed policies and reach out when necessary. We are monitoring State and Federal legislation looking for barriers to access (we will monitor state legislation around cord blood to intervene when necessary and educate that insurance is adequate).

Discussion:

Dr. Delaney: I'm a stem cell transplant MD. We need to be sure everyone has a donor. The challenge is that it's not really known which is the best patient-specific donor. Each of these transplant centers has their own priorities, and development has facilitated this. It is confusing for the patient; you may get different answers from different centers. We need to focus on this. I agree we do have to focus on clinical trials; we have a lot of data but we need to provide evidence via trials as to which donor is the best for a certain patient. A lot of people feel it should be either a cord blood or a haploid if they don't have a suitable source. The message is either of those choices can be possible, but our mantra should be that every patient has a donor.

Dr. Hartzman: The problem is clinically around the ability to get the patient out of the hospital. So the big issue around cord blood is utilization. My belief had been the expanding cells *in vitro* may offer some promising techniques, but I've gotten negative responses that it would be very problematic. But, there's an opportunity around trials. Is there a possibility for NMDP or government to change utilization? What are the things you can do to get the patient out of the hospital? I think this happens by accelerated neutrophil recovery of the patient. That might be one reason why people hesitate to use cord bloods.

Mr. Walsh: Has that been looked into?

Ms. Beaver: We haven't looked at it from a policy perspective. I could see something like an act around funding a specific clinical trial. We've stayed away from reimbursement for those from specific cell sources (traditionally we've been cell source agnostic), but with therapy coming online and now that CMS is struggling with how to reimburse, the conversation maybe we could have a public policy position to encourage development of a product that could expand cord blood.

Dr. Laughlin: The unusual circumstance is that you have clinicians selecting, on the one hand, a cellular product that is FDA regulated and licensed, and on the other hand, and family-donated cellular product that is not under any agency regulation. We should focus on literature, which is retrospective, which focuses mainly on short-term outcomes and focuses on a relative paucity of comparison with long-term outcomes. With FDA, the concern is overall survivals. NMDP and HRSA might focus on these parameters and longer-term overall survival is improved with one cellular source over another. This could improve practice.

Dr. Bracey: Medicare reimburses approximately 85 percent. Is their information suggesting that, for stem cell therapies, the ratio is different? Treatment groups vie for increasing support that may not happen because we're trying to bend the curve, but if there's good data on a cost and reimbursement ratio, which seems out of range compared to other Medicare reimbursements that might offer an advantage in seeking some sort of modification.

Ms. Beaver: That would be interesting. I'd have to dig into data we now have. If we could pull it out to see if the ratio of reimbursement to actual transplant costs are not in line with other services, then we could maybe use that as another argument to CMS as to why they should increase their reimbursement.

Dr. Delaney: I echo Mary Laughlin. Long-term follow-up of a donor is a real achievable goal for NMDP. Expansion of cord blood cells to enhance engraftment – lots of data will come out. Most of the technologies in clinic now have been moved to industry trials, which will be reported on. In the last few years, time to engraftment has gotten shorter. We need education and awareness around this. We need more information on the cause of high-resolution typing and we need better units to select from, as well as knowing how to select units.

Overview of the National Marrow Donor Program's (NMDP's) 2019 Physicians Summit

Donna Regan, Director, Customer Ready Products, National Marrow Donor Program

Key topics from the June 2019 Physician Cord Blood Summit:

- How to create "NMDP's s first innovation lab
- The look of the cord blood bank space if started today
- Provider:
 - Develop high touch relationship with BTM HLA expert
 - Engage cord blood consultation service
 - Utilize cord blood selection criteria
 - Communicate search prognosis—product and timing
 - Learn why patient did not proceed

