ADVISORY COUNCIL ON BLOOD
STEM CELL TRANSPLANTATION (ACBSCT)
U.S. Department of Health and Human Services (HHS)

Summary of Conference Call Meeting
November 8, 2011

Welcome and Introductions

Patricia A. Stroup, MBA, MPA, Executive Secretary, called the meeting to order at 10:09 a.m. and welcomed the Council members and participants. Edgar Milford, Jr., MD, ACBSCT Chair, asked that presenters keep their remarks brief to allow for discussion and voting on several issues. (A summary of the recommendations and action items from this meeting is included in attachment 1. The list of participants is included in attachment 2.)

Realizing the Potential of Cord Blood Work Group Update

Liana Harvath, PhD, Work Group Chair, and Bertram Lubin, MD, Work Group Member
Dr. Harvath reviewed the purpose of the Work Group and summarized its efforts over the past few months. The Work Group held a joint conference call with the ACBSCT's Scientific Factors Necessary to Define a Cord Blood Unit (CBU) as High Quality Work Group that resulted in a recommendation (to be presented by the chair of the Scientific Factors Work Group) regarding the Food and Drug Administration's (FDA's) biologics license application (BLA) and investigational new drug (IND) application requirements, as described in the FDA Guidance for Industry, *Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution for Specified Indications.*

The Work Group is considering various research questions, such as whether double CBU transplantation is superior to single CBU transplantation. The National Institutes of Health (NIH) is funding a study of the question, with enrollment expected to be completed by the end of this year.

Sickle cell disease (SCD) is excluded from the FDA's indications for licensing for unrelated allogeneic hematopoietic stem cell transplantation (HSCT). Two literature reviews have been published on allogeneic HSCT for SCD, and three NIH-funded clinical trials are underway. Twelve clinical studies are evaluating reduced-intensity HSCT regimens for hemoglobinopathies. The NIH's SCD Advisory Committee met in October 2011 to discuss barriers to HSCT for SCD and to hear overviews of the three NIH-funded clinical trials. The SCD Advisory Committee discussed challenges to studying HSCT for SCD (e.g., poor enrollment, questions about measuring outcomes).

Dr. Lubin pointed out that SCD affects 80,000–90,000 people in the United States and millions worldwide. While effective treatment exists, bone marrow transplantation (BMT) is the only cure. Treatment is expensive, and there are few comprehensive treatment centers. The disease can cause neurocognitive impairments in adults and multiple disabilities related to chronic organ damage. People with SCD often have chronic pain, and they are sometimes labeled as drug addicts because of their efforts to seek pain management medications. There are far fewer care providers for adults with SCD than for children.

Over the past few years, said Dr. Lubin, we have seen dramatic improvements in survival of children with SCD into adulthood. But little is known about adults with SCD. Many providers see BMT as too risky, and trials are limited. Even experienced hematologists delay referring patients for BMT until complications of SCD are severe.

A number of social factors pose barriers to treatment of SCD:

- lack of insurance coverage
- lack of awareness/education (fears and concerns among families and health care providers about treatment, failure to inform families about using sibling donors)
- disparities in access to health care
- lack of communication between hematologists and transplant physicians
- challenges of collecting cord blood from African Americans

An investigator found that providers do not always refer eligible patients for clinical trials and that eligible patients may choose not to enroll because of past experiences with treatment-related complications, misgivings about biomedical experimentation and participation in clinical trials, religious convictions, the uncertainty of transplant results, and uncertainty of disease progression (often perceived as manageable without BMT). Specific challenges to trials of BMT for patients with SCD include the difficulty of explaining the risks and benefits, the inability to predict outcomes, and the lack of suitable donor sources. Socioeconomic factors must be addressed, said Dr. Lubin, and investigators must target motivated families and encourage their participation in trials.

More studies are needed to demonstrate the benefits of BMT in preventing stroke among children with SCD, for example. Dr. Lubin said stem cell transplantation offers a potential cure for SCD and should be included in FDA's indications for unrelated cord blood transplantation.

The Realizing the Potential of Cord Blood Work Group recommends that ACBSCT establish a work group on advancing HSCT for hemoglobinopathies. Dr. Harvath presented a draft charter for the new work group, should it be approved.

Discussion

Council members expressed support for a new work group on advancing HSCT for hemoglobinopathies. Dr. Harvath pointed out that the HHS Secretary has convened an interagency working group whose goal is to advance treatment options for hemoglobinopathies. She said a new ACBSCT work group could provide unique expertise about the role of transplantation in curing SCD and outline the barriers to access to transplantation. Joanne Kurtzberg, MD, said that African Americans have a harder time finding matched donors than other populations, and CBUs can play a big role in treatment for them. We should prioritize treatments that expand access, said Dr. Kurtzberg.

In response to a question, Dr. Harvath clarified that the FDA determined its indications for HSCT on the basis of data provided to support the use of CBUs from unrelated donors; the FDA has no data on the safety of unrelated allogeneic HSCT, and the new work group could help

bring forth such data. She also clarified that the proposed new work group would focus on HSCT but could also address CBU issues. The Council voted unanimously in favor of creating a new work group with the proposed charter.

Action Item
The Council will establish the Work Group on Advancing HSCT for Hemoglobinopathies, with the following charge:

> The Work Group will identify important gaps, including barriers to transplantation, and opportunities to more fully realize the potential of HSCT for individuals with hemoglobinopathies (SCD and the thalassemias). The Work Group will submit for consideration and adoption by the Advisory Council recommendations regarding high priority actions. The Work Group should involve in its work experts in related fields, including as needed experts who are not members of the Advisory Council. The Work Group should present a status report, and any recommendations developed by that time, at the next meeting of the Advisory Council.

Council members should submit to Drs. Milford and Harvath their recommendations on who should chair the new work group and suggest potential members.

Scientific Factors Necessary to Define a CBU as High Quality Work Group Report
Joanne Kurtzberg, MD, Work Group Chair
Dr. Kurtzberg explained that the Scientific Factors Work Group considers not only what constitutes a high-quality CBU from a medical perspective but also what constitutes a high-quality CBU for inclusion in the Health Resources and Services Administration's (HRSA's) National Cord Blood Inventory (NCBI)—and specifically, what units the NCBI would pay for. The types of CBUs vary, as do collection mechanism and storage methods, and questions remain about what technical parameters best correlate with outcomes. Those questions are complicated, because many factors affect successful engraftment. Typically, CBUs are selected on the basis of matching and total nucleated cell (TNC) count, but other parameters, such as colony-forming units (CFUs) and CD 34, may be better predictors of engraftment and may correlate better with quality. Donor and sample screening are also factors in assessing quality.

