

2.3 Cord Blood Coordinating Center

The Cord Blood Coordinating Center (CBCC) was established as one of the four components of the C.W. Bill Young Cell Transplantation Program to help more patients receive a successful umbilical cord blood transplant. It is administered by NMDP.

2.3.1 New Mission/Contract Requirements

Umbilical cord blood (cord blood) is recognized as an established alternative to bone marrow and peripheral blood stem cells as a transplant source for many of the same diseases. Cord blood units (CBUs) are used more often for pediatric recipients, but are also used increasingly in adults. The relative ease of CBU collection, along with less stringent HLA matching requirements, makes cord blood more accessible for patients from racial and ethnic minority populations and for those with rare HLA types.

The CBCC was established to:

- Increase access to transplantation by providing a comprehensive registry of CBUs;
- Facilitate the search and distribution of CBUs on the Registry;
- Support efforts to educate health professionals and the public about CBU transplantation, and reduce barriers to this therapy; and
- Manage the related cord blood donor program for families that are having a baby, and who have a first-degree (close) relative diagnosed with a disease that may be treated by a cord blood transplant.

The CBCC coordinates a national registry of CBUs through agreements with transplant centers, cord blood banks, international registries and laboratories. It also works closely with the other Program operators to coordinate and serve patients in need of a transplant.

2.3.2 Growth of Cord Blood Unit Registry

The NMDP has operated a registry of cord blood banks since 2000. Over time, there has been a steady increase in the number of CBUs available for transplantation (Figure 13). NMDP and HRSA sponsor programs to encourage cord blood banks to collect and process more CBUs from families of diverse ethnic and racial backgrounds (Figure 14).

