

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

Virtual Meeting

**May 16, 2013**

**Welcome and Introductions**

Edgar Milford, Jr., MD, ACBSCT Chair, called the meeting to order at approximately 10:00 a.m. and welcomed the Council members and participants to the first meeting of 2013. Patricia A. Stroup, MBA, MPA, Executive Secretary of the Council, introduced the new members of the Council: Andrew D. Campbell, MD; Joanie Y. Hare, MD; Thomas H. Price, MD; and Mark C. Walters, MD. Council members Edgar Milford, M.D.; Richard P. McQuellon, PhD, and Stephen Sprague have had their terms extended. (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.)

**Special Government Employees (SGEs) Serving on Advisory Committees**

*Laura Ridder, Ethics Advisor, Health Resources and Services Administration (HRSA)*

Ms. Ridder explained that, as SGEs, the Council members are required to file financial disclosure information and complete a questionnaire about their foreign activities. Financial conflicts of interest (COIs) can be a criminal offense and may apply to participation in Council decision-making and recommendations. Ms. Ridder urged Council members to be aware of potential COIs and recognize that a spouse's or dependent's job or holdings could introduce a COI. Similarly, the appearance of loss of impartiality is also a concern, and may include, for example, a relationship with a business partner that raises questions about impartiality.

Federal statute distinguishes matters of broad policy from those issues that affect a discrete class or specific parties. Federal agencies can obtain waivers for SGEs to allow them to continue working without violating statute. In such cases, the agency determines whether the need for the SGE's participation outweighs potential COI concerns or questions about the appearance of impartiality. Other methods for resolving COIs or questions about the appearance of impartiality include recusal or disqualification from a given area of discussion, divestiture of the financial interest in question, resignation from the position, and regulatory exemptions. Ms. Ridder emphasized that SGEs should contact their designated Federal official (DFO) if they have any questions about potential COIs or appearances of impartiality. The penalties for violating COI rules include imprisonment, fines, civil action, and removal from the position of service.

Ms. Ridder noted that SGEs may not receive compensation for representational services or act as agent or attorney for any other party before any Federal agency/court for any specific party matter that the SGE personally and substantially worked on. She added that representation includes meetings, phone calls, and email exchanges.

Like other Federal employees, SGEs may not receive compensation for teaching, speaking, or writing about matters that relate to their official duties (in this case, the work of the Council).

Ms. Ridder advised Council members to contact their DFO if they are invited to teach, speak, or write on the basis of their Council membership or if an invitation comes from a source that would be substantially affected by the member's official duties with the Council.

Ms. Ridder described the misuse of position, i.e., using public office for private gain, personal fundraising, or disclosing non-public information. She emphasized that an SGE may not imply that HHS or the Council endorses the SGE's private work. Also, SGEs also may not accept gifts related to their service. Ms. Ridder again urged Council members to contact their DFO with any questions about potential misuse of position or gift concerns. She also suggested Council members contact their own professional organizations to learn about ethical guidelines around gifts in their other professional roles.

While full-time Federal employees may never be involved in political fundraising, the Hatch Act permits SGEs to do so when they are not performing government business. SGEs may not conduct any political fundraising in any Federal workplace.

Finally, after completing their terms, there is a lifetime ban on SGEs representing anyone else before a Federal court or agency in a specific party matter that the SGE worked on while with the government and a 2-year ban when such matters were under the SGE's "official responsibility," said Ms. Ridder. She noted that Council members may contact the HRSA Ethics Advisor any time, even after they leave the Council, to discuss concerns.

#### *Discussion*

Asked how the regulations affect teaching or speaking overseas, Ms. Ridder noted that HRSA evaluates the foreign activity questionnaire that SGEs fill out when they begin their terms. Some engagements are permitted, others are not; Ms. Ridder suggested contacting the DFO for any overseas work, even if it is just a one-time event, to ensure it is within the boundaries of the law.

Ms. Ridder clarified that the 2-year post-employment ban applies to matters that were pending or under discussion while serving as an SGE and that the lifetime and 2-year bans refer to specific party matters (e.g., grants, contracts), not general matters such as policy decisions. Dr. Milford commented that the presentation raised many fears, and Ms. Ridder again urged Council members to contact their DFO in advance if they have any concerns to avoid violating the law.

#### **Program Report**

*Shelley Grant, MHSA, Chief, Blood Stem Cell Transplantation Branch, Division of Transplantation, HRSA*

Ms. Grant provided an overview of the C. W. Bill Young Cell Transplantation Program (a.k.a. the Program). She explained that HRSA awarded new contracts in late 2012 to support the Program to several cord blood banks, the National Marrow Donor Program (NMDP), and the Center for International Blood and Marrow Transplant Research (CIBMTR). The NMDP operates the most public interface of the Program, the Office of Patient Advocacy/Single Point of Access, which provides information to individuals about blood cell transplantation.

Ms. Grant described the roles of HRSA's Division of Transplantation, its contractors, other external organizations, and the Council in relation to the Program. The Program's registry has

about 10.5 million potential adult donors, of which 28% come from minority populations. In fiscal year (FY) 2012, the registry added more than 500,000 potential adult donors, of whom 47% identified as a racial/ethnic minority. The total number of cord blood units (CBUs) available through 2012 exceeded 163,000. Overall, transplants increased 4.7% from FY 2011 to FY 2012, and transplants for minority patients increased 6.9%. One-year post-transplant survival rates have increased significantly over the past 10 years. Ms. Grant said the figures demonstrate that the research community and others are working together to improve lives.

The National Cord Blood Inventory (NCBI) seeks to build a genetically and ethnically diverse inventory of 150,000 new, high-quality units for transplantation and make them available through the Program. In FY 2012, over 53,000 units were available. Of those, 714 were distributed for transplantation (3.5% more than in 2011), and over 27,000 were distributed for research. Ms. Grant praised the field for progress in informing pregnant women about their options for donating CBUs. She presented a breakdown of the units collected by race/ethnicity of the donors and the funding distributed by HRSA to support collection.

Ms. Grant said the Program and the NCBI face continuing challenges in identifying the barriers to transplantation and meeting the annual needs, recruiting enough adult units and CBUs of sufficient diversity, banking units of sufficient diversity and size, supporting and providing incentives to banks to increase inventory, ensuring adequate Federal funding, and finding the right balance in using Federal funds. Funding has remained steady for the past few years. The proposed budget for FY 2013 would freeze NCBI funding at \$11.8 million and Program funding at \$23.3 million.

For the remainder of FY 2013, priorities include monitoring contractor performance and focusing on use of available funds with a special emphasis on expanding cord blood activity. The website FedBizOpps (<https://www.fbo.gov/>) will soon release a request for information (RFI) about the NCBI's activities to gather public comments and spur organizations to propose demonstrations or outreach programs to increase collection and diversity of CBUs.

Having exceeded all of the goals originally set for 2010 (doubling the number of transplants and improving patient survival), the Program is finalizing its goals for 2020. The new goals will emphasize annual growth in overall transplants, transplants for minorities, domestic transplants, and the size of the registry. They also aim for improved 1-year survival rates in new subsets of recipients, such as older people.

#### *Discussion*

At the request of a Council member, Ms. Grant said she would provide data on transplants by indication.

#### **Action Item**

Ms. Grant will provide the Council with data on transplants by indication.

In response to a Council member, Ms. Grant explained that when the first contracts for CBU collection were awarded in 2006, the NCBI started at zero, although other banks were collecting CBUs and making them available through the program. The 53,000 units represent CBUs

available through the 13 NCBI-based contractors. The 163,000 units include those units plus units collected by other banks not participating in the NCBI. Ms. Grant later added that some overseas networks are members of the NMDP, but all 13 cord blood bank contractors are based in the United States.

Answering a Council member, Ms. Grant said the Office of Patient Advocacy and the CIBMTR are looking beyond 1-year survival rates to consider quality of life. Ms. Grant said the efforts underway further demonstrate how members of the transplant community are working together.