- Invite TC search coordinators to BTM
- Mentoring program facilitated by NMDP: Mentees would be junior faculty; we would like formal certification. Junior faculties', BMT fellows' Application process elements include: small review committee, letter of support, education didactic session, 1-2 months at major cord blood transplantation center, formal certification, funding for housing and travel, exposure to entire TC team and services, all graft sources
- CBC Consortium: Create standard of care cord blood protocol support for teams that use cord blood less frequently (selection, preparation, transplant, supportive care, immune reconstitution)

Innovation Lab Uptake:

- Revitalize CBAG (*Restructure CBAG to be mission driven and action oriented*)
- Evidence to drive change (provide physicians with evidence for proper *care*)
- Leadership *to promote visibility*
- High-resolution typing (*Perform high-resolution typing for a more accurate match*)

Additional Activities:

- Refresh CBAG (charter, composition, subgroup charges)
- Formalize consultation process
- Convene cord blood protocol group (pediatrics and adult)
- Support RAND recommendation to increase TNC criteria for NCBI funding
- Offer services in support of clinical trials in non-malignant space

Our feedback and recommendations follow. We:

- Support better engagement in the cord blood space as expressed by an immunogenetics doctor at "Be the Match"
- Support endorsement of using the cord blood criteria that guide the selection
- Support NMDP to communicate stronger recommendations pertaining to sub-optimal CBUs not selected
- Support that we learn more about why patients didn't proceed to transplant when they had the option
- Support that we invite coordinators to teach them about the search practices occurring in the field
- Support remedying the lack of standardization in cord blood standards spectrum of success; "Be the Match" could create a cord blood standard of care best practices (we will host a meeting on this at the upcoming cord congress)
- Support restructure and recomposition of CBAG, which should be action oriented and mission driven under the advisement of board of directors; working subgroups there can be given specific deliverables to feed up to the board of directors
- Support formalizing the consultation process
- Support convening a cord blood protocol group covering guidelines and procedures for standard and predictable pediatric and adult transplants
- Support RAND recommendation to increase TNC criteria for NCBI funding

- Support NMDP commitment and responsibility to protect stem cell source, with the acknowledgement that this must be done sensibly

Discussion:

Dr. Laughlin: The committee members would want to understand the primary view of 990 reporting by NMDP. Who collects millions of dollars of fees for distribution of cord units? How could those resources be used to address some of these goals? *Ms. Regan:* Finances will be addressed in October. Absence of high-level typing is an impediment for transplant centers to do better matching. We need high resolution HLA typing on cord blood segments so it would also improve time to transplant.

Efforts to Increase Cord Blood Utilization

American Society for Transplantation and Cellular Therapy Cord Blood Special Interest Group

Dr. Juliet Barker, Director, Cord Blood Transplantation Program, Memorial Sloan Kettering Cancer Center, American Society for Transplantation and Cellular Therapy, Special Interest Group

The many benefits of cord blood transplantation (CBT): extending transplant access through rapid availability and easy scheduling; reduced requirement for HLA-match; it is sometimes the only available stem cell source. Long-term advantages include good immune recovery, better GvHD treatment response, low rates of chronic GvHD, low relapse rates (no ATG), advantages in GVL biology, and long-term cost benefits.

However, not all of the transplant community agrees about the value of cord blood and cord blood has declined because of unit selection, cost of units, complexity in early post-transplant, selective focus, conceptualizing of CBT as “last ditch” therapy, and expansion.

CBT is needed because of the ongoing disparity in unrelated donor access according to patient race. Additional volunteer access is not appreciably improving for southern and non-European patients. The U.S. population is becoming more diverse and young donors are less likely to match patients of any age. Therefore, the cord blood inventory becomes very important:

- The majority of units with adequate TNC do not have adequate CD34+ dose. Four percent are adequate as single units.
- With lower dose (TNC 1.5 and CD34+ 1.0) threshold, 22 percent of units had adequate dose for a double unit graft, which supports that the major focus should be on increasing inventory of high dose units (i.e., increase lower limit of TNC for banking). On the other hand, despite small inventory, there were adequate cord blood graft: 88 percent.
- Graft availability is much better than for the unrelated donor (e.g., more than triple for African ancestry patients). There was no cord blood graft at the rate of 12 percent. (Nearly all non-European; median weight 98 kg).

