

May 14, 2007

Dear Colleagues:

We are entering an exciting new era for research in hematopoietic stem cell transplantation as we prepare for the July 2007 launch of the Stem Cell Therapeutics Outcomes Database (SCTOD) of the C.W. Bill Young Transplantation Program. As was announced in the attached article from the December 2006 CIBMTR[®] Newsletter, CIBMTR, along with our partner the National Marrow Donor Program (NMDP), was awarded the federal contract to establish and maintain the SCTOD. Explanations of the SCTOD and the C.W. Bill Young Program can be found at www.cibmtr.org. Implementation of the SCTOD in July 2007 will bring significant changes for transplant centers. Following are highlights of these changes.

Federal Legislation Reporting Requirements

Under new federal legislation, U.S. centers are now *required* to submit outcomes data on all allogeneic transplants, related and unrelated. To meet the federal requirements, we have modestly expanded the Transplant Essential Data (TED) form to include all necessary data elements. Starting in July 2007, eTED (for expanded TED) forms will be required for all related and unrelated donor transplants. Additionally, unrelated adult donor and unrelated cord blood transplants that are facilitated by the C.W. Bill Young Transplantation Program will require a Product Form that includes data on HLA typing, graft characteristics and donor infectious disease markers. These data will be used for evaluation of C. W. Bill Young Program operations, including federally required research such as analyses of center-specific outcomes and optimal registry/cord blood bank size. A Federal Register notice of these forms was published on May 8th: http://frwebgate.access.gpo.gov/cgi-bin/getpage.cgi?dbname=2007_register&position=all&page=26136 including estimates of the time required to complete the forms. These estimates were derived from pilot studies in a dozen transplant centers. There is a 30 day comment period for this notice.

Research Reporting

CIBMTR will continue to collect data for scientific research, both at the eTED level (for autologous transplants and international transplants) and comprehensive research Report Forms on a subset of allogeneic and autologous transplants at all CIBMTR Research Centers. Although these activities are not part of the SCTOD, we have taken advantage of the many changes required to implement the SCTOD to make some additional changes that we think will significantly enhance our research program and assist centers who participate in that program.

CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Medical College of Wisconsin
P.O. Box 26509, 8701 Watertown Plank Road
Milwaukee, WI 53226 USA
(414) 456-8325

3001 Broadway St. N.E. Suite 110
Minneapolis, MN 55413-1753 USA
(612) 884-8600



These include:

1. Harmonized Report Forms. The CIBMTR and NMDP recently completed harmonizing their data collection instruments into a unified series of harmonized Report Forms. Going forward from July, there will be a single set of Report Forms used for all types of transplants. An electronic data entry system will be available for both the eTED and the new Report Forms (see below).
2. Selection of cases for Report Form submission. CIBMTR Research Centers submit TED data on all patients and comprehensive data (Report Forms) on a subset. Centers that are currently Research Centers (i.e. submitting comprehensive data on a subset of patients for scientific studies) will continue to be Research Centers under the new program. When the NMDP and IBMTR formed our research affiliation in July 2004 and created the CIBMTR, all NMDP centers became CIBMTR Research Centers, as they were already reporting comprehensive level data on their unrelated donor transplants. NMDP centers will continue to be Research Centers; however, under the new program, comprehensive research data will only be required *for a proportion of unrelated donor transplants*. No center should see its reporting burden increase and some will have a decrease in the number of Report Forms requested.
3. Reimbursement. The reimbursement for all Report Forms (whether for autologous, related or unrelated donor transplants) submitted for transplants performed after July will be at the current NMDP levels, \$245 for the first set of forms (baseline and 100 day) and \$65-\$85 for six-month and annual follow-ups. Details of the new forms and forms submission schedules will be distributed shortly.