Asked about NCBI targets and how the NCBI negotiates reimbursement, Ms. Grant said that targets are based on the level of Federal funding available and the cost per unit negotiated with the banks. In the past few years, under current prices, banks have collected and made available through the NCBI about 9,000 CBUs per year. Every few years, HRSA renegotiates those totals with the banks.

Ms. Grant noted that the RFI is in the clearance process. When it is ready for release, HRSA will post a notice on its website, <http://bloodcell.transplant.hrsa.gov/>. It will also be posted on FedBizOpps (<https://www.fbo.gov/>), and interested parties will receive email notification.

**Analyzing the Threshold for Total Nucleated Cell Concentration (TNCC) for NCBI CBUs**  
*Overview of Combined Work Group Call: Realizing the Potential of Cord Blood and Scientific Factors Necessary to Define Cord Blood Units as High-Quality Units*

Liana Harvath, PhD, Chair, Realizing the Potential of Cord Blood Work Group, and  
Joanne Kurtzberg, MD, Chair, Scientific Factors Necessary to Define Cord Blood Units  
as High-Quality Units Work Group

Dr. Harvath reviewed the purpose, activities, and membership of both the Realizing the Potential of Cord Blood Work Group and the Scientific Factors Necessary to Define Cord Blood Units as High-Quality Units Work Group. The Work Groups met jointly via teleconference in April 2013 to analyze the results of CIBMTR data and consider whether the TNCC threshold for NCBI CBUs should be increased from  $90 \times 10^7$  to  $125 \times 10^7$ .

In previous ACBSCT meetings, concerns have been raised that the large inventory of CBUs with TNCC between  $90 \times 10^7$  and  $125 \times 10^7$  is underutilized. The Realizing the Potential Work Group has focused on financial aspects, while the Scientific Factors Work Group has addressed the quality of the units. Both Work Groups have concerns about raising the cutoff to  $125 \times 10^7$ . In the April call, the Work Groups discussed who would use the lower-concentration CBUs and whether the evidence supports increasing the threshold.

Dr. Kurtzberg presented a breakdown by age and race/ethnicity of the NMDP's distribution of CBUs with TNCC between  $90 \times 10^7$  and  $125 \times 10^7$  from 2008 to 2011. The percentages of use range from 39–50% for children ages 0 through 8 years and drop into single digits for those over 16 years old.

Dr. Kurtzberg provided detail data from her organization's cord blood bank about mother-infant donor pairs in relation to birthweight and gestational age at birth. In addition, Dr. Kurtzberg's

data show that concentrations of total nucleated cells (TNCs), colony-forming units (CFUs), and CD34 differ between African Americans and Caucasians. African Americans have different adhesion properties, so when you collect liquid blood, you don't get as many cells from African Americans as from Caucasians, she said. Thus, to ensure diversity of the CBUs in the registry, we need to collect more from African Americans than Caucasians to get the same quality of material and proportions representative of the U.S. population, and the effort will cost more. Dr. Kurtzberg also showed that all the parameters of high-quality units are negatively affected by delays in the time from collection to processing (which may be an important consideration for new collection models, such as collection kits for remote settings). Finally, Dr. Kurtzberg suggested that if the criteria for CBU potency goes beyond TNCC, the combination of TNCC and CFUs would be a potential target for evaluating potency.

On the basis of the data and discussions, the Work Groups do not recommend increasing the lower TNCC limit to  $125 \times 10^7$  for the following reasons:

- CBUs with a TNCC between  $90 \times 10^7$  and  $125 \times 10^7$  are successfully used in pediatric and non-Caucasian recipients.
- The TNC, CFU, and CD34 concentrations are approximately 30% lower in CBUs collected from African American donors.
- Increasing the lower TNCC limit will result in the banking of fewer CBUs from African American donors.
- CBUs with a TNCC between  $90 \times 10^7$  and  $125 \times 10^7$  are currently used successfully in multi-CBU transplantation and in ex vivo expansion clinical trials. As these technologies develop, CBUs may become more widely used, particularly when the CBUs are from diverse donor populations with less common human leukocyte antigens (HLAs), enabling closer HLA matching.
- The CBU TNCC obtained from Caucasian donors is steadily increasing in the NCBI to more than  $125 \times 10^7$  because of business practices, and the higher TNCC CBUs are requested more frequently by transplant physicians.
- It is costly to collect and bank diverse minority CBUs in the NCBI because many more collections are needed to obtain eligible, high-quality units with an adequate TNCC.
- The NCBI needs to increase the number of minority donor CBUs with TNCC greater than  $125 \times 10^7$ .
- It is important to strategically and prospectively model collection strategies to increase the probability of banking high-TNCC, highly potent, and diverse CBUs in the NCBI.

The Work Groups agreed that the ratio between collected and frozen units is different for different ethnic/racial groups at any TNCC, and the reimbursement by HRSA should be consistent with those ratios. The proper ratios should be calculated by a committee of banks and HRSA representatives so that the results are as fair as possible.

Dr. Harvath proposed the following recommendation:

Cord blood banks receiving a NCBI contract administered by HRSA for collecting diverse, high-quality CBUs for transplantation are required to meet all Federal, State, and local regulatory requirements. The cord blood banks must also demonstrate progress

toward achieving financial self-sufficiency. To date, the individual cord blood bank contracts have provided a fixed rate of reimbursement per qualified unit added to the NCBI. This reimbursement subsidizes only a portion of the actual costs associated with donor recruitment, CBU collection and testing, CBU storage, and the distribution of units. Recognizing that there are finite funds available for the NCBI program, and in spite of the fact that a higher rate of reimbursement would reduce the speed at which HRSA is able to achieve its statutory goal of building an inventory of at least 150,000 new units of cord blood, the ACBSCT strongly recommends that HRSA reimburse contracted cord blood banks at a level that will allow the banks to cover the increased costs associated with meeting regulatory requirements while continuing to increase the genetic diversity of CBUs added to the NCBI. This will also assist the banks as they work to demonstrate progress toward achieving financial self-sufficiency.

### *Discussion*

Richard Champlin, MD, pointed out that outcomes are better with bigger units; therefore, we should increase screening and store more of the larger-TNCC units. More low-TNCC units would be discarded, but the result would be more large, diverse units. Dr. Kurtzberg said that for children, especially African American children with sickle cell disease (SCD), who are now candidates for CBU transplantation, discarding the smaller units would be a mistake, because they may be sufficient and offer a better HLA match. Further discussion of the recommendation was held until after the three scientific presentations scheduled.

### *The Promise of Expanded Cord Blood Progenitor Cells for Clinical Applications*

Colleen Delaney, MD, Fred Hutchinson Cancer Research Center, Seattle, WA

Dr. Delaney said that cord blood engineering could provide more opportunities to use units that are currently considered too small for transplants. Even among patients who receive double cord blood transplantation, recovery is slow; to improve efficacy of transplants and survival rates, we need novel methods to decrease the time to neutrophil recovery.

Dr. Delaney and colleagues are developing a method to expand cells *ex vivo* or increase the number of stem and progenitor cells available within a single CBU. The Notch ligand uses a protein that activates signaling pathways in the stem cells, which expands the number of progenitor cells available for transplant. The goal is to create a myeloid bridge for patients who take a long time to engraft. Clinical trials at multiple centers looked at the feasibility of locally manufacturing an expanded cord blood product and shipping it overnight to patients in need.

Dr. Delaney described the treatment schema in detail, noting that it is based on a double cord blood platform. The patients who received expanded cells with an unmanipulated graft saw neutrophil recovery at a median of 11 days, compared with 25 days for patients who received a double cord blood transplant (both with the same conditioning regimens). Thus, the expanded product successfully decreased neutrophil recovery time, and many of the subjects achieved engraftment earlier than the conventionally treated patients. However, the approach is neither commercially economical nor feasible, so Dr. Delaney and her colleagues have moved on to other work.