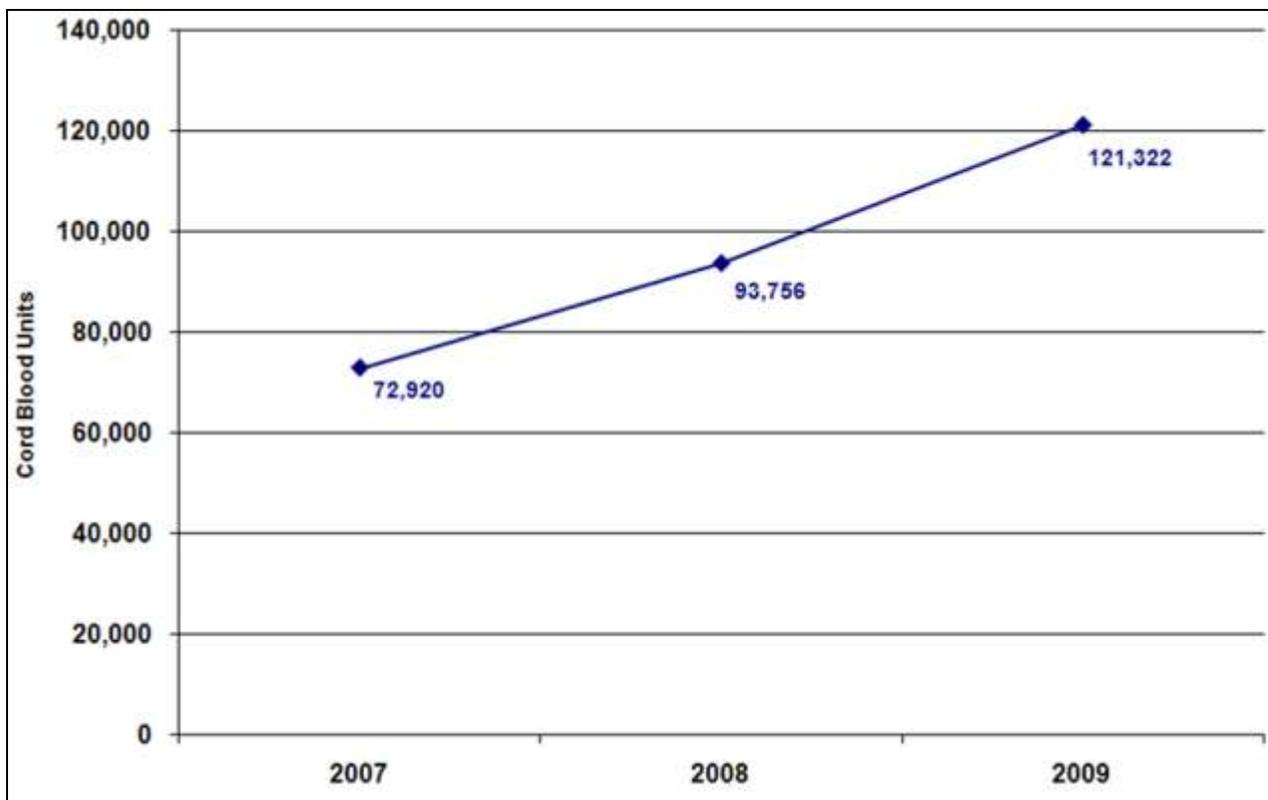


Figure 13. Cord blood units on the Registry - Calendar Years 2007 – 2009

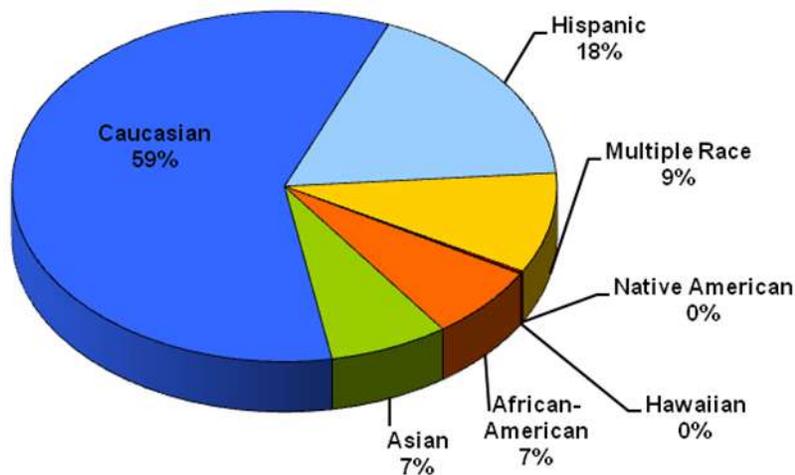


Figure 14. Race/ethnicity of cord blood units on the Registry as of 12/31/09

Note: Caucasian includes patients who chose a broad race of Caucasian, Declined, Other or Unknown without Hispanic ethnicity. Hispanic includes patients who chose a broad race of Hispanic or Caucasian, Declined, Other or Unknown with Hispanic ethnicity.

2.3.3 Recruitment Programs through NMDP: Challenges to Recruitment

Although the number of cord blood donors has increased significantly since 2000, there are several factors that make recruiting them and storing the CBUs for clinical use challenging.

The first is expense: although there is no cost to families for donating cord blood to a public cord blood bank, there is considerable cost for collecting, processing and storing the CBUs. The total costs average \$1,500-\$2,000 per unit.

The second challenge to the use of CBUs is that they must be processed within 48-hours of collection. These two factors mean that many cord blood banks focus on efficiency by recruiting new mothers who deliver in hospitals with large, active obstetrics programs that are physically close to their facility. However, the majority of pregnant women do not give birth at a hospital associated with a public cord blood bank. In some cases, it is possible for women to receive a collection kit through the mail, have their physician perform the collection and return the CBU to the cord blood bank. NMDP is currently conducting a pilot program for non-fixed site collections with three cord banks. The results of the pilot will be evaluated to determine the feasibility of expanding the program network-wide.

Funding that is available through the NCBI program (see 2.3.5 below) is helping increase the national inventory of CBUs. Between 2007 and 2009, HRSA provided funds to cord blood banks to help build their inventories of high quality CBUs. This funding has enabled the addition of over 9,400 CBUs during this reporting period, of which about half were from ethnic and racial minority donors.