Dr. Kurtzberg noted that FDA has set quality standards for the NCBI regarding donor screening, collection, and storage. HRSA has also established requirements regarding race/ethnicity to stimulate accrual of units from non-Caucasian populations.

In response to some of the issues that HRSA asked the Scientific Factors Work Group to address, Dr. Kurtzberg noted that there is more work to do to address the use of remote cord blood collection kits. In addition, the Work Group believes that factors other than TNC may be important in cord blood selection, and processing, storage, and thawing methods affect CBU potency. Data from the Center for International Blood & Marrow Transplant Research (CIBMTR) will inform future recommendations from the Work Group on criteria for NCBI payment.

Regarding stability, Dr. Kurtzberg said blood banks are charged with predicting the potency of units before they are released from the bank, but processing, freezing, and thawing all affect potency. Therefore, efforts are underway to identify assays that can provide information to help transplant centers select CBUs. Dr. Kurtzberg described some of the approaches her blood bank has discussed with FDA, such as evaluating potency of six units from each year of banked units. Standardized norms for the results of such evaluation are needed.

Evaluation of patient outcomes using samples from the Duke University blood bank ranging from 1 to 10 years old found no significant difference in the median time to engraftment of neutrophils, development of platelets, recovery TNC counts, or CD 34. The development of recovery CFUs appears to decrease as the unit gets older, but Dr. Kurtzberg cautioned that different centers evaluate CFUs differently. She noted that, ideally, CIBMTR will undertake such an analysis of samples from all blood banks and transplant centers. Dr. Kurtzberg said it is possible that Duke's success in maintaining the stability of its samples may be related to the fact that it stores them in liquid nitrogen, but she pointed out that the effects of various storage methods represent exactly the kind of information we need to know.

Dr. Kurtzberg noted that hundreds of thousands of units are in storage, and there is no way to label those units with expiration dates without destroying them. Therefore, it has been proposed that blood banks attach labels with expiration dates via tie-tags to each unit when it's removed from storage for release to a transplant center. Pablo Rubinstein, MD, said his bank has reached an agreement with FDA to use the tie-tag approach.

Currently, laboratories require two weeks to provide results of assays to evaluate CFUs of a thawed unit. Dr. Kurtzberg and colleagues have developed an effective assay of aldehyde dehydrogenase (ALDH) bright cells that takes only a few hours and appears to be predictive of engraftment. They hope to demonstrate that the rapid ALDH bright assay could be used instead of the time-consuming CFU assay. In addition, Duke University investigators are proposing a scoring system that transplant centers could use to select units for an individual patient given various parameters.

Discussion
Dr. Kurtzberg said the age of the stored unit is not usually a factor in selection. Dr. Rubinstein noted that his bank has obtained similar data as Dr. Kurtzberg's on the stability of units over time. Dr. Kurtzberg said her organization has new data correlating units with engraftment outcomes, but banks and transplant centers need to standardize their assays and refine their methods to identify potency and stability. Donna Regan, MT (ASCP), SBB, pointed out that modern vapor freezers provide more consistent temperatures than older models, and she hoped analysis of CBUs would take that into account. Dr. Kurtzberg said that a CIBMTR analysis could override biases by doing an evidence-based analysis of such variables.

Joint Work Group Recommendations on FDA BLAs and INDs
Joanne Kurtzberg, MD, Chair, Scientific Factors Necessary to Define a CBU as High Quality Work Group
Dr. Kurtzberg said that FDA's guidance on use of CBUs does not include BMT for sickle cell anemia, other inherited metabolic conditions, and other rare indications. The failure to include

these indications may lead to confusion and reduce access to transplantation. The ACBSCT sent a letter to the HHS Secretary on October 14 spelling out its concerns. The Scientific Factors Work Group and the Realizing the Potential of CBUs Work Group discussed the issue in depth and identified the following concerns about FDA's failure to include the stated indications in its guidance:

- Increased time to procurement of CBUs for patients because of the need to apply for a compassionate-use IND could lead to otherwise avoidable disease progression.
- In cases in which the patient's condition does not allow time for an IND to be prepared and approved, or transplant centers lack the resources to quickly prepare an IND, transplant centers may feel compelled to choose a less optimal but licensed CBU or an alternative donor for the patient (e.g., a haploidentical family member) to avoid the increased regulatory burden of an IND.
- Third-party payers may not reimburse cord blood transplantation for conditions that are not specified in the guidance or for unlicensed CBUs.
- Selective licensure of a single or a few banks for specific clinical indications will lead to inferior donor selection for a patient in need.
- Patients of ethnic and racial minorities will be further disadvantaged because their best donor is more frequently a cord blood donor.

The Work Groups jointly proposed the following:

1. FDA should broaden the 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.
2. All cord blood products should be approved for the same license indications.
3. FDA should implement a transition plan to allow time for the FDA to review recommendations 1 and 2 above and to allow for implementation of any changes by transplant centers who will need to put these changes through their institutional review boards (IRBs).

In addition, the following issues require clarification before implementation of the FDA guidance:

- Appropriate protocol when multiple institutions hold INDs that would affect the same patient
- Harmonization of recipient consent requirements
- Clarification of the extension period to allow time required to amend INDs and resubmit them to IRBs
- Addressing insurance denials secondary to the new IND structure (e.g., when centers use units that do not have a license)

Dr. Kurtzberg noted that the National Marrow Donor Program (NMDP) plans to revise its IND. Once it does, all of the 160 transplant centers that operate under the NMDP's IND will have to resubmit their protocols to their local IRBs, followed by months of review. The issues related to INDs also affect BLAs.

Discussion
Dr. Rubinstein said FDA has allowed his organization, the New York Blood Center, to continue operating under its existing IND as long as it is progressing toward establishing a new IND compliant with the new guidance. However, FDA has signaled that the indications in the new IND could be modified, allowing the New York Blood Center to treat all conditions that can be treated with HSCT from other sources. Dr. Rubinstein did not believe that FDA's decision to extend the indications was restricted to the New York Blood Center.

Participants discussed the confusion surrounding the question of who must hold the IND, with Dr. Kurtzberg noting that it's the bank's responsibility to ensure that the product is used under an IND. Dr. Rubinstein added that the bank must either have its own IND, subscribe to NMDP's IND, or confirm that the transplant center has an IND. Ms. Regan pointed out that the NMDP's IND trumps all other INDs. Dr. Kurtzberg said confusion remains when different INDs cover different aspects of treatment. Ms. Regan said the FDA should clarify the switch from requiring donor consent to requiring recipient consent. Dr. Rubinstein said his organization has consent processes for both. Participants offered some suggestions to revise the wording of the recommendations, primarily to ensure that they refer to both licensing and INDs.