Through funding from the Biomedical Advanced Research and Development Authority (BARDA) for products to treat radiation exposure, Dr. Delaney and colleagues began working on a product for use as a universal donor. They work with public cord blood banks to obtain fresh units of any size, expand them, then cryopreserve them for future use. Good evidence suggests the product could potentially be used as a third-party donor product without regard to HLA matching, said Dr. Delaney.

Phase-II trials are now comparing standard cord blood transplant with and without the new product. Dr. Delaney described the treatment schema for the transplant trial and said the expanded product yielded a reduction in the time to neutrophil recovery, although not as dramatic a reduction as with the previous product. Comparing various protocols over time, Dr. Delaney noted, platelet engraftment has been encouraging regardless of which expanded cell product the patients received. Six centers are taking part in a phase-II randomized study to gather clinical data on hospital stays, infection rates, and other regimen-related toxicities. The universal donor cryopreserved product does have limitations, said Dr. Delaney. She and her colleagues hope to figure out a better manufacturing process that is less labor-intensive and also to address scalability.

*Strategies to Increase Cell Dosing for Unrelated Donor Cord Blood Transplantation*  
Joanne Kurtzberg, MD

Dr. Kurtzberg said two new pieces of information have emerged from studies that may influence the decision whether to increase the TNCC threshold for NCBI CBUs. First, the Blood and Marrow Transplant Clinical Trials Network (BMTCTN) 0501 randomized trial compared double with single umbilical cord blood transplantation in children with hematologic malignancies and found no survival advantage to using the double cord approach. Dr. Kurtzberg described the study design, treatment schema, preparation regimen, and other details. She pointed out that in both arms of the study, the greatest majority of subjects had an HLA matching grade of 4/6 or 5/6. The study results showed no significant differences between the double and single cord blood transplant groups in overall survival rates, neutrophil recovery times, non-relapse mortality rates, or relapse rates. In the single cord blood transplant group, platelet recovery times were better, and the incidence of grade III–IV acute graft-versus-host disease (GVHD) was lower.

Dr. Kurtzberg and colleagues compared the findings from the BMTCTN 0501 trial with those of the Cord Blood Transplantation (COBLT) study. The BMTCTN 0501 trial subjects had faster neutrophil recovery times, better platelet recovery times, lower rates of treatment-related mortality, and higher overall survival rates. In both survival and treatment-related mortality, Caucasians had a significant advantage over other ethnicities. Comparing the cell doses, Dr. Kurtzberg noted, those subjects receiving higher TNCC doses had a significant survival advantage over those who received lower doses.

Secondly, the promise of new technology, such as the Notch-mediated expansion described by Dr. Delaney and NiCord®, a different type of hematopoietic progenitor cell (HPC) expansion technology, may affect how we choose CBUs for transplantation. Dr. Kurtzberg and colleagues found that NiCord-expanded HPCs performed better than unmanipulated CBUs and prolonged

engraftment following double cord blood transplantation for high-risk leukemias. Another study is underway to assess NiCord for sickle cell anemia.

In response to BARDA's call for products to treat radiation injuries and exposure, Dr. Kurtzberg's team at Duke University developed CordBridge, a ready-to-use product stored in the cryopreserved state. CordBridge is the positive fraction only of the NiCord-expanded product, and it is produced from multiple CBUs. Studies demonstrated increased survival following high radiation exposure in mice that received expanded cells compared with controls. Dr. Kurtzberg and colleagues plan to examine the use of expanded single CBUs as proof of concept for CordBridge. If successful, they would test and mass-produce the CordBridge product. The technology makes use of multiple CBUs that are too small to bank.

*Cell Dose and HLA/U.S. Food and Drug Administration (FDA) Licensure Update*  
Andromachi Savaradou, MD

Dr. Savaradou pointed out that blood banks working with the NCBI must meet stringent Federal and State regulations. Those regulations have changed significantly in recent years, and banks have invested considerable time and resources to keep up. The HRSA subsidy covers a fraction of the costs that banks incur in collecting, manufacturing, and testing CBUs, but that subsidy is important revenue, Dr. Savaradou emphasized. For most banks, the subsidy is the only revenue banks collect other than transplant fees. At the same time, HRSA is encouraging banks to become financially self-sufficient.

The FDA's regulatory requirements make it clear that CBUs are biological products. According to the FDA's 2009 industry guidance, licensed products can be prescribed for specific indications; all other products, including CBUs, must be used under an investigational new drug (IND) protocol and require institutional review board approval. Dr. Savaradou said banks have undertaken a huge amount of work to submit applications to FDA for biologic licensure to comply with the new regulations. In addition to the intensive application process, banks will have to invest more resources in ongoing studies once they do receive licenses.

Dr. Savaradou described Hemacord, a product that was licensed by FDA for broad indications related to HPC transplantation procedures. The aim of seeking licensure is to ensure that all banked CBUs are of consistently high quality with reliable safety, purity, and potency to ensure maximum safety and efficacy for transplantation. The benefits of licensure to banks include regulatory oversight and guidance; inclusion in quality systems of manufacturing and testing; better monitoring of adverse events; and progress toward consistently safe, high-quality products. The transplant community benefits by improved access to high-quality products, translating to better safety and more patients benefitting from treatment. The challenges to licensure for banks are the substantially increased cost for the ongoing maintenance of licensure and increasing costs of manufacturing.

Dr. Savaradou noted that the FDA will not license existing products. Of the current inventory of 58,000 products, only 3,500 are licensed. Thus, banks are using their limited resources to submit license applications, increasing the cost of units substantially, and the number of licensed units is

only a fraction of the total. She concluded that any change in the HRSA subsidy affects the accumulation of new, licensed products and the financial stability and sustainability of the banks.

### *Discussion*

Dr. Milford clarified that because HRSA has a fixed budget for the NCBI, increasing the reimbursement rate for banks would mean that fewer units would be collected. Dr. Kurtzberg added that if the threshold for units were increased, the expense per unit banked would also increase, because banks would have to collect more just to achieve the required number of qualified units.

Dr. Harvath reiterated that HRSA's reimbursement rate subsidizes only a portion of the banks' costs. The proposed recommendation aims to give HRSA more flexibility to negotiate with banks individually and set rates based on individual banks' operating costs and fees associated with actual collection. Ms. Grant said that HRSA already has flexibility to negotiate with banks. In its requests for proposals, she said, HRSA has expressed its interest in discounts and does not anticipate funding the whole cost of collection. Rather, HRSA aims to allow for collection of as many units as possible. Ms. Grant said the proposed recommendation serves as a reminder that costs are going up, which may slow progress toward the collection goals. HRSA has been adding about 9,000 CBUs annually under the current appropriation, but Ms. Grant cautioned that funding decisions can change at any time.

In response to a Council member, Dr. Savaradou clarified that she is in favor of the recommendation. If subsidies are only provided for very large CBUs, she said, that would be a problem for banks.

Dr. Campbell asked whether the recommendation would significantly affect genetic diversity and whether there are other ways to increase diversity that do not affect the bottom line. Dr. Harvath said she believes that outreach for collecting from underrepresented ethnicities is extremely costly because more units must be collected and tested. Dr. Kurtzberg said that cell concentration varies significantly between African Americans and Caucasians, so it is necessary to collect 7–10 more units from African Americans compared with Caucasians to achieve the same quality. Increasing the threshold would decrease the number of CBUs from African Americans and further increase costs, she noted.

Dr. Milford asked whether the Work Groups have a recommendation to HRSA about how it should spend its fixed budget dollars. Dr. Kurtzberg said HRSA should consider other models that would help banks move forward. For example, HRSA could send money in advance to banks to set up collection sites, instead of paying 6–9 months after collection. Another option is offering higher reimbursement rates for units that cost more to procure, which would mean higher rates per unit and fewer units collected. Dr. Price said HRSA already offers a financial incentive by paying higher rates for units from minorities. He noted that Ms. Grant's presentation showed that HRSA has allocated more money than it is actually spending.