2.3.4 Selection and Use of Cord Blood Units

Every search of the NMDP Registry on behalf of a patient identifies potentially matched cord blood units and unrelated PBSC and bone marrow donors. When a patient needs a transplant for a life-threatening disease, his or her doctor considers many factors:

- Should the cells come from the patient (autologous transplant) or from a donor (allogeneic transplant)? The type of transplant to be used depends on which works best for that disease.
- Which graft source (bone marrow, peripheral blood or cord blood) is best for the patient? Each source has advantages and disadvantages.

Cord blood is especially useful for:

- Patients who need a transplant quickly, because CBUs are stored frozen and ready to use.
- Patients who have a hard time finding a matched bone marrow or PBSC donor. Cord blood does not have to match a patient's HLA type as closely as donated bone marrow or peripheral blood stem cells.

The use of cord blood for transplantation has been steadily growing. Approximately 22 percent of transplants facilitated by the NMDP in fiscal year 2009 used cord blood (Figure 6).

2.3.4.1 Race and Age of Cord Blood Transplant Recipients

The use of cord blood in transplants has increased for both children and adults. Cord blood is used more often in children because the umbilical cord and placenta hold a limited amount of blood and blood-forming cells. The number of blood-forming cells that a transplant recipient needs is relative to their size—smaller patients need fewer cells and larger patients need more cells. Some CBUs may not have enough blood-forming cells for larger patients (Figure 15).

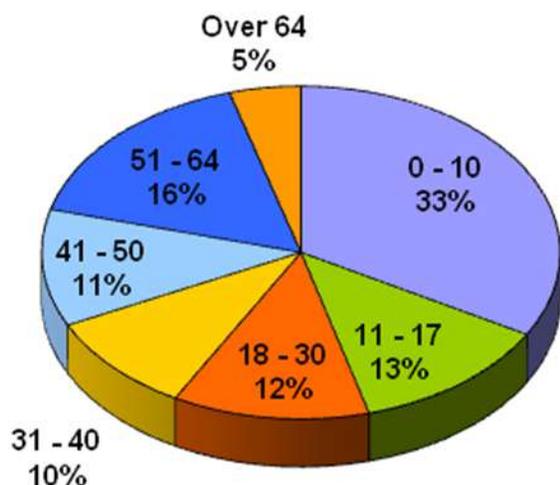


Figure 15. Age distribution of cord blood recipients, calendar year 2009

For a successful transplant, the tissue type of a bone marrow, PBSC donor or a CBU should match the patient's as closely as possible. Tissue types are inherited, so patients are more likely to match the HLA type of someone who shares their racial or ethnic heritage. Often, patients from racially or ethnically diverse communities have a harder time finding a match. Because cord blood does not need to match a patient as closely as donated bone marrow does, cord blood transplants may offer hope to these patients. In 2009, 33 percent of cord blood transplants were for patients from racially or ethnically diverse communities (Figure 16).

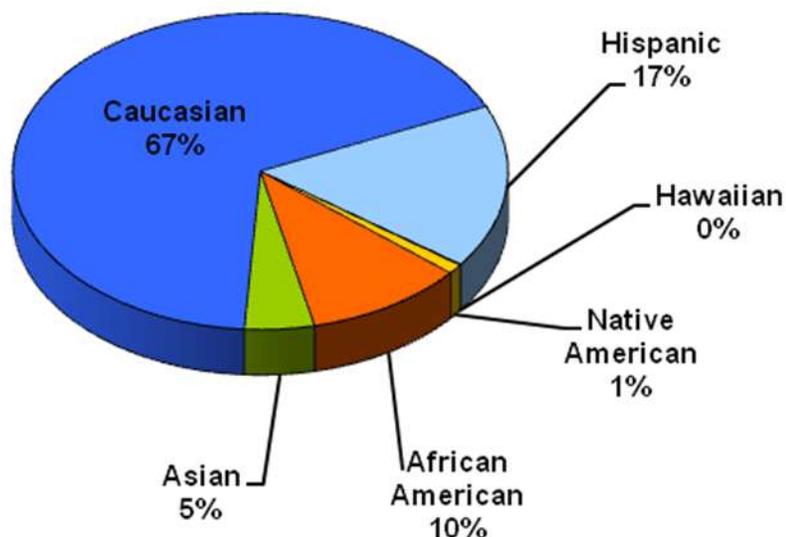


Figure 16. Race/ethnicity distribution of cord blood recipients, calendar year 2009

2.3.4.2 Increasing Transplants for Adults

Researchers are trying different ways to increase the number of cells in a CBU so they can use cord blood for larger patients. One method being studied is a way to increase the number of cells in a CBU in a laboratory before giving the unit to a patient. Another method being investigated is the use of two (or more) CBUs for a single patient. The use of dual CBUs for single recipients has increased in recent years (Figure 17).