Dr. Kurtzberg clarified that deadline for implementing the new guidance and FDA requirements (October 20, 2011) has passed, but some organizations were allowed to continue operating under their existing INDs, and enforcement of the restrictions on clinical indications was not implemented. Mary C. Hennessey, JD, said that, in relation to patient treatment, the transition process will continue until all blood banks have completed the new licensure process. FDA will have to address whether patients will be asked to consent to using what may be considered an unlicensed product when, from a scientific perspective, the same product from a different bank is licensed. Ms. Hennessey suggested thinking more broadly about the recommendation for a transition plan. Dr. Kurtzberg responded that the consent process is only required for INDs, not licensing, and FDA and NMDP agreed that the recipient is a research subject who must give consent to use of an unlicensed product. Following discussion, participants agreed to reference the date on which FDA enforcement was to have taken effect (October 20, 2011) in its recommendation.

Unrelated to the FDA issues, Dr. Kurtzberg offered an additional recommendation of the Scientific Factors Work Group:

- CBUs collected through distribution of kits sent to motivated maternal donors, collected by their obstetric provider, that meet all NCBI/FDA qualifications should be eligible for licensure and listing on the NCBI, which will enable more donations and has the potential to decrease collection costs.

Dr. Kurtzberg said evaluation is underway now to determine whether the NCBI has the capacity to accept thousands of donated units from Caucasian women as a result of the use of remote collection kits. Robert Baitty of HRSA said NCBI plans to reimburse for units if the bank has a license that covers them and has not yet met the contract goal for the population from which the

unit comes. Ms. Regan suggested rewording the recommendation so that it does not infer that a kit cannot be licensed unless it is also included in the NCBI.

Dr. Kurtzberg provided estimates of the cost of compliance with new FDA licensure guidelines, from hundreds of thousands per year for equipment and maintenance to millions for constructing new facilities. She asked whether the money spent to achieve compliance would result in any increase in safety, purity, potency, quality, or efficacy of the product.

The Council members unanimously agreed to accept all four recommendations pending review later in the meeting of revised versions.

Cord Blood Thawing and Washing Work Group Report
Jeffrey McCullough, MD
Dr. McCullough explained that the charge to the Work Group expanded from reviewing thawing and washing procedures to all activities at the transplant center laboratory and interactions between transplant centers, banks, laboratories, and clinicians as well as infusion-related policies, practices, and adverse events. He summarized the issues under consideration by the Work Group, noting that the Council recommended at its May 2011 meeting that HRSA disseminate a list of activities performed by transplant centers that could be used to plan training and operations. Robert J. Hartzman, MD, said the proposed list should include transplant center reporting requirements (cell counts, patient outcomes), and Adrian P. Gee, PhD, suggested including a broad statement indicating that transplant centers are responsible for tracking certain data.

> **Action Item**
> The Cord Blood Thawing and Washing Work Group will review the list of transplant center activities that it proposed with the May 2011 recommendation and consider how to address transplant center reporting requirements.

The Work Group is also reviewing the literature on various thawing and washing methods. Dr. McCullough hoped a draft of the Work Group's findings would be available for consideration by the Council at its spring 2012 meeting.

CIBMTR will undertake a clinical outcomes study to evaluate the impact of processing methods by banks and transplant centers. The protocol is in the early stages of development but will be a retrospective analysis using CIBMTR's data and follow-up mechanisms. It may be necessary to conduct a preliminary survey of bank practices to define the key variables for this study. Other Council members added that while CIBMTR has agreed to conduct this study, confusion remains about the logistics and scope of the study. Dr. Kurtzberg suggested the Council urge CIBMTR to elevate the study to a higher priority. Mr. Baitty noted that the next step in the process is for banks to discuss the measures that should be included in the analysis, and NMDP has included the issue on its agenda for a meeting later this month.

Dr. McCullough said the Work Group recognizes that transplant centers lack a unified structure for reporting adverse events, but NMDP has developed a system and software for banks and

transplant centers that helps them report data in a standardized form and meet their FDA reporting obligations.

Update on Cord Blood Thawing and Washing Work Group White Paper on Thawing and Washing Methods

Donna Regan, MT(ASCP), SBB

Ms. Regan said the Work Group is writing a white paper that reviews the literature on preparation in general. She noted that nothing has been published about automated methods of preparation.

It is critically important to provide a resource for banks and transplant centers that can serve as a template for validating units of all shapes and sizes, said Ms. Regan. The steps involved in preparation and use of CBUs all affect the quality of the CBUs. Ms. Regan said NMDP plans to post online the webinar it conducted in June that depicts at least three methods of validation. She said people in the field are eager for standardized approaches to preparation and validation.

> **Action Item**
> Ms. Regan will provide an update on the progress of the Cord Blood Thawing and Washing Work Group white paper on thawing and washing methods at the next Council meeting.

The Potential Impact of the Proposed FDA Guidelines on Laboratory-Developed Tests

Carolyn Hurley, PhD, D(ABHI), Professor of Oncology, Georgetown University Medical Center

Dr. Hurley stated that FDA has broad authority to regulate medical devices, which includes in vitro reagents for diagnosis and prevention. In June 2011, FDA published guidance in the form of frequently asked questions on commercially distributed in vitro diagnostic (IVD) products labeled for research use only (RUO) or investigational use only (IUO). While the guidance is not legally enforceable, industry takes it very seriously and has concerns about the potential loss of RUO/IUO labeling exemption and the possible impact on clearance for IVD products.

Dr. Hurley said the guidance could prohibit use of IUO/RUO reagents in laboratory-developed tests, prohibit off-label use of IVD cleared tests (despite laboratory validation), and limit access to IUO/RUO reagents. Notably, the guidance indicates that a company selling IUO/RUO products should halt sales to laboratories using these products for diagnostic purposes.