Ms. Grant reiterated that HRSA does have flexibility to negotiate with each bank. Also, government contracting typically involves reimbursement, not providing money up front, but HRSA is exploring other structures, and the upcoming RFI is one example. Ms. Grant added that

HRSA needs to address the broader question of informed consent for pregnant women. Dr. Milford noted that the proposed recommendation only addresses reimbursement, not alternative mechanisms for covering bank costs. Ms. Grant said the recommendation could be used as supporting documentation when HRSA has to report to Congress about the slowing progress toward meeting the goal of 150,000 units.

Dr. Milford tabled the recommendation and requested that the Work Groups revisit the issue.

**Action Item**

The Realizing the Potential of Cord Blood Work Group and the Scientific Factors Necessary to Define Cord Blood Units as High-Quality Units Work Group will talk with HRSA staff in more detail and present a revised recommendation at the next Council meeting regarding reimbursement for cord blood banks. HRSA and its contractor banks will discuss how to collect the maximum number of high-quality units with HRSA's limited funding.

**Advancing Hematopoietic Stem Cell Transplantation (HSCT) for Hemoglobinopathies: Work Group Report**

*Naynesh Kamani, MD, Chair*

Dr. Kamani reminded the Council that the Work Group was charged with identifying barriers to transplantation and opportunities to more fully realize its potential for treating SCD and thalassemia and making recommendations to address them. He pointed out that HSCT is the only curative therapy for children with SCD but is less frequently used than treatment with regular red blood cell (RBC) transfusions or hydroxyurea. Several clinical trials offer evidence that HSCT is associated with significant risk but also has very good outcomes and high rates of survival. The number of bone marrow transplants for SCD has been increasing dramatically since 2008, but HSCT is still underused for SCD, even when matched sibling donors are available.

The Work Group identified the following barriers to transplantation:

- Disease-related barriers
  - Heterogeneous nature of disease with lack of clinical/laboratory/genomic predictors of poor prognosis
- Patient/family barriers
  - Fear of transplant-related mortality and morbidity
  - Fear of risk of long-term complications (GVHD, infertility)
  - Comfort with transfusion programs for those with complications
  - Gaps in knowledge about natural history, progressive organ damage
  - Mistrust of medical professionals
- Health care provider barriers
  - Provider reluctance to recommend HSCT
  - Gaps in knowledge about role of HSCT
- Donor availability
  - Lack of matched sibling donors
  - Lack of well-matched unrelated donors for most patients
- Lack of insurance coverage (gaps in coverage have not been studied)

Dr. Kamani described some efforts underway to address these barriers. Of the more than 450 SCD trials reported to the website ClinicalTrials.gov, only 11% related to transplants, and fewer than half of those are currently recruiting. Of these, three are HSCT clinical trials for SCD funded by the National Institutes of Health (NIH); the rest are limited, investigator-initiated trials. Dr. Kamani also described the status of several studies underway regarding use of alternative donors. Finally, CIBMTR and NMDP are conducting focus groups to better understand patient, parent, and provider attitudes about participating in SCD clinical trials. The main barriers to participation are lack of access to information, misinformation about HSCT, lack of awareness of SCD complications, overestimation of the risks of HSCT, and distrust of medical professionals.

Furthermore, guidelines for the clinical management of SCD from NIH's National Heart, Lung, and Blood Institute (NHLBI) make little to no mention of HSCT as a potential therapy for SCD. In 2009, NHLBI established an expert panel to update the guidelines; that group has produced draft guidelines currently under review that still give little attention to HSCT.

The Work Group proposed the following recommendation:

Educational/outreach efforts should be made to the SCD patient and provider community to educate them about the progressive nature of SCD, increasing morbidity and mortality in early adulthood, and the role of HSCT and its complications.

Dr. Kamani suggested the Council further discuss ways to improve access to HSCT for SCD, such as studying and eliminating insurance barriers and increasing minority representation in volunteer donor registries and cord blood bank inventories.

Dr. Kamani also suggested the Council discuss how to update the NHLBI guidelines to include the option of HSCT for SCD and increase education of providers, patients, and parents about HSCT for SCD. The Council should discuss increasing NIH funding to identify predictors of poor prognosis that could facilitate early referral for HSCT and funding for more clinical trials to address knowledge gaps about HSCT for SCD.

#### *Discussion*

Jeffrey R. Schriber, MD, said we must overcome the disconnect between clinicians who address nonmalignant disease and those who address malignant disease. Doing so may also help with insurance issues, he added. He also emphasized that HSCT should be considered early in the course of disease, when patients are young, because it is likely to be more effective and less toxic. As the disease progresses, patients have more complications that affect treatment decisions.

Dr. Walters asked whether there are education or outreach initiatives underway to address the utilization gap. Ms. Grant said HRSA does not currently have educational materials developed about HSCT, but she offered to raise the issue with HRSA's Maternal and Child Health Bureau (MCHB) in the context of screening. Dr. Milford added that one of the Council's committees developed a list of indicators for HSCT that included hemoglobinopathies. That list was intended

for various Federal agencies, including NHLBI, which is charged with disseminating information about the appropriate indications for a given therapy. He asked how to move forward, using that list, to encourage more consideration of HSCT for SCD, and whether the Council should take that role.

Dr. Campbell pointed out that recent success with hydroxyurea to decrease morbidity and mortality of SCD may deter some families from considering HSCT for their young children. Other trials underway illustrate that the field of SCD is moving forward on treatment options, although, he said, HSCT remains the best chance for curing SCD. Robert Hartzman, MD, pointed out that only transplantation is curative and has the potential to eliminate the disease if performed early in life. Dr. Campbell said he believes in transplantation, but many practicing hematologists are balancing the procedure against the existing treatment options.

Regarding the suggestion to increase minority representation, Dr. Hartzman suggested focusing on African Americans, because they have so much more difficulty than other ethnicities finding donors. Dr. Schriber said that Arizona requires newborn screening for hemoglobinopathies. Linking those findings to cord blood banks could yield opportunities when searching for donors.

In response to questions raised by participants, Ms. Grant said that HRSA does work with private banks as well as public banks. Also, HRSA has a related cord blood demonstration project underway. Dr. Kamani asked whether HRSA has traditionally interacted with parent and patient SCD organizations, because the educational materials of these organizations generally do not mention transplantation and refer only to the future potential of gene therapy. Ms. Grant said HRSA is currently exploring options through the MCHB on how best to communicate and collaborate with patient and parent organizations.

In response to Dr. Milford, Dr. Kamani clarified that the recommendation about education and outreach is aimed at HRSA, not the Secretary, and that early adulthood refers to people between 16 and 35 years old. A participant noted that the MCHB supports newborn screening and followup for SCD and other conditions, so HRSA could incorporate education in that context. Ms. Grant said that, if passed, HRSA would act on the recommendation by reaching out to the MCHB first and then looking more broadly at how contractors could play a role.

The Council members voted unanimously in favor of the following recommendation:

**Recommendation to HRSA**

The Council recommends that HRSA undertake educational/outreach efforts to the SCD patient and provider community to educate them about the progressive nature of SCD, increasing morbidity and mortality in early adulthood (ages 16–35 years), and the role of HSCT and its complications.

**Action Item**

Dr. Milford requested that HRSA report back to the Council about its progress on educational/outreach efforts to the SCD patient and provider community.

Dr. Kamani said the NHLBI guidelines on SCD should have at least a section if not a separate subset of guidelines on the role of HSCT in SCD, because information is lacking in the current draft. Nancy L. DiFronzo, PhD, from the NHLBI pointed out that the guidelines are not intended for hematologists but rather for treating physicians who may not be familiar with SCD. Also, she said, the guidelines have been in development for several years and are very near completion, so amending them now probably is not an option. However, Dr. DiFronzo said, the Council could recommend developing guidelines for hematologists who treat SCD. Dr. Schriber said that if the guidelines are out of date, they should be updated, even if it's logistically problematic. Dr. Campbell agreed with Dr. Kamani that excluding transplantation from the discussion is shortchanging patients, parents, and providers. The other options (transfusion and hydroxyurea) are also provided by hematologists, he added. The appropriate role of transplantation should be addressed in the guidelines.