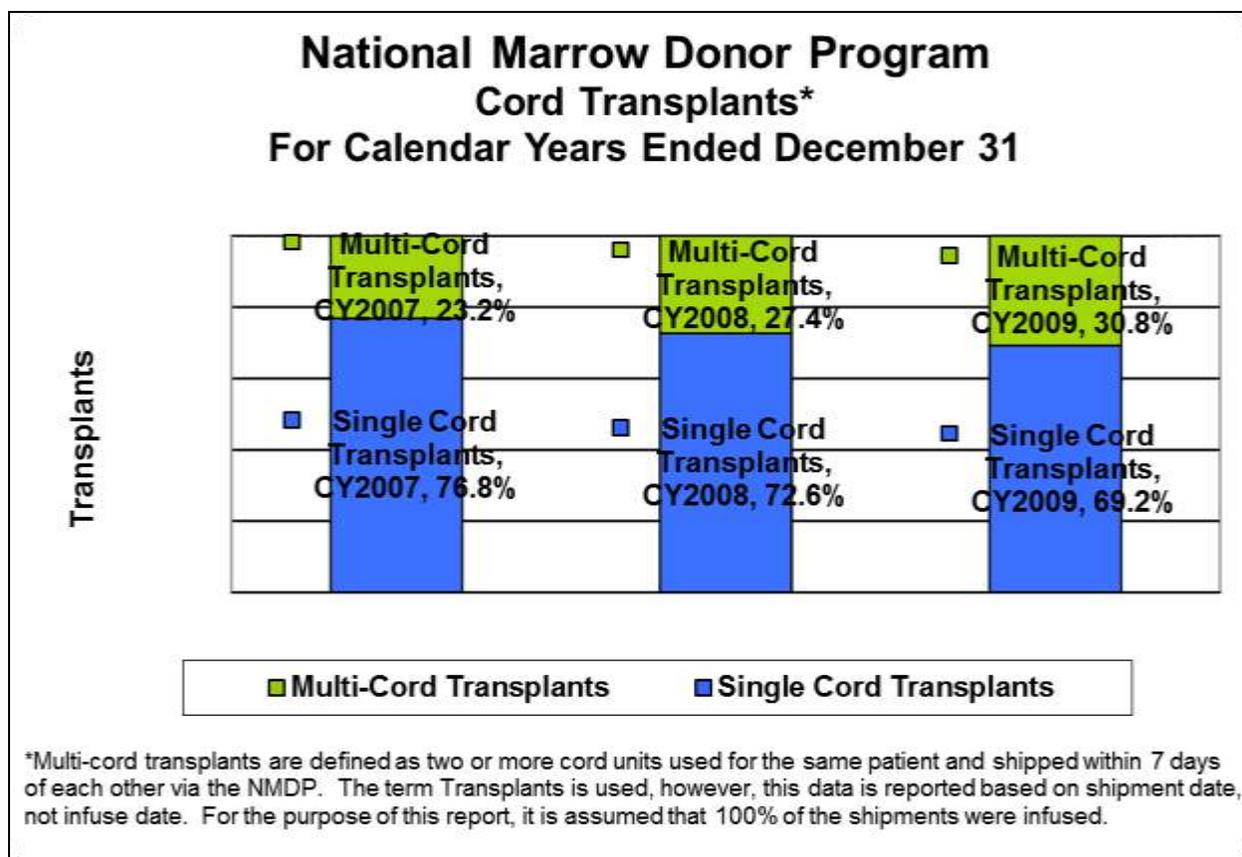


Figure 17. Single and multi-cord transplants, calendar year 2007-09

2.3.4.3 International Exchange of Cord Blood Units

Finding the best CBU for a patient often means getting it from an international cord blood bank or registry. Almost 45 percent of CBUs used for transplants come from a country other than the country of the patient receiving the unit.

