

October 2011

# NATIONAL CORD BLOOD INVENTORY

## Practices for Increasing Availability for Transplants and Related Challenges

U.S. Government Accountability Office

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## Why GAO Did This Study

Every year, many people diagnosed with diseases such as leukemia and lymphoma require transplants of stem cells from umbilical cord blood or other sources. The Stem Cell Therapeutic and Research Act of 2005 authorized funding for banking 150,000 new units of high quality and genetically diverse cord blood and directed the Department of Health and Human Services (HHS) to contract with cord blood banks to assist in cord blood collection. HHS, through the Health Resources and Services Administration (HRSA), established the National Cord Blood Inventory (NCBI) program to support banking of cord blood units and contracted with 13 cord blood banks to bank these units. The 2010 reauthorization required GAO to report on efforts to increase cord blood unit collection for the NCBI. As of May 2011, HRSA had reimbursed banks for over 41,000 units banked for the NCBI.

In this report, GAO describes (1) practices identified to increase banking of cord blood units for the NCBI and related challenges and (2) practices cord blood banks are using to lower costs and improve the efficiency of cord blood banking and associated challenges. To do so, GAO reviewed relevant regulations and documents, and interviewed officials from pertinent organizations. These included officials from HRSA, the Food and Drug Administration (FDA), which is responsible for regulating cord blood used in transplants for patients who are not related to the donor, the National Marrow Donor Program (NMDP), which operates a national registry of cord blood units and other sources of stem cells, and the 13 banks with contracts to bank cord blood units for the NCBI.

View [GAO-12-23](#) or key components. For more information, contact Marcia Crosse at (202) 512-7114 or [crossem@gao.gov](mailto:crossem@gao.gov).

# NATIONAL CORD BLOOD INVENTORY

## Practices for Increasing Availability for Transplants and Related Challenges

## What GAO Found

The 13 banks with NCBI contracts reported various practices that could increase the number of cord blood units banked at existing and new collection sites, as well as increasing the diversity of the units collected. However, challenges to increasing collection for these banks include resource limitations, as well as competition from other cord blood banks, which collect units for use only by family members of the donor, and slowing growth in demand for U.S. cord blood units. Cord blood banks reported that increasing staff at collection sites, providing feedback to those who collect cord blood, and lowering the age for those donating could increase the number of units collected for the NCBI at existing sites. Expanding the number of collection sites could also increase the number and diversity of NCBI units. However, the banks in our review reported financial challenges related to increasing the number of units collected at existing or new collection sites, such as a limited ability to address the costs associated with hiring additional staff to cover more hours of collection or to support bank and hospital staff salaries at new sites. These banks identified additional practices for increasing the diversity of the units collected for the NCBI, but also reported that the units collected from some racial groups have lower volumes or cell counts compared to other groups, making such units less likely to meet standards for inclusion in the NCBI. Further, growth in sales of U.S. cord blood units, banks' primary source of funding, has slowed and could challenge banks' efforts. Demand for cord blood could increase or decrease depending on a number of variables, such as whether new research identifies ways to increase the benefits of cord blood or conversely, the development of alternative treatments to cord blood transplantation.

Most of the 13 banks with NCBI contracts reported adopting practices to reduce costs and improve the efficiency of cord blood banking, but also reported some uncertainty about the effect on costs and revenues of complying with FDA licensure regulations that now apply to cord blood. These banks reported practices such as using an early screening process to identify units that do not meet NCBI or the bank's own requirements prior to incurring the costs of processing these units. Further, banks with NCBI contracts reported that efforts to comply with applicable FDA regulations could increase the costs of banking cord blood. For example, some banks reported hiring external consultants or additional staff, reorganizing staff duties, beginning building renovations, or purchasing new processing equipment in attempts to comply with FDA regulations regarding cord blood manufacture and licensing. Some banks also said they were uncertain whether these efforts would comply with FDA requirements or if their collection sites would have to register with the FDA as an establishment that manufactures cord blood. However, FDA officials told GAO that neither individuals nor collection sites that have agreements with banks to collect units will be required to register, though banks must ensure the collection sites comply with FDA regulations. Further, some banks also reported that they were uncertain whether potential increased revenue from licensed units will offset their costs of cord blood banking.

HHS provided additional information regarding our findings, which was incorporated as appropriate.