Dr. Walters said he wrote the section on HSCT in the 2002 edition of the NHLBI guidelines and had the opportunity to comment on the current draft. At present, transplantation is addressed in one sentence and is described as investigational. Thus, the Council appears to have a fundamental disagreement with the expert group that drafted the current version. Dr. DiFronzo said she could not get permission to review the draft at this point. She said she did not know how to give the Council any further guidance given the procedure for producing the guidelines.

Participants agreed that the Council should recommend to the Secretary that the expert panel should review the draft guidelines and ensure they include discussion of the role of HSCT as a curative option for SCD. Dr. Kamani and others agreed to draft a recommendation for consideration by the Council later in the meeting.

### **Current Thawing and Infusion Practice of Cryopreserved Cord Blood: The Impact on Graft Quality, Recipient Safety, and Transplantation Outcomes**

*Salem Akel, PhD, Scientific and Laboratory Director, Saint Louis Cord Blood Bank/Cellular Therapy Laboratory*

Dr. Akel described the results of his literature review on thawing and infusion practices, which sought to compare various methods and suggest an algorithm selecting thawing methods. Dr. Akel briefly gave a brief risk assessment and analysis for dimethyl sulfoxide (DMSO), plasma stored in citrate phosphate dextrose, synthetic colloids, ABO-incompatible RBCs, and free hemoglobin/RBC lysate.

Dr. Akel summarized the pros and cons of bedside thawing practices and various wash methods. Wash protocols vary from laboratory to laboratory and result in substantially different cell recoveries. To promote a more consistent, safe, and fast wash method, automated options were developed but are not commonly used or feasible in transplant centers. A consistent method would require use of a qualified centrifuge and classified biosafety cabinet, training and ongoing practice at the transplant center to maintain proficiency in aseptic techniques and thaw procedure, and pilot validation of the wash method at the transplant center (site specific) using practice units in the same product category and from the cord blood bank of origin.

The dilution/no wash method has been recommended by Dr. Akel's own organization, but data are insufficient to recommend it for RBC-replete products. It is more direct than the wash

method, but success still requires a controlled environment for preparation and sampling, a staff well-trained in aseptic techniques, and a site-specific pilot validation of the method using RBC-reduced practice units from the cord blood bank of origin.

On the basis of the literature review, Dr. Akel proposed an approach for selecting the thaw method but noted that the suggested protocols do not supersede the manufacturers' directions. The optimal thaw method should be determined on the basis of patient characteristics and product contents, including viable nucleated cell dose, DMSO dose, and amount of ABO-incompatible RBCs. The proposed algorithm addresses thawing as well as steps for dilution and washing. When finalized, it will include an appendix describing the equipment, reagents, and supplies needed as well as steps for receipt, verification, and thaw preparation.

Regarding the stability of thawed products and the optimal time to infusion, post-thaw stability studies support prolonged stability but not necessarily optimal cell survival; therefore, clinicians should not withhold infusions needlessly, Dr. Akel said. The time from thaw to infusion should be minimized as much as possible. The NMDP Cord Blood Advisory Board Group developed a list of considerations for thaw infusion practices. In response to these considerations, Dr. Akel noted that further studies by manufacturers are needed to validate blood filters. It must also be kept in mind that different products behave differently under different methods. Finally, the New York Blood Center proposes starting infusion at a slower rate than that suggested by the NMDP.

Dr. Akel said there appear to be no significant differences in adverse events that are linked to thaw methods, with one exception. One study showed that unwashed RBC-replete infusions had a higher incidence of hemoglobinuria, but no life-threatening reactions were reported. A review of adverse reactions revealed that 70% of cases involved RBC-replete units. It is still not clear whether adverse events are related to product content, thaw method, or practices, but Dr. Akel said that washing methods for RBC-replete units should be strongly considered. Finally, Dr. Akel said limited data show no significant differences in transplant outcomes in relation to thaw methods. An ongoing retrospective study by CIBMTR would provide more helpful data.

Dr. Akel recommended further consideration of quality assurance, documenting communication, individualizing the selection of methods on the basis of patient and other characteristics, and encouraging manufacturers to validate and communicate the best methods for thawing and infusing their products.

### *Discussion*

A participant wondered whether there are few data on the toxicity of DMSO because DMSO is not very toxic. Another responded that high doses of DMSO, used in earlier days, are toxic, so amounts used now are smaller. Dr. Milford asked whether licensed units are required to specify their method of thawing and infusion. Pablo Rubinstein, MD, said the FDA expects that manufacturers will suggest a particular method for infusion and processing after thawing and also expects that manufacturers will have a rationale for their recommendations.

Dr. Rubinstein continued that the methods used over the years all share some characteristics. There is some support for not doing anything and infusing just-thawed material. In general, however, most clinicians believe that the evidence for toxicity of DMSO, for example, is real and

that decisions are complicated by individual patient idiosyncrasies. He said many complex issues are at play, and the FDA does not support any one method as superior. Dr. Kurtzberg added that in applying for an FDA license, her organization was required to validate its procedures for thawing, and all licensed banks have submitted a procedure as part of their package insert.

Dr. Milford asked whether transplant centers use the method for thawing and administration dictated by the bank where the unit originated or their own methods. Dr. Rubinstein believed that transplant centers use the method recommended by the manufacturer. He stressed that all of the methods are similar and any one may be satisfactory as long as it is done systematically and correctly. Dr. Kurtzberg added that transplant centers are not required to follow the manufacturer's recommendation.

### **Overview of AABB's Standards and Accreditation Program**

*Jean Otter, Division Director, Programs*

Ms. Otter explained that the American Association of Blood Banks has become an international organization and is now known as AABB. The organization and its Center for Cellular Therapies address all aspects of operations and provide education, advocacy, and resources. AABB also provides standards and accreditation for cellular therapy services, blood bank and transfusion service, relationship testing, and reference laboratories, among others. It accredits facilities in the United States and around the world.

Ms. Otter described the process by which AABB develops standards (through a multidisciplinary group of experts), gathers public comment, and updates and publicizes the standards. AABB has processes for interim and emergent standards when events warrant attention or new information come to light.

Standards undergo a rigorous process of technical and legal reviews; they incorporate quality standards and salient international and Federal requirements and guidelines. The Standards Committee can provide clarification as needed and consider requests for variances to allow for innovative practices or regional regulations as long as quality and safety are maintained. The standards apply broadly to all cell therapy products, and the standards evolve as new products and therapies emerge. The new (6<sup>th</sup>) edition of the *Standards for Cellular Therapy* will cover clinical use of the products and patient care. It will also emphasize more outcomes data.

AABB's accreditation program is designed for regulated environments. The initial accreditation process takes 18–24 months, and renewal takes about 8 months. The process offers a systematic view of the organization's operations over time, not a single snapshot, and uses robust auditing techniques. AABB accreditation has deemed status with CMS and is coordinated with the College of American Pathologists. AABB is recognized by HRSA, the World Marrow Donor Association, and NMDP as one of two accrediting bodies for HPC collection centers and cord blood banks. Both the accreditation program and its assessor training are accredited by the International Society for Quality in Health Care.

The AABB accreditation program is periodically validated by both internal and external sources. Ms. Otter summarized various mechanisms for evaluating the assessors who conduct accreditation and for ensuring continuous improvement of the accreditation program and its

assessors. AABB maintains a rigorous COI policy and has a review committee to address concerns about an assessor or any aspect of accreditation. The committee's decisions can be appealed to the AABB Board.