In fiscal year 2009, 233 CBUs used in transplants for U.S. patients facilitated by the NMDP were imported from other countries. Similarly, 272 CBUs were exported from the United States for patients in another country. This international cooperation is critical to providing the best options for patients who need transplants.

2.3.5 National Cord Blood Bank Inventory (NCBI)

The NCBI portion of the Stem Cell Therapeutic and Research Act of 2005 provides funds for collecting and storing 150,000 new units of high-quality cord blood. These CBUs are made available through the C.W. Bill Young Cell Transplantation Program to treat patients who need a transplant.

Cord blood banks that receive contracts to help build the inventory of CBUs will:

- Encourage more cord blood donations, with special emphasis on parents of racially or ethnically diverse backgrounds.
- Collect and store CBUs and make them available through the Program.
- Ensure the CBUs are of high quality and that they meet certain standards, such as having enough blood-forming cells. Cord blood units that do not meet these criteria may be made available for research studies intended to improve patient transplant outcomes.

- Protect the rights of donating mothers and their babies by obtaining informed consent from the mother to donate and by maintaining confidentiality of the mother and baby.
- Provide CBU data to the SCTOD contractor.

2.3.5.1 NCBI Participating Cord Blood Banks

Starting in late 2006, HRSA began entering into contracts with cord blood banks to participate in the NCBI program. These contracts are awarded through a competitive process. As of the end of fiscal year 2009, 12 banks had received contracts. They are:

- Carolinas Cord Blood Bank
- M.D. Anderson Cord Blood Bank
- New York Blood Center National Cord Blood Program
- Puget Sound Blood Center
- St. Louis Cord Blood Bank
- StemCyte International Cord Blood Center
- Texas Cord Blood Bank
- University of Colorado Cord Blood Bank
- LifeCord
- CORD:USE
- New Jersey Cord Blood Bank
- Cleveland Cord Blood Center

HRSA and each of the NCBI banks contract for specific recruitment goals. To better meet the needs of all patients, there is a heavy emphasis on recruiting donors of diverse ethnic and racial backgrounds.

2.3.5.2 Number of NCBI Units Used for Transplant

Before cord blood banks are permitted to start collecting CBUs under their NCBI contract, they need to make changes to their consent forms and sometimes other changes to their operations. After a slow start because of these requirements, NCBI recruitment is steadily increasing.

As of 12/31/2009, approximately 30,000 NCBI units have been added to the registry, of which 633 have been shipped for transplantation, as shown in Table 8 and Figure 18.

Patient Race	2007	2008	2009	Total to Date
AFA	3	16	47	66
API	1	7	19	27
CAU	7	72	222	301
DEC	0	0	6	6
HAW	0	0	0	0
HIS	0	0	0	0
NAM	0	1	4	5
OTH	0	0	1	1
UNK	2	63	162	227
Total	13	159	461	633
Minority*	4	24	70	98
HIS Ethnicity**	2	18	89	109

** Minority includes the broad races of AFA, API, HAW, HIS, and NAM.

Patient Race	2007	2008	2009	Total to Date
Total Minority/Ethnicity	6	42	159	207

Table 8. National Marrow Donor Program. Cord Shipments Using NCBI Funded Units by Patient Race For Calendar Years Ended December 31