The argument goes, “Nearly everyone has a cord blood graft and you don’t have to worry about donor availability.” That is true, “but engraftment is slow and early TRM is high” and “you can only do CBT with expansion,” which means it is more complicated with possible compromise of T-cells with T-add back platforms.

However, there are strategies to reduce mortality without expansion. Efficient unrelated donor/cord blood searches, unit selection, and optimized immune suppression and focusing on optimizing multiple components of the transplant improve post-transplant survival.

Despite multiple centers and trials showing outstanding results, CBT has declined in the United States and Europe. There is a need for increased utilization of CBUs to help patients and save the banks.

Concerning the NMDP, does the United States have enough cord inventory? For example, of those units that would be suitable as a single unit graft, 4 percent of the units would be adequate for a single unit transplant. We don’t have a huge number for bigger patients. So, our major focus should be increasing inventory of high dose units. Does so few units mean we can’t find a cord blood graft for a whole bunch of people? Sloan Kettering says 88 percent had a cord blood graft.

Proposal: Create a U.S. CBT Network to:

- Facilitate rapid collaborations and information exchange
- Create/share practice guidelines and protocols and share nationally
- Speed publications
- Perform clinical trials
- Train junior MDs/other transplant staff

Suggestion: These efforts would be promoted by ACBSCT and NMDP to increase CBT visibility and make CBT more mainstream. This initiative is ambitious and will require funding.

Discussion:

Dr. Bracey: I’m wondering about shared decision-making. If the patient had alternatives when there is not an ideal match, is it really appropriate to give patients a voice in the decision? *Dr. Barker:* Absolutely. During unrelated donor searches, the patient was never told “there is no find in the unrelated donor search,” if their center doesn’t do cord blood and doesn’t refer to a center who does, or if/that the center has different expertise or research preferences. *Dr. Delaney:* These areas are obtainable. I look forward to talking with you further.

Dr. Gandhi: This needs to be brought forward. Also, transfusion support must be addressed since blood banks are not getting enough donors and starting to talk of paid donations for platelet donors.

Dr. Laughlin: Providing an infrastructure such as a network is a no-brainer, but we want to emphasize, in addition to these advantages, further benefit is because the cellular therapy field is buffeted by rapid pendulum changes in clinical practice. It doesn’t mark another area in clinical

practice because transplant physicians completely manage the treatment and aren't constrained. There is also the risk of draining the inventory but also of losing a generation of physicians knowledgeable in cord blood transplant. This center could save that. *Dr. Barker*: I agree. Training the younger physicians needs to be addressed. For example, T cells, which can be dangerous. There are clear standard operating procedures, we could institute a similar paradigm with cord blood.

Overview of Cord Blood Transplant Consultation Services – National Marrow Donor Program

Donna Regan, Director, Customer Ready Products, National Marrow Donor Program

Cord Blood Consultation Service

Search Strategy Advice (SSA)

- SSA team comprised of immunogenetic specialists
- SSA review will automatically list cord blood donors when no or few 10/10 matched unrelated donors are identified
- Transplant Center (TC) can directly request this service
- Present best options from which to choose
- Special cord blood consult as an extension of SSA Service began in December 2015
- External physicians rotate requests

NMDP sends information to MD performing consult:

- Cord search report or cord list
- SSA report (if done)
- TC contact, specific questions, additional TC requirements
- Patient demographics, disease, age, weight, transplant time frame
- MD contacts TC to discuss their recommendation.