For NCBI banks, assessors evaluate the bank's conformance to HRSA specifications using an HRSA assessment tool in addition to AABB auditing tools. An interim self-assessment is due within 1 year of the last on-site assessment and is reviewed by AABB professional staff. Summary reports are sent to HRSA within 30 days. AABB reports annually to HRSA about accreditation issues, program changes, the accreditation status of NCBI banks, and any other information requested by HRSA, Ms. Otter concluded.

### *Discussion*

Dr. Milford noted that the Council was charged with deciding early on which organizations would be allowed to accredit banks doing stem cell collection, and Ms. Otter's presentation gives a more thorough picture of what AABB is doing in that regard. Ms. Stroup said AABB is working closely with Council member Jeffrey McCullough, MD, who chairs the Cord Blood Thawing and Washing Work Group. At an upcoming meeting, the Council will hear a presentation from the Foundation for the Accreditation of Cellular Therapy, said Ms. Stroup.

### **Recommendation of the Advancing HSCT for Hemoglobinopathies Work Group**

Dr. Kamani presented a revised recommendation for consideration. The Council members voted unanimously in favor of the following recommendation:

#### **Recommendation to the Secretary**

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

### **Cell Therapy Data Collection Work Group Report**

*Claudio Anasetti, MD*

At a previous ACBSCT meeting, participants discussed the lack of participation in data collection efforts by entities that are pursuing cell therapy indications not related to hematopoietic reconstitution. A CIBMTR representative requested that the Council work with HRSA and contractors to clarify the scope and priorities of data collection. Dr. Milford appointed Dr. Anasetti to chair a Work Group on the topic. Dr. Anasetti and Dr. Kurtzberg worked with Ms. Stroup and HRSA legal counsel to evaluate the issue and lay the foundation for the Work Group's efforts.

Dr. Anasetti summarized various cell types and therapies and indications for cellular therapies. Hematopoietic reconstitution and immunotherapy for blood disorders fall within the Council's expertise, while treatment of solid tumors and regenerative medicine (currently used in cardiology and neurology) do not. The Council has already raised the following considerations:

- CIBMTR navigates easily the field of HSCT but is not at ease with other disciplines, e.g., cardiology.

- Centers are reluctant to share confidential data gathered under IND studies that involve intellectual property rights.
- The law is silent on the data reporting obligation by parties that manufacture cells.
- Reporting is unfunded.

The Work Group should clarify the scope of the CIBMTR mandate and identify potential partners who have an interest in cellular therapies for indications other than hematopoietic reconstitution. Dr. Anasetti provided a list of stakeholder organizations and individuals to consider appointing to the Work Group. He noted that his term ends at the end of 2013, but he hoped that would be enough time for the Work Group to develop and present a report to the Council.

#### *Discussion*

Dr. Price said some alternative medicine practitioners use autologous stem cell therapy but do not believe they are subject to regulatory guidelines; he wondered whether the Work Group's efforts would address such practices. Dr. Anasetti responded that he had no personal experience or knowledge of such practices, but stem cell therapy is a large, emerging field that is expanding around the world. Such practices are not within the scope of HSCT, but the Work Group could advise HRSA on whether to restrict them.

Dr. Hartzman asked Dr. Anasetti to clarify the intention of the Work Group's focus. Dr. Anasetti replied that CIBMTR currently is tasked with developing approaches to collect data on therapeutic cell infusion outcomes broadly. CIBMTR has asked for more direction, because it has not been successful so far in, for example, creating a comprehensive database on stem cell transfusions in heart transplant recipients.

Dr. Walters asked whether the Work Group should have members with expertise in neurology or cardiology. Dr. Anasetti said the group could expand to include other experts as needed.

Dr. Milford said it would be helpful to better understand what is happening now and in what directions cell therapies are heading. The Council does not necessarily have to weigh in on these issues. However, said Mr. Milford, the Council's authority does go beyond hematopoietic transplants. Ms. Grant agreed that the authorizing legislation covers other cellular therapies and it would be helpful to have a better understanding of the landscape. She said that Marcelo Pasquini, MD, of CIBMTR should be able to help in that respect.

Dr. Kurtzberg said the proposed members would also have insight on non-hematopoietic applications. Dr. Milford said it may not be possible to get a clear picture of what is going on in private industry. Dr. Kamani reminded the group that these therapies go beyond academic institutions; they are practiced in private clinicians' offices and elsewhere. Thus, the Work Group should be clear about the scope of its intelligence-gathering effort. Ms. Grant said the focus is on transplants facilitated through HRSA, so data can be collected from cord blood banks and NMDP, but private clinics and other facilities are beyond the reach of HRSA's programs.

Drs. Champlin, Kamani, and Walters, and Mary C. Hennessey, JD, expressed interest in joining the Work Group. Ms. Stroup will take part and will ensure there is program representation on the

Work Group. Dr. Walters suggested inviting Evan Snyder, MD, PhD, of the Sanford Burnham Medical Research Institute in San Diego to join the Work Group.

### **Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) Update**

*James Berger, MS MT (ASCP) SBB, Executive Secretary*

The ACBTSA last met in December 2012 to discuss the policy implications of emerging research on blood and tissue products, specifically relating to emergency preparedness and response. It recommended addressing the lack of a system for managing tissues during a disaster and enhancing the blood system's capabilities for disaster preparedness, response, and recovery. The ACBTSA formed subcommittees on disaster preparedness and response for blood and tissue systems. Another subcommittee will look at blood requirements during emergencies.

The ACBTSA identified several areas of potential enhancement of the blood system:

- Stable government funding to support AABB's Interorganizational Task Force for Domestic Disasters and Acts of Terrorism (currently funded by AABB alone)
- Advancement of new products
  - Reserves of end products
  - Logistic support for transport of blood and tissues in an emergency, including information technology and communication
  - Connectivity with other disaster response systems
  - Designation of committed donors and essential staff as priority health care responders
  - Extended storage of blood products in an emergency that do not require cold storage
  - Rapid "low-tech" screening tests for infectious diseases (with increased sensitivity and specificity and faster processing time)
  - Pathogen-reduced blood components (currently used widely in Europe)
  - Stem-cell-based products and growth factors
- Regulatory flexibility
  - Identifying unmet needs, including funding
  - Characterizing and addressing barriers
  - Establishing evidence to project risks and benefits of possible interventions

To improve disaster preparedness of the tissue system, the ACBTSA recommended support for a gap analysis to address safety and availability of tissue products.

The ACBTSA will meet next in June 2013 to address whether the current blood center system is designed to function appropriately in the new health care system and how the field of transfusion medicine will be defined over the next decade. Mr. Berger noted that a 2011 survey to be released soon will show that blood collection and blood usage are going down, primarily because of changes in blood management that emphasize transfusing blood only when necessary.

#### *Discussion*

Ms. Stroup suggested the Council members consider where its efforts may overlap with those of the ACBTSA.

## **New Business and Updates**

No new business was raised.

## **Review of Tabled Recommendation Cord Blood Bank Reimbursement**

Dr. Milford noted that Dr. Rubinstein was unable to give his input earlier in the meeting during the discussion of recommendations about the perceived difficulty that cord blood banks face in keeping costs down while meeting new requirements and still providing a diversity of genotypes. He invited Dr. Rubinstein to comment.

Dr. Rubinstein said his main concern was discussed—that is, given the cost of collecting units from minority groups, especially from African American donors whose cord blood is somewhat deprived of hematopoietic cells, there may be an advantage to assigning reimbursement values to units that are not just provided by minority donors but also achieve the targets for cell dose, particularly CD34 and CFU content. That way, if the money available is not increased, at least banks are compensated proportionately for their actual costs.

Dr. Harvath said her group's recommendation did not put forth a specific proposal for reimbursement because the group believed that HRSA needed more flexibility to negotiate with cord blood banks. She believed that HRSA and the banks should discuss approaches that both parties feel are fair and feasible. Dr. Harvath said HRSA should take the lead to find out whether money can be shifted and tradeoffs made such that banks receive higher subsidies for cord blood from underrepresented groups. The two Work Groups did not have the time or expertise to address financing models in detail. Dr. Harvath asked that HRSA report back to the Council about its discussions with the banks.