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## Abbreviations

|      |  |
|------|--|
| FDA  | Food and Drug Administration                 |
| HHS  | Department of Health and Human Services      |
| HLA  | human leukocyte antigens                     |
| HRSA | Health Resources and Services Administration |
| IND  | investigational new drug                     |
| NCBI | National Cord Blood Inventory                |
| NMDP | National Marrow Donor Program                |

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G A O

Accountability \* Integrity \* Reliability

United States Government Accountability Office  
Washington, DC 20548

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### Congressional Committees

Every year, thousands of people are diagnosed with diseases such as leukemia and lymphoma, which damage their blood-forming cells. Many of these patients require transplants of stem cells from umbilical cord blood or the bone marrow or bloodstream of an adult donor to supply healthy blood-forming cells.<sup>1</sup> While the best match for such a transplant is cells from a sibling or other family member, the majority of patients will not find a matching donor in their families and must rely on stem cells from other sources, such as those from unrelated adult donors or umbilical cord blood. In 2005, the number of usable cord blood units<sup>2</sup> in the United States available to the public for transplant was estimated to be about 44,000 units, according to an Institute of Medicine report.<sup>3</sup> In recognition of the need for high quality and genetically diverse units to help those who need a cord blood transplant, Congress passed the Stem Cell Therapeutic and Research Act of 2005 (Stem Cell Act).<sup>4</sup>

The Stem Cell Act directed the Secretary of Health and Human Services (HHS) to enter into contracts with cord blood banks to assist in the collection and maintenance—known as banking—of 150,000 new units of high quality and genetically diverse cord blood.<sup>5</sup> The act directed that these units be made available for transplantation and authorized the appropriation of \$60 million in federal funds through fiscal year 2010.

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<sup>1</sup>For purposes of this report, stem cells refer to blood-forming stem cells.

<sup>2</sup>A cord blood unit available for transplant refers to the stem cells isolated from the blood extracted from a single umbilical cord and the placenta.

<sup>3</sup>The Institute of Medicine report estimated that there were more than 44,000 cord blood units available in the United States, but estimated that not all publicly available cord blood units would meet clinical standards for transplant. See E. A. Meyer, K. Hanna, and K. Gebbie, (Eds.). *Cord Blood: Establishing a National Hematopoietic Stem Cell Bank Program* (Washington, D.C.: National Academies Press, 2005).

<sup>4</sup>Pub. L. No. 109-129, 119 Stat. 2550 (Dec. 20, 2005).

<sup>5</sup>Prior to 2005, cord blood was already being banked for public use in the United States. A 2005 Institute of Medicine report estimated that at least 100,000 new, high quality units should be made available to provide as many potential recipients with a high probability of receiving an effective cord blood unit.

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HHS, through the Health Resources and Services Administration (HRSA), established the National Cord Blood Inventory (NCBI) program, which supports the banking of stem cells derived from umbilical cord blood for use in transplantation.

The Stem Cell Therapeutic and Research Reauthorization Act of 2010<sup>6</sup> (Reauthorization Act) changed the number of cord blood units that are to be available from the NCBI from a total of 150,000 to “at least” 150,000 cord blood units and placed new emphasis on actions such as exploring innovations in cord blood collection and increasing the number of collection sites.<sup>7</sup> The Reauthorization Act authorized additional federal funds to support the growth of publicly available cord blood units and in meeting the inventory goal of the Stem Cell Act to increase the genetic diversity of the supply to improve the probability that all racial and ethnic groups might find a suitable cord blood unit.

Since fiscal year 2007, HRSA has entered into contracts with 13 cord blood banks (banks) to contribute cord blood units to the NCBI. Each contract specifies goals—by racial and ethnic group—for the number of cord blood units to be banked for the NCBI under that contract.<sup>8</sup> As of May 31, 2011, HRSA had reimbursed these banks \$45.7 million for more than 41,000 cord blood units that were banked under contracts for the NCBI.<sup>9</sup> One condition of contracts with HRSA for the NCBI is that the banks will list the units banked for the inventory on a registry maintained by the Cord Blood Coordinating Center,<sup>10</sup> which is operated by the

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<sup>6</sup>Pub. L. No. 111-264, 124 Stat. 2789 (Oct. 8, 2010).

<sup>7</sup>The Reauthorization Act also authorized \$112 million to fund cord blood unit collections through 2015.

<sup>8</sup>HRSA contracts for cord blood units using the following racial and ethnic categories: American Indian/Alaskan Native, Black/African American, Asian, Native Hawaiian/Pacific Islander, White/Caucasian (non-Hispanic), White/Caucasian (Hispanic), and Multi-race.