The guidance includes language specific to transplant center laboratories and could potentially affect the following areas:

- Human leukocyte antigen (HLA) typing of patients, families, and donors, including registry typing, because high-resolution typing IVD reagents, software, and equipment for DNA sequencing are not cleared by FDA
- Antibody screening/monitoring, because equipment may not be approved by FDA for specific applications and using antibody assays for antibody quantification is an off-label application
- Crossmatching tests, both real and virtual, because reagents and equipment are not cleared by FDA

Dr. Hurley said histocompatibility laboratories are already subject to Clinical Laboratory Improvement Act (CLIA) regulations, and FDA approved exemptions for CLIA-certified laboratories to develop and validate tests of specific and general reagents. Furthermore, histocompatibility laboratories must comply with quality-assurance requirements to maintain CLIA certification and accreditation. Finally, she noted, histocompatibility is recognized as a specialty that requires subjective interpretation and different external proficiency testing requirements, so extensive documentation exists for most tests developed by histocompatibility laboratories. Dr. Hurley emphasized that laboratory-defined tests already fall under extensive oversight.

The unintended consequences of the new FDA guidance may be as follows:

- Inability to identify allele-matched donors for HSCT in the context of a racially/ethnically diverse U.S. population
- Reduced access to transplantation for HLA-sensitized candidates
- Reduced deceased donor availability for non-renal candidates without "virtual crossmatches"
- No desensitization or post-transplant monitoring, except in research protocols
- Loss of incentive for industry and academic center medical laboratories to develop new assays

Dr. Hurley suggested that FDA should 1) exempt laboratory-defined tests for which there is documentation of validation and clinical benefit and 2) recognize and accept the review of laboratory-defined test validation performed in CLIA-certified, high-complexity laboratories.

Discussion
Dr. Hurley clarified that investigators and clinicians need the flexibility to develop tests in the absence of demonstrated clinical benefit to determine how they could be used in the future. She further clarified that laboratories may use HLA assays to predict sensitization, which goes beyond the FDA-approved indication for the products. Frederick R. Appelbaum, MD, agreed that the guidance poses some real problems, but it does not prohibit using reagents in early research efforts. He suggested that any recommendation to FDA should focus on the issues of documentation and validation of clinical benefit.

Dr. Hurley said concerns about uncontrolled genetic testing in the context of personalized medicine prompted FDA to publish the guidance, but she was not sure why it contained specific references to transplantation. Dr. Milford said the Council would review recommendations made by the HHS Advisory Committee on Organ Transplantation (ACOT) to FDA on this issue later in this meeting and consider adapting them to address stem cell transplantation.

FDA Licensure Update
Celia Witten, MD, FDA
Dr. Witten emphasized that FDA does not want to impede access to cord blood transplantation. She noted that all CBUs must be shipped under either a license or an IND.

On September 22, an FDA advisory committee reviewed the New York Blood Center's BLA, not to vote on the indications but to consider the safety and efficacy of cord blood transplantation for certain indications and the overall risk/benefit profile of HSCT for those indications. The advisory committee supported the use of cord blood transplantation, although agreement was not unanimous, said Dr. Witten.

Dr. Witten emphasized that when sponsors contact FDA with concerns about implementation of the new guidance regarding INDs, FDA makes it clear that the agency will consider indications beyond those described in the guidance. FDA is willing to discuss the matter with any sponsor. Dr. Witten said FDA sometimes needs to take action quickly, and guidance takes longer to modify, but FDA will look back at the cord blood guidance in the near future and think about updating it.

Dr. Witten said FDA does not prescribe which entity should hold the IND. However, the unit must be used under an IND. For a given patient, only one IND is needed, and it can be held by any entity involved in the process (the blood bank, the transplant center, or the NMDP for an affiliated transplant center). Dr. Witten added that sponsors can ask FDA about cost recovery issues.

Discussion
Dr. Kurtzberg asked whether proposed changes under an IND also apply to licenses, specifically the broadening of clinical indications. Dr. Witten suggested that an entity with a license contact FDA to discuss the matter. Dr. Kurtzberg asked whether FDA intends to license different banks for different indications or whether approved clinical indications for one bank would be applicable to all licensed banks. Dr. Witten responded that FDA considers the data provided to support a licensed indication and is primarily concerned with data on effectiveness. If a licensed entity provided data that apply only to that entity, then the indication would apply only to that entity. To the extent that FDA makes conclusions based on public data, said Dr. Witten, those conclusions would be applicable to all entities. She emphasized that decisions are made on the basis of data in the docket and the published literature.

Dr. Kurtzberg asked why the FDA advisory committee has not requested that the docket be updated, given that it affects FDA licensing decisions. Dr. Witten explained that FDA does not ask that the community at large update the docket when FDA is considering a specific BLA. If the community develops data on new indications, dosing, etc., FDA would be interested in learning more. Dr. Kurtzberg said the purpose of the docket was to gather clinical outcomes data from multiple banks; she added that a single bank will not have sufficient data to support a rare indication. Dr. Witten said the data currently in the docket are accessible to all banks, and thus the docket achieves FDA's purpose. She emphasized that the field should collaborate to aggregate data but she did not believe the docket was the best mechanism for such collaboration.

Ms. Hennessey asked if FDA considers each BLA independently, and the public docket is not the mechanism for getting data about broad indications to FDA, how does FDA believe BLAs will not be inconsistent? Early BLA recipients will have certain data in the public docket; later on, there will be new data on new indications that are not captured for any bank that did not already have a license. Ms. Hennessey said her question reflects just one example of the

disconnect about which she is concerned. Dr. Witten said FDA has not yet issued its first license under the new guidance, so it's difficult to respond to the question. However, the public data are accessible to all banks. Individual BLAs can draw on the safety and effectiveness data that are generally available.

Dr. Milford returned to the question of licensing different banks for different indications, and Dr. Witten said that is not FDA's goal. She again noted that FDA makes decisions based on publicly available data.

In response to Dr. Kurtzberg, Dr. Witten said all INDs must consider the recipient as the research subject and thus include an informed consent process. She noted that FDA has talked with IND holders about the transition period and is willing to discuss the issue with any IND holder. Dr. Witten acknowledged that the terminology may be a source of confusion; research data can be gathered under a treatment IND, but the primary goal of a treatment IND is to ensure patient access.

Richard Champlin, MD, said there should be a worker and patient-friendly process to ensure that a cord blood source is available to all those who would benefit. FDA should harmonize indications so that all cord blood banks can provide units to transplant centers for general use, rather than licensing each bank for specific indications supported by that bank's own data. Dr. Witten agreed, noting that the FDA advisory committee recognizes that indications evolve over time.