### **Action Item**

Dr. Milford agreed to follow up with HRSA to ensure that the agency considers all the possibilities for addressing cord blood bank financing.

## **Public Comment**

Kathy Loper of AABB complimented the HRSA staff and the Council for the success of the Council's first virtual meeting.

## **Adjournment**

Dr. Milford thanked all the participants and adjourned the meeting at 3:30 p.m.

## **ATTACHMENTS**

- 1) Summary of recommendations to the Secretary and Council action items
- 2) List of attendees (by type)

## Attachment 1

# ADVISORY COUNCIL ON BLOOD STEM CELL TRANSPLANTATION Summary of Recommendations and Action Items May 16, 2013

## RECOMMENDATIONS

### **Advancing Hematopoietic Stem Cell Transplantation (HSCT) for Hemoglobinopathies**

#### **Recommendation to Health Resources and Services Administration (HRSA)**

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

#### **Recommendation to the Secretary**

The Council recommends that the Secretary consider appropriate mechanisms to assure that the revised National Heart, Lung, and Blood Institute publication “Management and Therapy of Sickle Cell Disease” includes expert opinion about the curative option of hematopoietic cell transplantation for this disorder.

## ACTION ITEMS

### **C. W. Bill Young Cell Transplantation Program Update**

Shelley Grant, MHSA, Chief of the Blood Stem Cell Transplantation Branch in the Division of Transplantation at HRSA, will provide the Council with data on transplants by indication.

### **Cord Blood Bank Reimbursement**

The Realizing the Potential of Cord Blood Work Group and the Scientific Factors Necessary to Define Cord Blood Units as High-Quality Units Work Group will talk with HRSA staff in more detail and present a revised recommendation at the next Council meeting regarding reimbursement for cord blood banks. HRSA and its contractor banks will discuss how to collect the maximum number of high-quality units with HRSA’s limited funding.

Dr. Milford will follow up with HRSA to ensure that the agency considers all the possibilities for addressing cord blood bank financing.

### **Advancing HSCT for Hemoglobinopathies**

Dr. Milford requested that HRSA report back to the Council about its progress on educational/outreach efforts to the SCD patient and provider community.

**Attachment 2**

**ADVISORY COUNCIL ON BLOOD  
STEM CELL TRANSPLANTATION**

**Meeting Attendees  
May 16, 2013**

**Salem Akel**

**Claudio Anasetti, M.D.**  
Senior Member and Chair  
Department of Blood and Marrow  
Transplantation  
Moffitt Cancer Center  
Tampa, FL 33624

**Ellen M. Areman, M.S., S.B.B. (A.S.C.P.)**  
President and Senior Consultant  
Ellen Areman Consulting, LLC  
Glen Burnie, MD 21060

**Sue E. Armitage, B.S.**  
Assistant Director of Operations, Cord Blood  
Bank  
Stem Cell Transplantation & Cellular Therapy  
M.D. Anderson Cancer Center  
University of Texas  
Houston, TX 77030

**Marla Arnold**  
Captioner  
Caption Colorado

**Aleksandar Babic, M.D., Ph.D.**  
Medical Director  
St. Louis Cord Blood Bank  
St. Louis, MO 63110

**Robert Baitty, M.P.P. (Retired)**  
Consultant  
Potomac, MD 20854

**James J. Berger, M.S., M.T. (A.S.C.P.), S.B.B.**  
Senior Director, Blood Safety Policy  
Division of Blood and Tissue Safety &  
Availability  
Office of the Assistant Secretary for Health  
Rockville, MD 20852

**Michael Boo, J.D.**  
Chief Strategy Officer  
Administration and Business Development  
National Marrow Donor Program  
Minneapolis, MN 55413

**Janet Brunner, P.A.-C.**  
Program Director, Data Operations  
Center for International Blood & Marrow  
Transplant Research (CIBMTR)  
Milwaukee, WI 53189

**Andrew Campbell, M.D.**  
Assistant Professor  
Director, Comprehensive  
Hemoglobinopathies Program  
Department of Pediatric Hematology &  
Oncology  
University of Michigan  
Ann Arbor, MI 48105

**Tom Carpenter, B.A.**  
Vice President  
Wexler & Walker  
Washington, DC 20004

**Rafael K. Cassata, M.S., R.A.C.**

Deputy Director, Regulatory Affairs - Cellular Therapies  
American Association of Blood Banks  
Bethesda, MD 20814

**Christina M. Celluzzi, Ph.D.**

Technical Specialist Cellular Therapies  
American Association of Blood Banks  
Bethesda, MD 20814

**Richard Champlin, M.D.**

Chairman  
Department of Stem Cell Transplantation and Cellular Therapy  
M.D. Anderson Cancer Center  
University of Texas  
Houston, TX 77030

**Jeffrey W. Chell, M.D.**

Chief Executive Officer  
Administration  
National Marrow Donor Program  
Minneapolis, MN 55413

**Anne C. Chenoweth, M.B.A., M.T. (A.S.C.P.)  
C.M., C.Q.A. (A.S.Q.)**

Deputy Director  
American Association of Blood Banks  
Bethesda, MD 20814

**Dennis Confer, M.D.**

Chief Medical Officer  
National Marrow Donor Program  
Minneapolis, MN 55413

**Alexandra Constantini**

Gift of Life Bone Marrow Registry

**Colleen Delaney, M.D., M.Sc.**

Associate Member  
Director, Program in Cord Blood Transplantation  
Fred Hutchinson Cancer Research Center  
Seattle, WA 98109

**Ulyana V. Desiderio, Ph.D.**

Senior Manager for Scientific Affairs  
American Society of Hematology  
Washington, DC 20036

**Sarah Dickerson, M.T., (A.S.C.P)**

Lab Manager  
Department of Defense  
Rockville, MD 20852

**Nancy L. DiFronzo, Ph.D.**

Program Director  
Division of Blood Diseases and Resources,  
Transfusion Medicine and Cellular Therapeutics Branch  
National Heart, Lung, and Blood Institute  
U.S. Department of Health & Human Services  
National Institutes of Health  
Bethesda, MD 20892

**Suanne Dorr, M.B.A., M.T. (A.S.C.P.), S.C.**

Executive Director  
JP McCarthy Cord Stem Cell Bank  
Karmanos Cancer Institute  
Detroit, MI 48201

**Jill A. Evans, M.T. (A.S.C.P.), A.S.Q., C.Q.A.**

Vice President of Quality  
Quality Assurance  
LifeSouth Community Blood Center  
Gainesville, FL 32607

**Jay Feinberg, Hon. D.H.L**

Chief Executive Officer  
Gift of Life Bone Marrow Foundation  
Boca Raton, FL 33431

**Randy Gale**

Health Resources and Services  
Administration  
Rockville, MD 20857

**Shelley Grant, M.H.S.A.**

Chief, Blood Stem Cell Transplantation  
Branch  
Division of Transplantation  
Health Resources and Services  
Administration  
Rockville, MD 20020

**Linda M. Griffith, M.D., Ph.D.**

Medical Officer  
Division of Allergy, Immunology, and  
Transplantation  
National Institute of Allergy and Infectious  
Diseases  
National Institutes of Health  
Bethesda, MD 20892

**Amanda Gauch**

Transcription  
Caption Colorado

**Rebecca Haley, M.D.**

Medical Director  
Cord Blood Services  
Puget Sound Blood Center  
Seattle, WA 98112

**Joanie Y. Hare, M.D.**

Physician  
Department of Obstetrics  
Houston Perinatal Associates  
The Woman's Hospital of Texas  
Houston, TX 77054

**Robert J. Hartzman, M.D.**

Director, C. W. Bill Young Marrow Donor  
Recruitment and Research Program  
Bone Marrow Research Directorate  
Naval Medical Research Center  
Rockville, MD 20852