Current Process:

- Recommendations are based on latest cord blood selection criteria
- Recommendations are advertised on network website, at Council Meeting (One Forum). They include: site visits with :1) 24 requests to date specific to CB Consultants 2) cases moved forward to transplant with the recommended CBU

Recommendations:

- Service is valuable despite very low usage
- Dependent on external colleagues
- Experienced MD to provide guidance and to be direct

- Leverage BMT CTN 1702 and DOTS to fine tune the program: 1) BMT CTN1702 – alternative donors presented 2) Donor Optimization for Transplant Success – alternative donors in software

Ours is a work in progress too. There is a subgroup in “Be the Match” for donor search and cord blood. They are not physicians but can give HLA advice.

SSA team of immunogenetic specialists--extension of SSA, NMDP physicians consult on:

- Cord search report
- Search strategy
- TC contact
- Patient demographics

There are a couple things we can do: a new trial to find a well-matched donor, or go directly to an alternative donor without waiting around.

The Diverse Use of Cord Blood for Hematologic and Non-Hematologic Indications

Marcie Finney, Executive Director, Cleveland Cord Blood Center

Umbilical cord background: Cord blood is used in 13 percent of all stem cell transplants. Over 35,000 CBUs have been released by public banks for allogeneic transplantation.

- Approximately every 3 minutes, one person in the United States is diagnosed with a blood cancer
- Cord blood is used in 13 percent of all stem cell transplants
- Cord blood is an option for patients with uncommon HLA types, including many of African American ancestry (only 30 percent of patients have a match within their family)
- Cord blood is an option for patients who have an immediate need for a transplant

Use of cord blood for hematologic indications: Leukemia (Majority of patents from our center are leukemia patients).

Malignancies:

- ALL, AML, CML, myelodysplastic disease, lymphomas, non-Hodgkin's, Hodgkin's disease, myeloma

Non-Malignant Disorders:

- Hemoglobinopathies, thalassemia, sickle cell disease, bone marrow failure syndromes, severe aplastic anemia, Fanconi anemia, Diamond-Blackfan anemia, immune deficiencies, Wiskott-Aldrich syndrome, SCID, DiGeorge syndrome

Research Efforts in Transplant for Hematologic Indications:

- Improve immune reconstitution
- Speed engraftment
- Reduce relapse
- Expand cord blood
- Derive MSCs from cord blood
- Augment homing

Potential Uses of Cord Blood for Non-Hematologic Indications:

- Allogeneic, inborn errors, stroke, autism, multiple sclerosis

Autologous:

- Neural injury, cerebral palsy, autism, type I diabetes

Cell Therapy Clinical Trials:

- Over 100 CB, over 60 Phase I/II, 3 in Phase III

Research Examples for Non-Hematologic Disorders:

- diabetes; Parkinson's disease; chronic, non-healing wounds; autism; cerebral palsy; ischemic stroke

Approximately, there are 780,000 publicly banked cord blood units worldwide. In the United States, 6.5 million people currently have chronic wounds, 1 million have Parkinson's disease, 3.5 million live with an autism spectrum disorder, 9,500 children diagnosed with cerebral palsy each year, 795,000 people have a stroke each year. If even one of these research approaches resulted in a safe and efficacious cellular therapy product, the public cord blood inventory could be more effectively utilized.

Public Cord Blood Banking Future Directions to Optimize HPC, Cord Blood Inventory:

- Identify industry drivers
- High TNC CBUs
- Unique HLA types
- Reduce cost of inventory acquisition
- Streamline processing procedures
- Optimize collection strategies
- Develop clinical pathways and product pipelines
- In-house research and development
- Support external researchers
- Make research CBUs available
- Leverage existing resources to diversify utility
- Support movement of cord blood derived products from research and development to FDA approval
- Experience with FDA BLA process

- Diverse partnerships
- Supply chain management

Key points: Incidence of leukemia and lung cancer are not going away. Cord transplant is important for many, including African Americans; it is also good when tissue typing is an issue.

Discussion:

Dr. Bracey: Regarding coverage and social economic status (SES), in terms of Medicaid across the States, what do we know about SES and State variation related to coverage for Medicaid? With the African American population, SES delta, how might that play into access to cord blood?