Dr. Harvath pointed out that SCD is not a licensed indication, and Dr. Witten noted that there currently are no licensed indications. Dr. Harvath noted that the guidance refers to data from the public docket that applies to specific indications, and SCD is missing from that list. She asked how best to present to FDA data that have been accumulated since the public docket was last reviewed about 10 years ago. Dr. Witten said the community should consider combining data rather than reporting a lot of small studies. Dr. Harvath asked whether publication of a study is sufficient to warrant inclusion in the docket or whether data need to be presented directly to FDA. Dr. Witten said it sounded as though Dr. Harvath would recommend modifying FDA's guidance to include a specific indication, and she suggested Dr. Harvath send a formal comment to FDA to that effect.

Dr. Kurtzberg asked for clarification about INDs when a patient receives both a licensed and an unlicensed product in the context of an experimental protocol. Dr. Witten said she presumed that both products would be described and covered by a single IND, and she reiterated that the process only requires one IND.

Ms. Stroup said a participant asked via e-mail whether only CBUs manufactured after licensing are eligible for a license. Dr. Witten said the issue is covered in the guidance, but FDA would discuss it with license applicants. Mr. Baitty wondered how transplant centers, banks, and NMDP feel about the risks of enforcement of FDA guidance during the transition period. Dr. Witten responded that FDA expects every unit to be used either under a license or IND. As long as an IND holder is taking steps toward compliance, FDA does not intend to take action. Dr.

Witten emphasized that each IND must obtain IRB approval and informed consent from the research subjects (i.e., recipients).

Ms. Regan said it is not clear how entities should transition from gathering procedural consent from the donor to obtaining research consent from the recipient. Dr. Witten said IND holders should be moving toward amending their protocols, resubmitting them to their IRBs, and matching the informed consent process with the new IND requirement. During the transition, FDA will be flexible, she added. Ellen Lazarus, MD, said FDA is working with IND holders, who are aware that they need to update their INDs to come into compliance with the new guidance. Dr. Witten noted that there have been extensive discussion with FDA compliance evaluators about the transition period, and there has been no disagreement.

Dr. Witten left the call, and Council members continued discussion. Dr. Milford noted that FDA seems to consider each bank as a unique manufacturer of widgets with no sense of commonality. Dr. Witten did not indicate that FDA would establish its own set of indications applicable to all licensed entities. She stated that each entity applies for a license individually, yet FDA does not intend for banks to have heterogeneous indications. However, Dr. Witten did mention modifying the guidance, so Dr. Milford suggested the Council consider that mechanism. Mark McGinnis, JD, pointed out that revising guidance can take years, so it's not an immediately practical solution. He added that FDA will update the public docket at some point.

Ms. Hennessey said it was not clear what the fastest mechanism is to provide FDA with current data to inform new BLAs or modify existing licenses that can then be applied across the board. It was noted that licensing takes into account the safety of product manufacturing, whereas IND indications are considered in terms of efficacy. Dr. Harvath said the goal of the public docket was to make data available for individual reference in BLAs. She said Dr. Witten did not seem enthusiastic about efforts to get more data into the public docket. Dr. Harvath suggested writing to FDA, referencing the FDA advisory committee and the Council's discussion, and providing information gathered from registries and the literature on the efficacy of unrelated allogeneic cord blood transplantation. She said that in addition to the recommendations put forward by the Scientific Factors and Realizing the Potential Work Groups, the Council should work with HRSA staff and its Office of General Counsel to determine the best method for getting current data to FDA.

Dr. Harvath continued that it's still not clear how to address indications that are not specifically referenced in the guidance. Sending data directly to FDA may be easier and faster than seeking to include that data in the docket. A participant asked whether modification of an individual bank's license to include new indications would translate to approval of the new indication for all other licensed banks, but no response was provided.

Dr. Champlin said the Council should send its recommendations to broaden the indications in the guidance directly to FDA. Dr. Milford said the joint recommendations of the Scientific Factors and Realizing the Potential Work Groups had already been sent to the HHS Secretary in a letter, and Ms. Stroup pointed out that the Council makes recommendations directly to the Secretary, who then decides whether to pass them on to specific HHS agencies.

Dr. Harvath said that from her experience working at FDA, the more data the community can provide, the better. Data published in respected, peer-reviewed journals are most welcome. Dr. Harvath said it's critical to work with CIBMTR on data analysis, because CIBMTR has tremendous data resources. She noted that information is needed particularly from investigators treating hemoglobinopathies, including SCD, with CBUs from unrelated allogeneic donors. FDA is receptive to data that are published or thoughtfully collected from registries. Dr. Harvath urged the Council to include in any correspondence to FDA the need to broaden the indications for licensing and to include data.

Dr. Rubinstein said that many members of the FDA advisory committee that reviewed his organization's BLA were unhappy that data were left out. He felt their recommendation to broaden the indications for the license was based on new data beyond that used by FDA for the review. Thus, FDA is aware of new data, said Dr. Rubinstein, but it was not clear from Dr. Witten how that data weighs into FDA's decisions.

Jeffrey Schriber, MD, hoped that the Council's recommendations would highlight the issue of rare, or orphan, diseases. He asked that the recommendation state that if FDA approves an indication for one source (i.e., bank), all sources should have the same approval. Dr. Kurtzberg noted that FDA seems reluctant to include metabolic diseases as a broad category of indications, which would capture rare indications. Dr. Champlin said the Access to Transplantation Work Group has included cell source and donor selection in a recommendation that it will put forth.

There was general consensus that no new recommendations are needed. Dr. Harvath added that the recommendations will have more weight if they are supported by data.

Adverse Event Reporting

Willis Navarro, MD, NMDP

Dr. Navarro said that adverse event reporting and product complaint forms became available online on October 1, and the adverse event follow-up form went online on October 13, so both items were available through the FormsNet system ahead of the October 20 deadline for CBU licensure. Dr. Navarro emphasized that the system accepts reporting from any source in the CBU transplant community, regardless of its relationship with NMDP. The reporting timeframes were conveyed to all of the transplant centers, but NMDP can expedite reporting if it becomes aware of an event that meets FDA's adverse event criteria. Dr. Navarro noted that a serious adverse event that occurs in relationship to a transplant but is not caused by CBUs will be submitted to FDA through annual reporting. The system enables near-real-time reporting; information on reportable events goes directly to the FDA if the bank is licensed or to the IND holder, allowing adequate time to report adverse events to FDA as required.

NMDP will investigate and report on adverse events and product complaints for all NMDP facilities; for others, NMDP will pass the information on to the appropriate stakeholder. By collecting basic information on adverse events from all sources, NMDP is building a database that will facilitate monitoring of trends and allow NMDP to alert stakeholders to potential signals.