New Electronic Identification (ID) Number Assignment System

A web-based system to assign unique numbers to transplant recipients will be released in July. Centers will use this system to identify patients prior to submission of TED forms. To generate the unique ID, centers will enter the recipient's name, address, country of birth, mother's maiden name, and social security number. This level of identifying data is necessary to ensure that recipients are not already entered in the system and will decrease the chance of duplicate entries/numbers for the same recipient. The identifying data used for generating the unique ID will be stored in a secure database separate from the outcomes database. These identifying data will never be used for any purpose other than generating the unique ID. Once assigned, the unique ID will be used in all data submissions to the SCTOD and CIBMTR.

Systems for Electronic Submission of Data

In July we will launch FormsNet 2.0, a web-based application for submission of outcomes data, both at the eTED and Report Form level. This system will allow centers to electronically submit data to the CIBMTR. Errors can be immediately corrected and Forms Due Reports in FormsNet will be real time reports. Training on the FormsNet application will be offered this summer. **It is important the data managers and clinical research coordinators receive adequate training in these new systems. In addition to the web-based training being provided this summer, centers should plan to send at least one representative to in person training sessions scheduled for November 2007 and February 2008.**



The CIBMTR and NMDP are also working on AGNIS, an electronic messaging system. This system is currently in the pilot phase but will eventually be available to all centers. AGNIS will allow centers to directly transmit data from their center's database into the CIBMTR database. Both FormsNet 2.0 and AGNIS will greatly streamline the data submission process. For centers choosing to do so, paper forms may still be submitted for the near future.

Research Database and Research Sample Repository Protocols

The NMDP's research database and research sample repository protocols have been revised to include the CIBMTR research activities and related donor and autologous transplants. These protocols are currently going through IRB review at the NMDP and the Medical College of Wisconsin and will be provided to centers once IRB approval has been obtained. Centers will be asked to submit these protocols to their local IRB for review and approval. All recipients should be asked to provide research consent regardless of whether eTED data or research level data will be collected. This will enable the CIBMTR to use eTED data for research. If a recipient declines to provide consent for research, eTED data must still be submitted on allogeneic transplant recipients to fulfill the legislative requirements. In these cases the recipient's data will not be used for research but only used to fulfill federal contract requirements such as the transplant center-specific outcomes analysis.

Data Management Codes

All NMDP and CIBMTR centers will be assigned a new data management center code that will be used for submitting data to the CIBMTR.

CIBMTR Campus Assignments

Centers will be assigned to either the Minneapolis or Milwaukee campus for support. If centers are submitting paper forms they will submit the forms for all transplant types, allogeneic related and unrelated, and autologous to the campus to which they are assigned.

Continuous Process Improvement (CPI) for Forms Submission

The NMDP's current CPI program to assess and maintain standards for timely submission and accurate completion of required forms will be expanded. The CPI program will remain the same for unrelated donor transplants and continue uninterrupted. In July, we will begin to apply this program to related donor and autologous transplants, phasing the program in gradually over the ensuing 18 months. More information on this will be provided in the near future.

On-site Audit Program

We are in the process of redesigning the on-site audit program and combining the current audit programs of the NMDP and CIBMTR into one single audit. The audit process will be streamlined and cover all types of transplants. This new audit program will be launched in January 2008. Through December 2007 the current NMDP and CIBMTR audit programs will continue.



NEXT STEPS

In May you will receive a “Launch Packet” from the CIBMTR giving you all of the information you will need to get started with the program. This packet will contain:

- A sheet indicating your reporting status: Research Center or Registration Center
- A flow chart for data submission
- List of contacts at CIBMTR Milwaukee and NMDP
- CIBMTR website URL
- Information on how to access the database and repository protocols
- Data transmission agreements
- A FormsNet 2.0 training schedule
- A forms completion training schedule
- A sample set of research forms and eTED forms
- Your new data management team number and campus assignment

We are excited about the new program and all the opportunities it holds for advancing research in hematopoietic stem cell transplantation. We also realize that the change will require a good deal of work on your part. We are committed to making the transition process as easy as possible and to continually look for ways to make supplying data more efficient. We look forward to continued partnership with you in this endeavor.