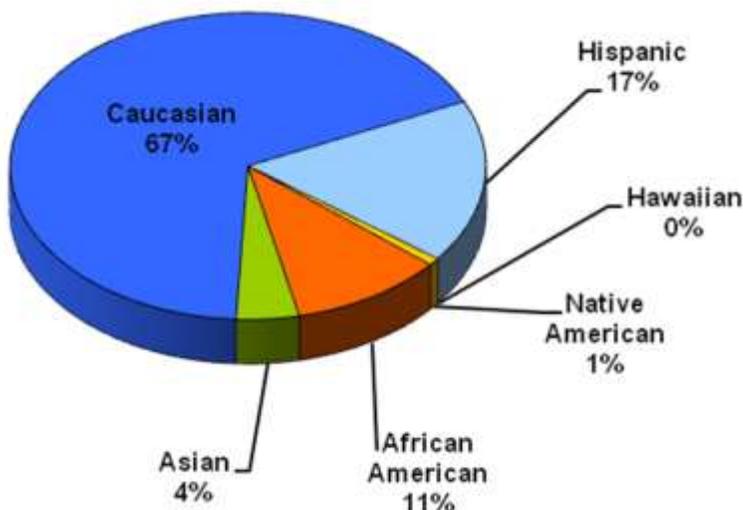


Figure 18. Race/ethnicity distribution of NCBI cord blood units, calendar year 2009

2.3.6 Developing Standardized Unit Inventory Requirements

The NCBI banks and NMDP have been working together since 2000 to identify and adopt practices to improve the quality of stored CBUs. Together, they have established standards for:

- Testing for infectious diseases
- The minimum number of cells in new units for the supplier to be eligible for reimbursement. (This recognizes the fact that larger units are more likely to be chosen and useful for more patients.)
- The level of HLA typing that is needed to provide the best information to patients and their physicians for their search reports
- Screening questions that should be asked of mothers and what should be included in the baby's family medical history

Much of the information obtained through these criteria is available in the NMDP database to make selection of units for patients easier and faster.

2.3.7 HLA-related Projects

It is important that high-quality, timely tissue-typing information is available to patients and their physicians, so that suitable CBUs can be identified. NMDP offers several programs to improve information about available CBUs to physicians.

2.3.7.1 Use of a Central Confirmatory Typing Laboratory

One of the challenges for cord blood banks and transplant centers is that a limited number of samples are available for additional testing. Since CBUs are small, the cord banks need to save

*** HIS Ethnicity includes only patients who chose a racial group of CAU, OTH, DEC, or UNK and an ethnic group of HIS. HIS Ethnicity is updated on a quarterly basis so the data for prior months may change. Broad race does not change.

as many of the cells as possible in the CBU itself. To make best use of the samples and the information that additional testing might provide, NMDP has a contract with one central laboratory to do additional and confirmatory testing on CBU samples. The advantages of this process are:

- A rigorous quality control program is maintained. Results are reported each quarter. The central laboratory has a more than 99 percent accuracy rate for typing.
- The central laboratory keeps a small number of extra cells for potential future use.
- Typing results are available electronically through the SPA search (see Section 2.1.3). Once this confirmatory typing is done, it does not have to be performed again and the unit can be ordered quickly, if needed.

2.3.7.2 Prospective Cord Blood Unit Typing

Many patients who receive transplants have aggressive diseases. They may be medically unstable, which means that they must receive a transplant very quickly. By prospectively performing the second (confirmatory) level of tissue typing before the unit is actually requested on behalf of a specific patient, it becomes available immediately. More than 21,000 CBUs in the Registry are already confirmatory typed, making them more quickly available when needed.

2.3.7.3 Search Process Improvements

Continuing to improve processes or operations is an important goal for the CBCC and NMDP as a whole. Several projects have helped streamline operations:

- **Multi-cord tool.** When a transplant center is searching for two CBUs for a single recipient, each unit must match the patient and the other CBU. NMDP developed an electronic tool to compare the match between units and the recipient to make it easier to identify and order CBUs.
- **Online cord blood unit eligibility assessment.** The FDA has established requirements for determining “eligibility status” of CBUs. They are based on the results of maternal donor screening, medical history and infectious disease marker test results. The CORD Link Web® software that NMDP developed and provides free to cord blood banks includes an automated assessment of this eligibility status. This application also generates the form that accompanies the unit when it is shipped.
- **Providing additional shippers to banks.** The increase in number of cord blood transplants has resulted in an increased need for the special shipping containers used to transport CBUs from the bank to the transplant center. NMDP has provided more than 80 “dry shippers” to network cord blood banks to better meet this need.