Dr. Navarro said NMDP continues to educate stakeholders about reporting roles, primarily through meetings and webinars. Webinars are available at marrow.org. NMDP plans to launch adverse event and product complaint forms for marrow, peripheral blood stem cells, and therapeutic cells as early as February 2012. Since the system launched, NMDP has received no adverse event reports, three reports of product deviation, and one product complaint, which Dr. Navarro said demonstrates that the system is functioning as intended.

Discussion
Dr. Navarro emphasized that NMDP will maintain files locally on adverse events that occur at facilities not related to NMDP. If potential safety signals are identified, NMDP will follow up, as it did when cardiomyopathy issues arose about one and a half years ago. Dr. Navarro added that, through FormsNet, NMDP collects cell dose, viability, and thaw data.

Access to Transplantation Work Group Report: Update on Technical Expert Panel: Insurance Guidelines/Covered Diagnoses and Costs
Richard Champlin, MD
Dr. Champlin said the Work Group is making progress on a document that summarizes the indications for HSCT, with the goal of supporting access for patients. The draft is circulating to Work Group members and other experts in the field for input. The document should serve as guidance to insurers, physicians, and patients about appropriate and inappropriate indications for HSCT; it is hoped that insurers in particular will refer to the comprehensive list of indications for HSCT in making coverage decisions. The document addresses logistic issues, such as timely insurance authorization to allow for treatment and the importance of clinical trial access to advance knowledge in the field. It will include data describing growth and changes in transplantation.

Dr. Champlin said the Work Group seeks to finalize the document with input from within and outside the group and to ensure that it is scientifically accurate. It categorizes indications as either “standard of care,” “consider,” or “generally not recommended” and recognizes that the field changes rapidly.

The document draws on consensus lists developed by other entities but provides more detail on uncommon genetic and nonmalignant diseases. It will also establish general principles regarding cell source and donor selection. Specifically it states that bone marrow, peripheral blood, and umbilical cord blood are all effective cell sources, and coverage policies should not restrict use of any of these cell sources. Similarly, the draft document states that matched related, related haploidentical transplants, unrelated donor transplants, and cord blood transplants are all effective, and coverage policies should not restrict use of any of these donor sources.

The Work Group needs assistance from HRSA to broaden the list of nonmalignant indications for HSCT, particularly to gather critical references to support HSCT for rare disorders. For both malignant and nonmalignant indications, the document will group indications by the type of disorder and indicates the category (“standard of care,” “consider,” or “generally not recommended”) for both allogeneic and autologous sources.

Dr. Champlin said physicians disagree about some issues, so the Work Group hopes to reach consensus about when transplantation should be considered, even if it's only appropriate for some patients. Eventually, the Work Group will hold a face-to-face meeting to hammer out the final document following input from a wide circle of stakeholders, including Council members. Dr. Champlin hoped Council members would provide him with suggestions for the document.

Discussion
Dr. Milford asked how the document might be used in light of the discussion about FDA indications. Dr. Champlin said the Work Group has discussed publishing the document and making it broadly available. One fundamental goal is to frame the document as a formal recommendation to the medical community. Once it's published, the Work Group can seek to have it included in the public docket. Susan K. Stewart suggested the document address the cost-benefit of transplantation when compared with medical therapy, because coverage decisions are sometimes made by employers, not insurers, on the basis of cost. Dr. Champlin said the document may discuss cost-benefit briefly, noting that in general, curing a disease with one outlay of money is less expensive than a lifetime of treatment. Ms. Stewart asked that the document emphasize that the treatment decision is not whether to use transplantation or not but rather weighing transplantation against long-term treatment.

Clive O. Callender, MD, DSc, said the document does not address access to cord blood for minority populations that can't afford it. Dr. Champlin responded that the document supports the use of cord blood, which can be a better option for minority patients who don't have a matched donor. He said cost is a big obstacle to transplantation in socioeconomically deprived areas, and he agreed that access is important. Dr. Callender said he was more concerned about the cost to minority populations of donating cord blood. Mr. Baitty said NCBI is making progress toward its diversity goals, although efforts are limited by the resources available to banks to collect and store CBUs. He clarified that donors incur no costs when they donate to public banks. Dr. Callender said minority communities need more information about donating and the distinction between public and private banks, and Mr. Baitty agreed.

Unmet Need
Jeffrey W. Chell, MD, NMDP
Dr. Chell pointed out that transplants have increased, but questions remain as to whether access has improved. NMDP facilitates more transplants every year, said Dr. Chell, but has demand grown faster and, therefore, access to transplants declined as a percentage of need? The short answer is that we have improved access in real terms, he said.

Recent analysis of need confirms that the NMDP goal of facilitating 10,000 transplants per year by 2015 is an appropriate goal consistent with data from CIBMTR and others. Real progress can be seen in the increase in transplants among racial/ethnic minorities and in older adults. NMDP drilled down into the data to assess relative access to transplantation, first by identifying need by ethnicity, then by breaking down access to each step in the process.

In 2010, 79% of African Americans in need of transplantation received a preliminary search, up from 50% in 2004. Access at the preliminary stage has improved for African Americans and for Asian Americans, said Dr. Chell, but not for Hispanics. (He noted that data collection methods

may affect the data for Hispanics.) The number of African Americans who successfully progress to the next step, formal activation of the transplant process, is lower than the number of Asian Americans, Hispanics, or Whites who do so, partly because of a lack of suitable sources. The same holds true for actual transplantation. Dr. Chell noted that Whites and Asian Americans are fairly close in their progress from preliminary search to transplantation.

Dr. Chell noted that transplant centers collect ethnicity data differently than collection centers do, which poses a challenge to data analysis, and efforts should be made to improve the consistency of collection of ethnicity data. The data indicate, however, that while initial access to transplantation has improved, more work remains to meet the transplantation needs of African Americans in particular.

Over the past decade, the number of transplants among people 51 years of age and older has increased dramatically. There has been incremental growth in the number of transplants across all age groups and a 4.5-fold increase in the number of transplants among minority patients. In the next decade, Dr. Chell predicted, we will see increased application of transplants for SCD. (If 10% of SCD patients would benefit from a transplant, that translates to 700 transplants per year, he noted.) Furthermore, we may see increased use of transplants for autoimmune disorders as transplant mortality and morbidity improves. The use of non-hematopoietic and immune reconstitution may increase, as will autologous and cord blood transplants.

On the other hand, over the next decade, the success of haploidentical transplants, novel therapies, health care rationing, and declining reimbursement for transplants all may contribute to a decrease in need for transplants.