Sincerely,

Mary M Horowitz, M.D., M.S.
Chief Scientific Director, CIBMTR

Note: The Office of the General Counsel, US Department of Health and Human Services has determined, with the concurrence of the Office of Civil Rights, that the CIBMTR meets the Privacy Rule’s definition of a public health authority (PHA) and is authorized by law to collect the information necessary to fulfill the legislated mandate to collect data needed to assess outcomes of hematopoietic cell therapy. It is therefore not a “covered entity” under HIPAA. Additionally, transplant centers who fit the definition of covered entities may disclose certain individually identifiable health information to the CIBMTR under 45 CFR 164.512 (Privacy Rule), which allows for the disclosure of an individual’s protected health information without the individual’s written consent or authorization when such a disclosure is made to a PHA that is authorized by law to collect information for the purpose of preventing or controlling disease, injury or disability.

CIBMTR Awarded HRSA Contract to Administer the C.W. Bill Young Cell Transplantation Program Outcomes Database

By J. Douglas Rizzo, MD, MS

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

The Center for International Blood and Marrow Transplant Research (CIBMTR) is pleased to be the recipient of the contract (administered by the United States Health Resources and Services Administration (HRSA)) to establish and maintain the Stem Cell Therapeutic Outcomes Database (SCTOD) for the C.W. Bill Young Cell Transplantation Program. This is the beginning of an exciting new era for research in hematopoietic cell transplantation (HCT).

The C.W. Bill Young Cell Transplantation Program (the Program) builds on the infrastructure for donor procurement and outcomes analysis developed by the National Marrow Donor Program (NMDP), which has held the U.S. contract to maintain a National Bone Marrow Donor Registry (NBMDR) for unrelated donor transplantation since its inception in 1987. In December 2005, the U.S. Stem Cell Therapeutic and Research Act of 2005 (Public Law 109-129) established the C.W. Bill Young Cell Transplantation Program to succeed (and enhance) the NBMDR. The Program is named after C.W. Bill Young, a recently re-elected 36 year veteran Congressman from Florida who has been a strong advocate of biomedical research and who was instrumental in the founding of the U.S. donor registry. The Program will include five key components: a Bone Marrow Coordinating Center (BMCC); a Cord Blood Coordinating Center (CBCC); an Office of Patient Advocacy and Single Point of Access for health care professionals and patients (OPA/SPA); and a Stem Cell Therapeutics Outcomes Database (SCTOD). Several cord blood banks will also receive contracts to develop a National Cord Blood Inventory. See Figure 1.

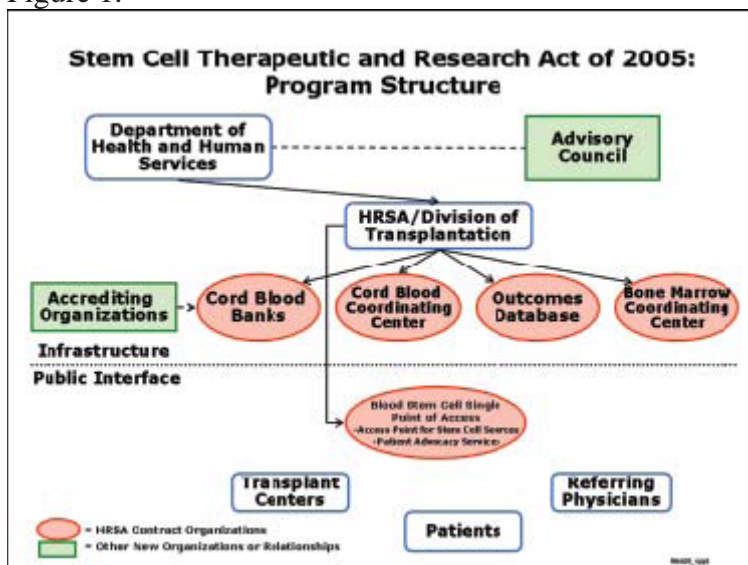


Figure 1.