<sup>9</sup>From 2006 through the end of fiscal year 2010, HRSA had obligated \$56.4 million for the collection of units for the NCBI.

<sup>10</sup>The Cord Blood Coordinating Center is a component of the C.W. Bill Young Cell Transplantation Program, which was established by the Stem Cell Act. The C.W. Bill Young Cell Transplantation Program was designed to help patients who need a stem cell transplant by making information about bone marrow and cord blood transplantation available, providing efficient and effective processes for identifying sources of stem cells through a single electronic system, increasing the numbers of stem cell donors and units that are available, and expanding research to improve patient outcomes.

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National Marrow Donor Program (NMDP) under a contract with HRSA.<sup>11</sup> NMDP's registry is the largest registry worldwide, where physicians and others can search for a stem cell match for patients who need transplants.

The Reauthorization Act required GAO to submit a report reviewing efforts to increase cord blood unit donation and collection for the NCBI to ensure a high quality and genetically diverse inventory of cord blood units. In this report, we describe (1) practices identified to increase banking of cord blood units for the NCBI and related challenges, and (2) practices cord blood banks are using to lower the costs and improve the efficiency of cord blood banking and associated challenges.

To describe the practices identified to increase banking of cord blood units for the NCBI and related challenges, we interviewed officials from HRSA, NMDP, and the 13 banks that have contracts with HRSA for the NCBI. We also attended meetings of the Advisory Council on Blood Stem Cell Transplantation (Advisory Council) and reviewed Advisory Council meeting minutes and reports.<sup>12</sup> We obtained and analyzed reports, publications, and other documents, including those about studies, demonstration programs, and outreach efforts conducted in response to the 2005 Stem Cell Act that focused on efforts to increase the NCBI. We analyzed the NCBI contracts and NMDP data to identify information about goals for collecting cord blood from various racial and ethnic groups, the numbers of cord blood units in this inventory, and HRSA reimbursement rates for cord blood units stored in the NCBI. To assess the reliability of NMDP's data about cord blood units and adult donors listed in NCBI and NMDP's registry, we reviewed relevant documentation about the data and interviewed officials about how the data were compiled. We determined that the data we used for our report were sufficiently reliable for our purposes.

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<sup>11</sup>One of the requirements of the contract with HRSA for the NMDP requires the maintenance of a national registry of cord blood units, including units from the NCBI. Other requirements include working with cord blood banks to recruit cord blood donors and coordinating a network of organizations, including public cord blood banks and transplant centers, to work together to provide quality cord blood transplants.

<sup>12</sup>The Advisory Council was established by the Stem Cell Act to advise, assist, consult with, and make recommendations to the Secretary of HHS on matters related to the activities of federal cell transplantation programs.

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To describe the practices banks use to lower costs and improve the efficiency of cord blood banking and associated challenges, we interviewed representatives from the 13 banks that have HRSA contracts for the NCBI, along with HRSA and NMDP officials. We also attended relevant NMDP and Advisory Council meetings that focused on the financial components of cord blood banking. We reviewed guidance promulgated by the Food and Drug Administration (FDA) in October 2009 that provides recommendations for how to comply with applicable regulatory requirements for licensure of cord blood units, including required activities such as testing, processing, and storage of units. We also reviewed the applicable FDA regulations and interviewed FDA officials. We also reviewed scientific literature about stem cell technologies.

For each of our interviews with the 13 cord blood banks, we used a question set that included open-ended questions about cord blood banking activities. These activities included increasing the number of cord blood donors from various racial and ethnic groups, expanding the number of cord blood units collected at existing collection sites, lowering costs and improving efficiency when collecting and processing cord blood, and complying with regulatory and administrative requirements associated with cord blood banking, including FDA requirements. The open-ended questions asked banks to consider the cord blood banking activities and, for each activity, to describe (1) challenges or barriers the cord blood bank experienced related to this activity; (2) practices, innovations, or incentives used successfully or heard of by the bank; and (3) any other practices, incentives, or technology that could increase the number and genetic diversity of cord blood units in the NCBI. The cord blood bank officials we interviewed provided varying levels of detail when answering our open-ended questions, and may not have provided an exhaustive list of all challenges or barriers cord blood banks have experienced, or all practices, innovations, or incentives that cord blood banks have used or identified.