Dr. Finney: I can't speak from the transplant side. We need someone who actually treats patients. We try to collect from many sites, but we can't speak to coverage from an insurance perspective.

Dr. Barker: There are a lot more broad issues with cord blood. It's three-fold. First, what the specific center will accept politically and financially when the transplant physician wants to offer expensive therapy. At Sloan, we have the luxury to get away with that. Second, if we get trouble from the insurance companies we have an army of people that will fight for the patient and we win frequently. Third, access to cord blood transplant; it's worse in particular with minority patients. There may be SES and educational and English as a second language issues that can make the care after discharge much more challenging.

Dr. Bracey: With a kidney transplant, it's nationally a case with Medicare. But what about a payment scheme like the one for kidney transplants, would that be a better model?

Dr. Arnold: We can loop back under reducing barriers to transplant and policy initiatives and prior recommendation examples such as getting policy reimbursement to align with solid organ transplant.

Dr. Gandhi: I will present on what Dr. Bracey said with a similar recommendation. My belief is you do the map of the areas at risk. Is that true? How often do you revise that? Because my belief is the current map should be revised quite a bit if you went back and used the criteria you used for your original suggestion; the criteria were much lower. An update of the map might radically change the travel issue.

Dr. Marks: The map was changed within the last 2 months. One of the issues, as Dr. Gould said, is that there is not a lot of reliable surveillance in a lot of countries.

Dr. Gandhi: But the problem is that we flag a lot of CBUs for reasons that might not be correct. Can the CDC go back and look?

Dr. Marks: The CDC doesn't make separate maps for tissues. The question is, "Is there Zika in the country, and could there be information then used for travel guidance?" We are not going to be able to solve the problem of inadequate surveillance across the world; CDC can't do it. A potentially better way would be if it could be a test like blood. The world would have a test that would be a

good step forward, but there are inherent problems in typing tests.

Dr. Gandhi: There should be a way to develop a test for this. At least it gives you population estimates of the frequency of infection.

Mr. Walsh: If we are to pass a recommendation, we need to finalize language and vote at this meeting. We have to do it now (not via email) or by follow-up meeting next year, April or May. When you're making a formal recommendation you need the language right and cannot do it on the fly. I attempted to put together what I heard from Dr. Gandhi and the follow-up conversation and that's in the notes section of Adobe Connect for people to review, and I'd like to hear from members of council. Is there a second?

Dr. Laughlin: Is there a third alternative for the committee to assign a small work group to rework the wording for review and approval?

Mr. Walsh: There is definitely that possibility for a recommendation at a future meeting. The note section is not available on everyone's view on Adobe Connect.

Dr. Gandhi: I have a generic recommendation, but it's based on the morning presentations. Parts of the recommendation use available testing and follow-up of mother and baby for 1 year. I agree, to get a much more specific recommendation that would be helpful, but if it takes a whole year, is there any other way?

Mr. Walsh: I think our colleagues at FDA and CDC and we at HRSA have heard it and will have further discussion as it's worded on the note. Right now, it may not be necessary for that purpose, but if we want to get into it in a more thorough way I recommend we get it into a working group before we make a recommendation. If we put forward a general recommendation as you have on the notepad, I assume if the FDA would come back to the committee with any questions – they're hearing this needs to be addressed in a timely fashion. I think if the general recommendation is as effective at triggering that review, as far as Zika, we need to review this sooner rather than later. Am I hearing this motion as a second for what's written on the notes page?

Text of Recommendation from Adobe Connect Notes, September 10, 2019, Meeting:

Based on current data and reduction in observed and confirmed Zika infection, ACBSCT recommends that HHS review the current FDA Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components as the guidance relates to utilization of cord blood.

Dr. Laughlin: I second.

Mr. Walsh: Any further discussion or amendments on this recommendation? I'll do a quick roll call. Just say approve or deny the recommendation.