Working with its NMDP partner, the CIBMTR submitted the winning proposal to administer the SCTOD. The NMDP also was awarded the BMCC, CBCC and the OPA/SPA contracts. Although the landscape of HCT will change because of this legislation, the contract awards to CIBMTR and NMDP represent a substantial benefit to transplant centers, who have become accustomed to collaborating with these organizations. Current, long-standing relationships will not be disrupted as the NMDP and CIBMTR work to implement new and modified requirements of the Program. The CIBMTR and NMDP will use their substantial experience and adapt proven, in-place methods and systems to ensure a successful transition to the new Program.

Implementation of the new Program will present new challenges and opportunities for the HCT community. Important aspects of the program are: development of new systems to collect HCT data electronically, enhanced efforts to develop a standard dataset of HCT data, new requirements for U.S. centers to report outcomes data for all allogeneic transplantations, development of a related donor recipient research sample repository, systems to make more data publicly available, broadened reporting of U.S. transplant center-specific survival rates, and data collection on uses of stem cells for new therapeutic applications (e.g., regenerative medicine).

Data collection for the SCTOD component of the Program will include collection of data for: allogeneic HCTs done in the U.S. using related or unrelated donors; allogeneic HCTs done using cells obtained through the Program, whether the transplantation is done in the U.S. or elsewhere; and use of allogeneic hematopoietic cells for emerging clinical applications other than HCT. In order to minimize the burden of data collection and assure that the most relevant data is collected, CIBMTR has begun discussions with U.S. authorities, the American Society of Blood and Marrow Transplantation (ASBMT), the European Blood and Marrow Transplant Group (EBMT), the Foundation for Accreditation of Cellular Therapy, the World Marrow Donor Association, cord blood banks and others in the international HCT community arrive at consensus on a reasonable set of common data elements to be collected for all patients. The current Transplant Essential Data form (corresponding to the EBMT Med-A form) will serve as a starting point (http://cibmtr.org/DATA/registering_centers.html). [Of note, centers participating as Research Centers in the CIBMTR will still be asked to complete comprehensive Report Forms on a subset of these patients; in a separate initiative the NMDP and CIBMTR have been working to harmonize the forms used for related and unrelated donor transplants.] The CIBMTR and NMDP are adapting established electronic data collection systems to collect these data under the HRSA contract. It is anticipated that these electronic systems will also allow centers to access their own HCT data as one of the benefits of participation. CIBMTR will work with consultants from PACT (Production Assistance for Cellular Therapies) and the SCCT (Specialized Centers for Cell-Based Therapy) and others to develop an approach to collect and analyze data on the use of hematopoietic cells for clinical applications other than HCT. Finally, CIBMTR and NMDP will work to expand the current unrelated donor-recipient specimen repository to include specimens obtained from related donor-recipient pairs. The databases and specimen repository created by these additional requirements of the C.W. Bill Young Program will serve as a resource for HCT investigators to address important research questions.

The new Program will also require publication of an annual report of Transplant center-specific outcomes similar to the report currently generated by the NMDP for unrelated HCT. CIBMTR

strongly believes in the importance of adjusting for difference in “case-mix” of patients across transplant centers using parameters for disease status and co-morbidities at the time of HCT. The experience held by the NMDP will facilitate generation of these reports, and CIBMTR will work closely with the ASBMT Quality Outcomes Committee, the CIBMTR Consumer Advocacy Committee, transplant center director representatives and HRSA to prepare a fair report that is useful for the transplant community and understandable to the general public.

Although change is often difficult, and will certainly require patience as new systems are implemented, the transition to the C.W. Bill Young Cell Transplantation Program promises to offer an enhanced platform from which to conduct clinical investigation into the outcomes of HCT for traditional and emerging indications.