Dr. Chell concluded that:

- access to transplants has improved over the last decade,
- data for Hispanics and people of multiple ethnicities are not complete,
- Caucasian transplants are likely overstated, and
- NMDP's approach to collecting ethnicity data needs to be more consistent between donor and recipient and offer more precise characterization (work is underway to implement new methodology in 2012).

NMDP validates its research findings through site visits to transplant centers. In fiscal year (FY) 2011, NMDP visited 32 transplant centers and found that most were expanding their operations, thus growing the system's capacity for allogeneic transplants. Various barriers to transplantation were identified at the sites, such as missed or delayed referrals for transplantation, market competition, and concerns about the implications of treating high-risk patients, because poor outcomes might affect insurers' decisions about the transplant center.

NMDP polled transplant center administrators and found that the top three barriers to transplant were insurance, comorbidity, and availability of temporary housing near the transplant center. The administrators identified staffing challenges across all clinical areas. Barriers to program growth were lack of space, lack of providers, external competition, reimbursement, lack of capital, internal competition, and, finally lack of patients.

Efforts to grow transplantation programs must identify the unmet need in the area to make the case for expansion. To address the issue, NMDP's bioinformatics department is mapping markets using U.S. Census and Survey Epidemiology and End Results (SEER) data to identify underserved markets. For a given geographic market, unmet need (or market potential) is defined as the demand for transplants minus the actual number of transplants.

Dr. Chell demonstrated the mapping project for two areas, Chicago and Miami. The process calculates a specific number for unmet need, and transplant center administrators can use that data to make the case for growing capacity in their areas. Dr. Chell said NMDP is analyzing data from all the markets now and will validate its findings with site visits in 2012. Additional data will help refine the model. In conclusion, Dr. Chell presented projections of the ethnic makeup of the United States in 2050; as Asian Americans, Hispanics, and people of multiple ethnicities make up a larger proportion of the population, matching challenges may become more significant, he said.

Discussion
Dr. Chell clarified that the model's definition of unmet need was intentionally broad and did not take into account a patient's ability to pay. He agreed that geography has an impact, and future modeling can look more closely at patients' zip code data to determine just how big a role geographic location plays in getting a transplant. NMDP is also evaluating best practices for housing transplant patients and their families, such as the Cities of Hope program.

Ms. Stewart said an assessment of unmet need should include long-term survival and management of comorbidities. Dr. Chell said NMDP is working to educate physicians about optimal timing of referrals to improve outcomes and management of post-transplant morbidity.

Dr. Milford wondered whether different strategies are needed to address the underserved. Dr. Chell said NMDP is trying to get a better picture of some of the barriers to transplantation. For example, homeless people are unlikely to receive transplants, because the health care system lacks mechanisms to deal with people who have no house and no caregiver. Dr. Chell said the lack of a transplant source is not the biggest barrier to transplantation.

To determine the effect that physician skepticism about transplantation has on access, NMDP conducted a survey comparing "believers" with "nonbelievers." The groups had very different patterns of referrals, said Dr. Chell. The nonbelievers tended to refer patients late in the course of disease, and as a result, those patients tended to have bad outcomes or insurance denials, which reinforced the nonbelievers' perception that transplantation is not effective or feasible.

Claudio Anasetti, MD, said the World Health Organization published data on geographic barriers to transplantation around the world. He and his colleagues used that data to support their request to grow their transplant center, and he believed NMDP's mapping project would provide similarly useful data for others who want to expand, especially for identifying underserved areas.

Discussion of Recommendations

In response to Dr. Hurley's request regarding new FDA regulation of laboratory-defined tests, Dr. Milford proposed that the Council modify the language of an ACOT recommendation to the Secretary asking that FDA recognize and accept the review of laboratory-developed testing performed in CLIA-certified, high-complexity histocompatibility laboratories. Participants discussed the ramifications of FDA's regulations, noting that suppliers of reagents would be banned from selling reagents to those laboratories that use their own validated in-house tests, which most laboratories do. Dennis A. Gastineau, MD, said there is a push in his institution to eliminate testing in laboratories as a risk management approach. A participant said the FDA regulation would drive academics out of testing altogether.

Dr. Milford pointed out that CLIA states explicitly that laboratories can generate their own tests if they are validated by an external organization. Members agreed that the current CLIA regulations seem to be workable. Participants then discussed adapting the background/rationale that was used to support the ACOT recommendations as a rationale for a Council recommendation. Council members voted unanimously in favor of the following:

Recommendation to the Secretary
The Council recommends to the Secretary that FDA recognize and accept laboratory-developed testing performed in CLIA-certified, high-complexity histocompatibility laboratories.

Action Item
HRSA staff will revise the ACOT background/rationale to be consistent with the ACBSCT charge and include it with the recommendation to the Secretary.

The Council reviewed revisions to the joint recommendations (numbered 1–3) of the Scientific Factors and Realizing the Potential Work Groups with some additional revisions. Council members voted unanimously in favor of the following:

Recommendations to the Secretary
Recommendation :The Council recommends that FDA broaden the IND and 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. This would allow licensed CBUs and CBUs distributed under IND to be used according to appropriate transplant patient and donor selection that occurs as part of the practice of transplantation medicine and would avoid the need to update lists for indications in this rapidly evolving field.

Recommendation : The Council recommends that all cord blood products have the same IND and BLA clinical indications; this is scientifically and medically sound.

Recommendation : The Council recommends implementation of a transition plan, initially stated as on or before October 20, 2011, to allow time for the FDA to review recommendations 1 and 2 above and to allow for implementation of any changes by transplant centers who will need to put these changes through their IRBs. During this transition period, the FDA can continue to exercise regulatory discretion for patients in

need of a cord blood donor for transplantation. This would result in less disruption of medical care and will not limit access to cord blood transplants.

Regarding remote CBU collection kits, members discussed the need to emphasize that some pregnant women are motivated to donate CBUs and have no mechanism for doing so other than the collection kits. It was noted that obstetric units and birthing hospitals also use the kits. As originally written, the recommendation excludes FDA licensure. Council members voted unanimously in favor of the following:

> **Recommendation to the Secretary**
> The Council recommends that CBUs collected through distribution of kits sent to motivated maternal donors or obstetrical units collected by an obstetric provider, which meet all NCBI/FDA qualifications be eligible for listing on the NCBI and for FDA licensure.