The following approved the recommendation as Mr. Walsh wrote it up: Drs. Arnold, Bishop, Bracey, Delaney, Gandhi, and Laughlin.

Mr. Walsh: It's unanimous then. Thank you very much. We will write this up as a recommendation to the department then. Are we still interested in a work group?

Dr. Arnold: Yes, I highly agree it's necessary. I suggest it include representatives from FDA, CDC, and the blood bank of New York, in addition to voting members to ensure there's balance in the information that's discussed and the final recommendation.

Mr. Walsh: We'll follow up with that. Any other new business?

Dr. Arnold: My other comment is on the concept of standardizing cord blood training/experience, which is a good one. I'm not sure how to enact that, with the caveat that more cord blood is needed as a focus but not in isolation because there are many options in cellular therapies and alternative donors that patient have access to. It may also lead to other donor options.

Mrs. Grant: We've had several work groups in the past and have reestablished some for these issues (e.g., "looking at potential of cord blood" and "aspects of cellular therapy"). This is a time for the council to think through what's discussed today and decide what work we want to do between today and the next meeting. You can have a dialogue to see what other working groups you may feel are necessary to do this work. We'll take the liberty of you saying yay or nay or not now. Ensuring we realize the potential of cord blood. Use your raised hands bar, raise your hand if want to do more on cord blood. (Pause.) We appreciate your typing. Keep it up.

Mr. Walsh: It's a split decision

Mrs. Grant: We'll stick with the one group we have focusing on Zika.

Mr. Walsh: It appears we have included the recommendations in new business. We did not receive any request from the general public to submit any comments at the meeting. However, if there are participants who wish to make a public comment we can allow you to speak. Anyone who wants to make a comment for consideration by the council from HHS, now's your opportunity.

Dr. Arnold: It seems there's an either/or value of going deeper into cord transplant, but I feel there were several different asks from the presenters. Maybe we can't fully capture them all but there were smaller actionable items that won't warrant a full working group. Someone listed standardized training or fellowship program. I'm curious if people think this is of value and moving forward on that.

Dr. Delaney: I thought whether there should be other working groups around any of the topics – sourcing cord blood. I'm confused. It seems to me this council's role is to provide recommendations around access to good health care especially around cell transplantation. How are we going to prioritize these on a phone call?

Mr. Walsh: Thank you. A number of issues were raised as potential future actions. The one working group is Zika and the FDA guidance. We passed the recommendation to establish a working group to continue discussion between now and the next meeting if there's a need for a more detailed

recommendation to come up at the next meeting.

Dr. Arnold: For example, Marcie and others suggested how banks could team up with researchers. Public-bank partnerships are important for me in developing cellular therapies for patients. It would be great to see how we can play a role in pushing this forward.

Mr. Walsh: Well said, we agree.

Ms. Regan: I'm making a public comment. I want permission before I proceed.

Mr. Walsh: Yes.

Ms. Regan: I'm following Shelley's lead of work done by the advisory council in the past. One concern is funding of the NCBI units that match demand for cord blood, which has been higher than units in the inventory in terms of nucleated cell count. I ask that new council recommendation of March 28, 2016, to increase fundable criteria for NCBI units, be re-considered. I know the solicitation has been closed. Perhaps we could define the TNC minimum threshold from the current small dose units that are unlikely in exchange for the larger units that would help the banks, incentivize them to move forward with banking larger units with better likelihood of being selected. There might be better minimum thresholds to use moving forward for NCBI funding.

Mr. Walsh: NCBI contracts are under review but we cannot comment on specifics. I believe we can adjourn. As a last thing, we are always seeking to add new members to the advisory council and have published on the *Federal Register* new ongoing requests for nominations on the advisory council and encourage those on the line today to nominate someone or themselves. They can do that via the link on the webpage. I thank the members for participation today. I greatly appreciate your knowledge and the time you shared with us.

Mr. Walsh adjourned the meeting at 4:50 p.m.