The C.W. Bill Young Cell Transplantation Program and the NMDP

By Dennis L. Confer, MD

Chief Medical Officer, National Marrow Donor Program, Minneapolis, MN, USA

The National Marrow Donor Program (NMDP) is a non-profit corporation that since 1987 has held a series of government contracts to operate the “National Bone Marrow Donor Registry”. In this role NMDP has facilitated more than 25,000 unrelated donor transplants for patients with blood disorders, such as leukemia and aplastic anemia, as well as immune system and genetic disorders. Currently more than 6.1 million adult donors and 52,000 cord blood units are listed on NMDP’s registry. New adult donors are recruited at about 280,000 annually. Cord blood unit numbers will grow significantly as a result of the Stem Cell Therapeutic and Research Act of 2005.

The new act created the C.W. Bill Young Cell Transplantation Program, a totally revamped system for delivering hematopoietic stem cell transplantation options to the U.S. public. This legislation is sweeping in its scope, but emphasizes a federal commitment to development of umbilical/placental cord blood. The legislation creates a National Cord Blood Inventory (NCBI), established by contracts awarded to individual cord blood banks that are charged with responsibility to begin collection of 150,000 new, high-quality cord blood units (CBU). The CBU inventories (both NCBI and non-NCBI units) of these contracted banks, as well as the inventories of other qualified member banks, will be listed, searched and distributed through the National Cord Blood Coordinating Center (CBCC). An analogous National Bone Marrow Coordinating Center (BMCC) will oversee adult donor recruitment, donor search, product collection and product distribution activities of the adult donor registry. The public interface to these coordinating centers will be provided through another contract awarded to establish an Office of Patient Advocacy/ Single Point of Access (OPA/SPA) function.

Six cord blood banks are charter members of the NCBI. They are: Carolinas Cord Blood Bank at Duke University Medical Center, MD Anderson Cord Blood Bank, Milstein National Cord

Blood Bank Program at the New York Blood Center, Puget Sound Blood Center, StemCyte, Inc., and the University of Colorado Cord Blood Bank. As described elsewhere in this issue, a contract for the outcomes database was awarded to CIBMTR. Contracts to operate the CBCC, BMCC and OPA/SPA were awarded to the NMDP. Because NMDP received these latter three contracts, much of the complexity inherent in the Program will be shielded from the public and from the transplant community.

Federal oversight of the Program rests with the Department of Transplantation in the Health Resources and Services Administration (HRSA). HRSA is a federal agency dedicated to improving health care access in the U.S. In HRSA's own words, "HRSA is the nation's access agency – improving health and saving lives by making sure the right services are available in the right places at the right time." Accordingly, the new contracts with NMDP include many requirements related to improving access to transplantation therapies. Some of the most interesting requirements relate to enhancing the information supplied to patients, their families and the public. For example, NMDP must develop software that allows patients, families, and the public at large, to conduct searches of the adult donor and CBU registries. This is envisioned as a public web site where any individual with HLA data can obtain information about the potential for matching adult donors and CBU. While this service clearly provides patients with greater access to health-related information, it also creates obligations to ensure that the information is accurate, properly represented and accompanied with important disclaimers. For example, the public search report cannot fully anticipate the transplant center's eligibility rules or HLA matching requirements.

The new contracts also require that patients are periodically updated about the status of their donor/CBU search that is being managed by a transplant center. If the search is interrupted or cancelled, the contractor must notify the patient. These requirements will be difficult to implement in a "fool-proof" manner, but will work best with solid collaboration between NMDP and the transplant centers. Additional contract requirements relate to increasing transplantation activity, improving efficiency and developing performance measures. These and other requirements will challenge NMDP, CIBMTR and their partners to create a working environment for innovation and collaboration.

The C.W. Bill Young Cell Transplantation Program has created a vision for the future of transplantation therapies in the U.S. Implementation of this vision has been entrusted to two well-known organizations, CIBMTR and NMDP, working in collaboration with federal officials and the transplant community. The demands are numerous, but rewards for our transplant community and the patients we serve are innumerable.