Government Accountability Office (GAO) Study Results
Randy Gale, HRSA
Mr. Gale summarized some of the methodology and key findings from the GAO's October 2011 report, *National Cord Blood Inventory: Practices for Increasing Availability for Transplants and Related Challenges*, which was required as part of Congress' reauthorization of NCBI. (The report is available online at http://www.gao.gov/products/GAO-12-23.) In addition to reviewing quantitative data from numerous sources and qualitative analysis of relevant recommendations and guidance documents, GAO conducted interviews with key stakeholders, including representatives from HRSA, FDA, NMDP, and all 13 NCBI banks. GAO staff also attended the NMDP's Cord Blood Sustainability Summit and reviewed the literature.

The report compares the racial/ethnic composition of units in the NCBI with those in the NMDP registry and finds that NCBI is more diverse in some respects. For example, CBUs from African Americans make up 14% of the NCBI compared with 6% of the NMDP registry. Similarly, CBUs from Caucasian Hispanics make up 30% of the NCBI compared with 10% of the NMDP registry. However, for marrow, African Americans account for 10% of the units in both the NCBI and the NMDP registry. Data show that since 2007, the number and percentage of total NCBI cord blood shipments have grown, and in the first half of 2011, NCBI unit distribution outnumbered non-NCBI distribution.

NCBI banks identified successful practices to increase collections at existing sites (such as longer hours) but noted that resource limitations are a barrier. To increase the number of new collection sites, banks suggested working with hospitals to identify target demographic groups and partnering with advocacy groups to broaden participation. However, resource limitations also affect new sites. Some banks use targeted outreach and recruitment efforts to increase the diversity of units collected—for example, by hiring bilingual collectors. The report also discusses the use of remote CBU collection to build up the inventory.

The report notes the slowing rate of growth in world demand for cord blood but does not address the growing demand for cord blood among racial/ethnic minorities in the United States, which

has increased access for those who have traditionally had more difficulty finding an adequate donor.

To reduce costs, some banks are carefully prescreening CBUs so only the largest units are processed and stored. Others have raised the minimum preprocessing TNC thresholds, but this practice may reduce genetic diversity, because banks must overcollect from some minority groups to meet the minimum threshold. Other efforts to reduce costs include processing and storing blood for family banks and collaborating with neighboring States to open new collection sites. Mr. Gale said banks expressed uncertainty about the impact of new FDA licensing regulations on public cord blood bank costs. Bank representatives felt it was unclear whether lifting cost recovery restrictions for units distributed under a license will adequately compensate for increased regulatory expenses, said Mr. Gale.

The report concludes with a high-level summary of where NCBI stands, with HRSA having contracted for 30% of the minimum inventory goal through the end of FY 2010. The report finds that the NCBI contributes to the genetic diversity of the U.S. public cord blood inventory, and continuing to expand the size and increase the diversity of the NCBI will reduce, but not completely eliminate, disparity in access to suitable cord blood units for transplantation. The future demand for cord blood is uncertain and may be influenced by technologic and scientific breakthroughs as well as the changing financial climate for CBU use and transplantation.

The report makes no recommendations for changing how HRSA administers the NCBI, how NCBI funds are distributed, or activities and actions undertaken by NCBI banks. Mr. Gale said the report should serve as a useful resource for banks, Congress, and the general public.

New Business: Continuation of Working Groups and Work Plan, New Working Groups
Patricia A. Stroup, MBA, MPA, Executive Secretary
Ms. Stroup suggested the Council annually review the status of work groups to determine whether they are still needed and what they should address in the future.

> **Action Item**
> At the next Council meeting, Work Group chairs should be prepared to discuss the status and future of their Work Groups.

Public Comments
There were no public comments.

Adjournment
Dr. Milford adjourned the meeting at approximately 3:50 p.m.

Attachment 1

ADVISORY COUNCIL ON BLOOD STEM CELL TRANSPLANTATION

Summary of Recommendations and Action Items
November 8, 2011

RECOMMENDATIONS TO THE SECRETARY

Laboratory-Developed Testing

The Council recommends to the Secretary that the U.S. Food and Drug Administration (FDA) recognize and accept laboratory-developed testing performed in Clinical Laboratory Improvement Act (CLIA)-certified, high-complexity histocompatibility laboratories.

FDA Guidance for Industry, *Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution for Specified Indications.*

Recommendation : The Council recommends that FDA broaden the investigational new drug (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 hematopoietic stem cell transplantation (HSCT) is the appropriate approach to treatment. This would allow licensed cord blood units (CBUs) and CBUs distributed under IND to be used according to appropriate transplant patient and donor selection that occurs as part of the practice of transplantation medicine and would avoid the need to update lists for indications in this rapidly evolving field.

Recommendation : The Council recommends that all cord blood products have the same IND and BLA clinical indications; this is scientifically and medically sound.

Recommendation : The Council recommends implementation of a transition plan, initially stated as on or before October 20, 2011, to allow time for the FDA to review recommendations 1 and 2 above and to allow for implementation of any changes by transplant centers who will need to put these changes through their institutional review boards. During this transition period, the FDA can continue to exercise regulatory discretion for patients in need of a cord blood donor for transplantation. This would result in less disruption of medical care and will not limit access to cord blood transplants.

Remote CBU Collection Kits

The Council recommends that CBUs collected through distribution of kits sent to motivated maternal donors or obstetrical units collected by an obstetric provider, which meet all National Cord Blood Inventory (NCBI)/FDA qualifications be eligible for listing on the NCBI and for FDA licensure.

ACTION ITEMS

The Council will establish the Work Group on Advancing HSCT for Hemoglobinopathies, with the following charge:

> The Work Group will identify important gaps, including barriers to transplantation, and opportunities to more fully realize the potential of HSCT for individuals with hemoglobinopathies (sickle cell disease and the thalassemias). The Work Group will submit for consideration and adoption by the Advisory Council recommendations regarding high priority actions. The Work Group should involve in its work experts in related fields, including as needed experts who are not members of the Advisory Council. The Work Group should present a status report, and any recommendations developed by that time, at the next meeting of the Advisory Council.

Council members should submit to Drs. Milford and Harvath their recommendations on who should chair the new work group and suggest potential members.

The Cord Blood Thawing and Washing Work Group will review the list of transplant center activities that it proposed with the May 2011 recommendation and consider how to address transplant center reporting requirements.

Ms. Regan will provide an update on the progress of the Cord Blood Thawing and Washing Work Group white paper on thawing and washing methods at the next Council meeting.

HRSA staff will revise the Advisory Committee on Organ Transplantation background/rationale to be consistent with the ACBSCT charge and include it with the recommendation to the Secretary that FDA recognize and accept laboratory-developed testing performed in CLIA-certified, high-complexity histocompatibility laboratories.

At the next Council meeting, Work Group chairs should be prepared to discuss the status and future of their Work Groups.