We conducted our work from March 2011 through September 2011 in accordance with all sections of GAO's Quality Assurance Framework that are relevant to our objectives. The framework requires that we plan and perform the engagement to obtain sufficient and appropriate evidence to meet our stated objectives and to discuss any limitations in our work. We believe that the information and data obtained, and the analysis conducted, provide a reasonable basis for any findings and conclusions in this product.

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## Background

Stem cells from healthy, unrelated donors have been used to treat patients with a variety of diseases, and are considered an appropriate course of treatment for numerous forms of leukemia, lymphoma, and other blood, metabolic, and immune-deficiency disorders. The first source of stem cells used for transplant was bone marrow, but now stem cells from the bloodstream and cord blood can also be used. The success of stem cell transplants depends, among other things,<sup>13</sup> on the extent to which certain blood cell proteins that are part of every donor's genetic make-up—human leukocyte antigens (HLA)—match those in the patient.<sup>14</sup> In general, the more closely related two people are, the more likely it is that their HLA will match. The HLA of members of different racial groups are typically less likely to match one another.

There is evidence that cord blood may not require as exact a match as stem cells from bone marrow or the bloodstream because the antigens in cord blood are less mature. This characteristic means that transplants involving HLA-compatible stem cells from cord blood are less likely to result in graft versus host disease because the donor's cells are less likely to perceive the patient's cells as foreign bodies and attack them.<sup>15</sup> This makes cord blood especially valuable to patients for whom a complete match cannot be found. Persons for whom a complete match may be difficult to find include those from communities with greater genetic diversity, such as African Americans and persons of mixed ethnic heritage. A broad selection of cord blood provides persons with rare HLA types greater access to stem cell transplantation.

In the event that a patient cannot find a sibling or other family member to donate, an HLA match may be sought among the stem cells donated and listed in transplant registries. While there are over 60 stem cell donor registries worldwide, NMDP operates the largest registry,<sup>16</sup> which is a

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<sup>13</sup>The outcome of a transplant also depends on common determinants of treatment success, such as patient age and disease severity.

<sup>14</sup>An antigen is a protein found on the outside of most cells in the body that induces the formation of antibodies. There are a number of antigens in the human body, and HLA are a set of these.

<sup>15</sup>Graft versus host disease occurs when donor cells attack the recipient's normal tissues after transplant, and can lead to organ damage.

<sup>16</sup>NMDP's registry, which lists adult bone marrow donors and cord blood units, is known as Be The Match<sup>®</sup>.

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database of information about cord blood units and adults<sup>17</sup> who are willing to donate stem cells from their bone marrow or bloodstream (adult donors). As of May 31, 2011, NMDP's registry included more than 6.5 million U.S. adult donors and nearly 135,000 cord blood units collected in the United States, of which almost 41,000 are from the NCBI.<sup>18</sup> In January 2011, NMDP estimated that at least 86 percent of most racial and ethnic groups have a close match using all available sources of stem cells listed in its registry.<sup>19</sup> Transplant centers may also find a suitable match through other U.S. and international registries.<sup>20</sup>

Table 1 provides a breakdown by racial and ethnic group of the U.S. cord blood units and adult donors in NMDP's registry. The NCBI is more diverse for some racial and ethnic groups compared to the inventory of cord blood units not in the NCBI or adult donors in NMDP's registry. For example, 14 percent of the NCBI units are from Black/African American

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<sup>17</sup>Adults who are willing to donate stem cells from their bone marrow or bloodstream are volunteers and must be between 18 and 60 years old. Cord blood donation is also voluntary.

<sup>18</sup>As of May 31, 2011, NMDP's registry also included 22,363 cord blood units and 2,797,958 adult donors from seven other countries. Based on GAO analysis of the most recent data from the World Marrow Donor Association, as of January 1, 2010, approximately 63,000 U.S. public cord blood units were not part of NMDP's registry. Transplant centers can use NMDP to search all of these other units for a match using NMDP's search process.

<sup>19</sup>In 2010, NMDP modeled the costs and benefits of cord blood inventory growth and estimated probabilities of a match for patients assuming cord blood from NMDP's registry as the only source of stem cells. The model was developed using the 94,199 cord blood units from the United States and four other countries in the NMDP registry as of December 31, 2008, and provided a 63 percent or better probability of finding a close match for all racial and ethnic groups. According to the model, an inventory of at least 1 million cord blood units would be required for a 90 percent or better probability of finding a unit that is a close match with a minimum treatment dose for most racial and ethnic groups. This model also showed that even with an inventory of 10 million units, the probability of finding such a unit for certain minority groups would remain below 90 percent. Thus, while adding a significant number of units to this inventory could increase the likelihood of finding more closely matched units for transplantation, it does not guarantee that all patients needing a transplant will find an appropriate cord blood match.