**Liana Harvath, Ph.D.**

Senior Consultant  
Liana Harvath, Ph.D., LLC  
Rockville, MD 20850

**Mary C. Hennessey, J.D.**

Senior Counsel  
American Society of Clinical Oncology  
Alexandria, VA 22314

**Mary Horowitz, M.D., M.S.**

Chief Scientific Director  
Center for International Blood & Marrow  
Transplant Research  
Froedtert and the Medical College of  
Wisconsin  
Milwaukee, WI 53226

**Naynesh R. Kamani, M.D.**

Faculty, Blood and Marrow Transplantation  
Chair, Institutional Review Board Medical  
Director, Office for the Protection of Human  
Subjects  
Principal Investigator, Children's Research  
Institute  
Center for Cancer and Immunology Research  
(CCIR)  
Children's National Medical Center  
Washington, DC 20010

**Kim Karras**

Captioner  
Caption Colorado

**Matthew J. Kuehnert, M.D., F.A.C.P.**

Director  
Office of Blood, Organ, and Tissue Safety  
Centers for Disease Control and Prevention  
(CDC)  
Atlanta, GA 30333

**Joanne Kurtzberg, M.D.**

Director, Duke PBMT  
Director, Carolinas Cord Blood Bank,  
Chief Scientific Officer, Robertson Clinical &  
Translational Cell Program  
Carolina Cord Blood Bank  
Duke University  
Durham, NC 27705

**Mary J. Laughlin, M.D.**

Professor of Medicine  
Cancer Center  
University of Virginia  
Charlottesville, VA 22903

**Judith Lawrence, R.N.**

Manager  
Department of Defense Cord Blood Bank  
Georgetown University  
Rockville, MD 20852

**Ellen F. Lazarus, M.D.**

Captain, USPHS, Medical Officer  
Division of Human Tissues  
Office of Cellular, Tissue, and Gene Therapies  
Center for Biologics Evaluation and Research  
(CBER)  
U.S. Food and Drug Administration  
Rockville, MD 20852

**Kathy Loper, M.H.S., M.T. (A.S.C.P.)**

Director, Center for Cellular Therapies  
American Association of Blood Banks  
Bethesda, MD 20814

**Juan Merayo**

**William D. Merritt, Ph.D.**

Director, Cancer Therapy Evaluation Program  
Division of Cancer Treatment and Diagnosis  
National Cancer Institute  
Bethesda, MD 20892

**Alyssa K. Mezochow, M.Sc.**

ORISE Infectious Disease Fellow  
Division of Blood & Tissue Safety & Availability  
Office of the Assistant Secretary for Health  
U.S. Department of Health and Human  
Services  
Rockville, MD 20852

**Edgar L. Milford, M.D. (Chairperson)**

Dover, MA 02030

**Elizabeth A. Murphy, Ed.D., R.N.**

Vice President, Patient and Health  
Professional Services  
National Marrow Donor Program  
Minneapolis, MN 55413

**Thomas J. Murphy, ALS Patient**

Consultant  
Gainesville, VA 20155

**Willis H. Navarro, M.D.**

Vice President  
Transplant Medical Services  
National Marrow Donor Program  
Minneapolis, MN 55413

**Steven S. Oh, Ph.D.**

Team Lead, Device and Combination Product  
Division of Cellular and Gene Therapies  
Office of Cellular, Tissue and Gene Therapies  
Center for Biologics Evaluation and Research  
Rockville, MD

**Jean Otter, M.T. (A.S.C.P.) S.B.B.**

Division Director, Programs  
American Association of Blood Banks  
8101 Glenbrook Road  
Bethesda, MD, 20814

**Effie W. Petersdorf, M.D.**

Professor of Medicine  
American Society for Blood and Marrow  
Transplantation  
Seattle, WA 98109

**Mujeeb Pirzada**

Technician  
OIT Department  
Health Resources and Services  
Administration  
Rockville, MD 20857

**Suzanne Pontow, Ph.D.**

Co-Director, Umbilical Cord Blood Collection  
Program  
Stem Cell Program  
University of California - Davis  
Sacramento, CA 95817

**Thomas H. Price, M.D.**

Professor Emeritus  
University of Washington  
Seattle, WA 98105

**Mercy Quagraine, Ph.D.**

Reviewer  
U.S. Food and Drug Administration  
Rockville, MD 20852

**Donna Regan, M.T. (A.S.C.P.) S.B.B.**

Director  
St. Louis Cord Blood Bank & Cellular Therapy  
Laboratory  
SSM Cardinal Glennon Children's Medical  
Center  
St. Louis, MO 63110

**Lisa C. Richardson, M.D., M.P.H**

Medical Officer  
Director for Science for the Division  
of Cancer Prevention and Control  
Centers for Disease Control and Prevention

**J. Douglas Rizzo, M.D., M.S.**

Associate Scientific Director  
Center for International Blood and Marrow  
Transplant Research  
Department of Medicine  
Medical College of Wisconsin  
Milwaukee, WI 53226

**Pablo Rubinstein, M.D.**

Program Director and Vice President  
New York Blood Center  
New York, NY 10021

**Ruben J. Rucoba, M.D.**

Patient Advocate  
Wheaton Pediatrics  
Wheaton, IL 60189

**Andromachi Scaradavou, M.D.**

Medical Director  
National Cord Blood Program  
New York Blood Center  
Long Island City, NY 11101

**Jeffrey R. Schriber, M.D.**

Oncologist  
Banner Blood and Marrow Transplant  
Program  
Phoenix, AZ 85006

**Marc Schulhof**

Senior Analyst and Technical Writer  
Columbia Telecommunications Corporation  
(CTC)  
Bethesda, MD 20817

**Stephen R. Sprague**

Patient Advocate  
Consultant  
Staten Island, NY 10301

**Susan Stayn, J.D.**

Senior University Council  
Stanford University  
Stanford, CA 94305

**Susan K. Stewart**

Executive Director  
Blood & Marrow Transplant Information  
Network (BMT InfoNet)  
Highland Park, IL 60035

**Pat Stroup, M.B.A., M.P.A.**

Director  
Healthcare Systems Bureau  
Health Resources and Services  
Administration  
Rockville, MD 20857

**Laura Tank, B.S.**

Cord Blood Registry  
Tucson, AZ 85756

**Carol Taylor, Ph.D., M.T. (A.S.C.P.)**

Director, Cord Blood Services  
Puget Sound Blood Center  
Seattle, WA 98104

**Passy Tongele, M.B.A.**

Management Analyst  
Division of Transplantation  
Health Resources and Services  
Administration  
Rockville, MD 20857

**Frances Verter, Ph.D.**

Director  
Parent's Guide to Cord Blood Foundation  
Brookeville, MD 20833

**Elizabeth Wagner, M.P.H.**

Scientific Program Coordinator  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
National Institutes of Health  
Bethesda, MD 20892

**Jon E. Walker, C.L.S.**

Co-Director, Umbilical Cord Blood Collection  
Program  
Stem Cell Program  
University of California - Davis  
Sacramento, CA 95817

**Mark Walters, M.D.**

Jordan Family Director, Blood and Marrow  
Transplant Program  
Children's Hospital & Research Center,  
Oakland  
Oakland, CA 94609

**Daniel J. Weisdorf, M.D.**

Professor of Medicine  
Department of Hematology, Oncology and  
Transplant  
University of Minnesota  
Minneapolis, MN 55455

**Theresa Wiegmann, J.D.**

Director of Public Policy  
American Association of Blood Banks  
Bethesda, MD 20814

**Rachel Witten**

**Keith Wonnacott, Ph.D.**

Chief, Cellular Therapies Branch  
Division of Cell and Gene Therapy  
U.S. Food and Drug Administration  
Rockville, MD 20852

**Roy S. Wu, Ph.D.**

Branch Chief  
National Cancer Institute  
Bethesda, MD 20892

**Shimian Zou, Ph.D.**

Health Scientist Administrator  
National Institutes of Health  
Bethesda, MD 20855