2.3.8 Cord Blood Education for Physicians and the Public

Professional medical education programs help physicians learn about appropriate timing and referring of patients for consultation and treatment; best practices for donor and cord blood selection; streamlining the search process; and providing post-transplant care when patients return home. Further information about professional education is contained in Section 2.1.5.

Cord blood recruitment education plan: NMDP works with network cord blood banks to help them achieve their recruitment goals. NMDP supports awareness and education programs for expectant parents and others to increase the number of cord blood donors, including:

- **Expectant parents and public/media:** NMDP has asked potential cord blood donors to identify what might be barriers and what might make them willing to donate. Based on that information, NMDP worked with cord blood banks to develop recruitment and educational materials. NMDP’s online resource center (<http://www.bethematch.org/cord>) helps educate expectant parents about their options for cord blood storage and helps them understand public cord blood donation. NMDP has also worked closely with the media to help disseminate accurate information to the public about cord blood.

- OB/GYN and labor/delivery staff: Discussions with cord blood recruitment staff, obstetricians and labor/delivery staff have indicated that these individuals need more education before they will support public umbilical cord donation. They need to be motivated before they will become involved. This process involves additional efforts on their part to educate their patients and support collection. Obstetricians and labor/delivery staff also need education to help ensure that they collect the CBUs correctly. An instructional DVD on correct collection techniques has been developed. An extensive market research study with expectant parents to learn about their current levels of understanding of and attitudes toward public cord blood donation has been completed.

2.3.9 Quality Assurance Activities

NMDP staff review data across the network of cord blood banks and transplant centers to identify areas of concern. These concerns might not be apparent if the information were collected at only one center. This review helps the network improve its collection, storage and search processes so that patients are receiving the highest quality transplant possible. NMDP has provided financial assistance to help cord blood banks receive and maintain accreditation by AABB (formerly American Association of Blood Banks) and/or the Foundation for the Accreditation of Cellular Therapy (FACT).

- Incident reporting, investigation and trending. NMDP receives reports from cord blood banks and transplant centers if an unusual or unexpected event takes place. These include difficulties with the thaw procedure or a reaction to the infusion of a CBU. These reports are investigated and monitored. Depending upon the severity of the incident, NMDP may notify HRSA and the FDA. NMDP reviews the reported incidents quarterly, and looks for trends in the data to identify patterns that may require changes to practice. This regular review is done to ensure that quality improvements continue throughout the network.
- Proficiency program. The NMDP has formed a partnership with StemCell Technologies (Vancouver, BC) to develop the first cord blood proficiency program. This program provides participants the opportunity to assess their individual competency in testing for nucleated cells, colony forming units, viability and CD34+ cells. It is available to all U.S. cord blood banks.

2.3.10 Making Cord Blood Units Available for Research

Individual cord blood banks make CBUs available for research studies to investigate how to improve outcomes for transplant patients. Cord blood banks providing these CBUs for research have different requirements about their use for studies. Most cord banks will ship CBUs to transplant facilities anywhere within the United States. NMDP provides an annual report to HRSA about the number of units provided for research by network cord blood banks.

2.3.11 Contingency Planning

Network cord blood banks also participate in activities related to the NMDP emergency response process. An Emergency Response Plan has been developed to help cord blood banks respond appropriately in the event of an emergency that might be marrow toxic, either natural or man-made. Drills and staff training are given regularly to assure that operations continue and patients are able to receive the transplants they need.

2.3.12 Related Cord Blood Donor Program

The Stem Cell Therapeutic and Research Act of 2005 called for establishing a three-year pilot program for banking CBUs from related donors. It was designed to help families in which a biological sibling or parent has been diagnosed with a medical condition that might be improved by a cord blood transplant. When a baby is born to an eligible family, there is no charge to the family to have that baby's umbilical cord blood collected and stored. It is estimated that as many as 2,500-5,000 families per year might benefit from this program.

The Related Donor Cord Blood Program launched on October 1, 2008, with the NMDP OPA serving as the central clearinghouse for information about the Related Donor Cord Blood Program to the public and professional organizations. HRSA is overseeing this process. In January 2010, a new version of the CORD Link Web application was successfully released, which included enhancements to accommodate the registration of cord blood units collected and banked for the purpose of related donor transplantation.