<sup>20</sup>NMDP's search process links users to an international repository of data from 65 stem cell donor registries and 47 cord blood banks that is maintained by Bone Marrow Donors Worldwide. As of August 15, 2011, Bone Marrow Donors Worldwide had matching information on 17.8 million adult donors and 492,000 cord blood units worldwide.

donors, compared to 6 percent of those U.S. cord blood units not in the NCBI, and 10 percent of adult donors registered in the United States.

**Table 1: Racial and Ethnic Composition of U.S. Cord Blood Units and U.S. Adult Donors in National Marrow Donor Program's Registry as of May 31, 2011**

| Racial/ethnic category                        | Cord blood unit inventories |                       |                |                           | Adult donor inventory     |                         | Total of units and donors <sup>b</sup> | Percent of total units and donors <sup>b</sup> |
|---|-----------------------------|-----------------------|----------------|---------------------------|---------------------------|-------------------------|--|--|
|   | NCBI units                  | Percent of NCBI units | Non-NCBI units | Percent of Non-NCBI units | Adult donors <sup>a</sup> | Percent of adult donors |  |  |
| American Indian/Alaskan Native <sup>c</sup>   | 40                          | 0 <sup>d</sup>        | 212            | 0 <sup>d</sup>            | 77,237                    | 1                       | 77,489                                 | 1  |
| Asian <sup>c</sup>                            | 1,760                       | 4                     | 3,304          | 4                         | 664,509 <sup>e</sup>      | 10                      | 669,573                                | 10   |
| Black/African American <sup>c</sup>           | 5,502                       | 14                    | 5,957          | 6                         | 657,648                   | 10                      | 669,107                                | 10   |
| Caucasian <sup>f</sup>                        |                             |                       |                |                           | 3,936,322                 | 60                      | 3,936,322                              | 59   |
| Caucasian – Hispanic                          | 12,230                      | 30                    | 9,269          | 10                        |                           |                         | 21,499                                 | 0 <sup>d</sup>                                 |
| Caucasian – non-Hispanic                      | 16,772                      | 41                    | 55,157         | 59                        |                           |                         | 71,929                                 | 1  |
| Hispanic – no race identified                 | 0                           | 0                     | 5,318          | 6                         | 831,731                   | 13                      | 837,049                                | 13   |
| Multi-race <sup>g</sup>                       | 4,373                       | 11                    | 9,487          | 10                        | 370,344                   | 6                       | 384,204                                | 6  |
| Native Hawaiian/Pacific Islander <sup>c</sup> | 54                          | 0 <sup>d</sup>        | 85             | 0 <sup>d</sup>            | 0                         | 0                       | 139                                    | 0 <sup>d</sup>                                 |
| Other <sup>h</sup>                            | 0                           | 0                     | 5,291          | 6                         | 0                         | 0                       | 5,291                                  | 0 <sup>d</sup>                                 |
| <b>Total</b>                                  | <b>40,731</b>               | <b>100</b>            | <b>94,080</b>  | <b>100</b>                | <b>6,537,791</b>          | <b>100</b>              | <b>6,672,602</b>                       | <b>100</b>                                     |

Source: GAO analysis of National Marrow Donor Program data.

<sup>a</sup>Includes adult donors recruited by U.S. donor centers, U.S. recruitment centers, and other U.S. member registries.

<sup>b</sup>Due to differences in the racial and ethnic classification for cord blood units and adult donors, the total numbers and percentages of the total by racial and ethnic group are approximate only.

<sup>c</sup>For cord blood units, this category includes persons of Hispanic ethnicity.

<sup>d</sup>The percentage for this category was greater than zero, but less than one.

<sup>e</sup>Includes Native Hawaiian/Pacific Islanders.

<sup>f</sup>For adult donors, the Caucasian category includes persons of Hispanic ethnicity.

<sup>g</sup>For cord blood units, Multi-race includes persons reporting two or more races. For adult donors, Multi-race includes persons reporting two or more races as well as Hispanic ethnicity plus Black/African-American, Asian, Native Hawaiian/Pacific Islander, or American Indian/Alaskan Native.

<sup>h</sup>Other includes National Marrow Donor Program categories of Other, Decline, or Unknown.

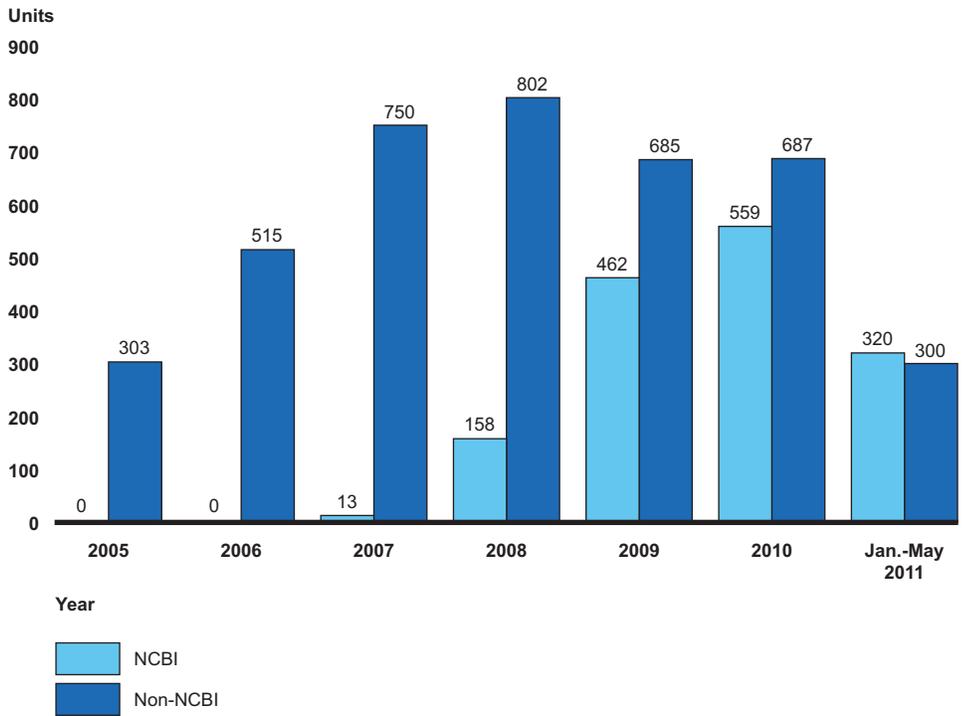
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Of all the U.S. cord blood units listed on NMDP's registry, between January 2005 and May 2011 NMDP facilitated the shipment of 5,554 units throughout the world for use in transplants. About 28 percent of these units were sent to transplant centers outside the United States. Similarly, U.S. transplant centers import cord blood units from outside the United States. As illustrated in figure 1, among U.S. cord blood units listed on the NMDP registry, and for which NMDP facilitated shipment, those from the NCBI represent a growing percentage of cord blood units shipped for use in transplants.<sup>21</sup> In the first 5 months of 2011, 52 percent of the U.S. units in the registry that were sold for use in transplants were from the NCBI.

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<sup>21</sup>Based on GAO analysis of data from the World Marrow Donor Association and NMDP, in 2010, NMDP facilitated 85 percent of the sales of cord blood units by U.S. cord blood banks in contrast to 33 percent in 2005. Where NMDP is not involved, the transaction is between another U.S. registry or a U.S. cord blood bank and the transplant center. With some exceptions, all of the sales facilitated by NMDP were of cord blood units identified through its registry.

**Figure 1: U.S. Cord Blood Units from National Marrow Donor Program's Registry Shipped for Transplant and Facilitated by NMDP, January 2005 through May 2011**



Source: GAO analysis of National Marrow Donor Program data.

A challenge associated with cord blood as a source of stem cells is the small number of cells contained in a typical cord blood unit, which may not be sufficient for a heavier patient. The higher the number of stem cells infused into a transplant patient, the better the outcome. The median number of blood cells in a typical cord blood unit listed in the NMDP registry is 1.07 billion cells, which is sufficient to provide a patient weighing 94 pounds or less a minimum therapeutic dose.<sup>22</sup> An adult bone marrow or bloodstream donor, on average, would provide the same patient with a dose of cells that is many times that which is provided by a single cord blood unit with a median number of cells.

<sup>22</sup>The minimum number of blood stem cells for a therapeutic dose is estimated to be 25 million cells per kilogram of patient weight.

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## Cord Blood Banking for the NCBI

Thirteen banks are currently under contract with HRSA to contribute cord blood units to the NCBI and list the units on the NMDP registry.<sup>23</sup> Each contract specifies goals—by racial and ethnic group—for the number of cord blood units to be banked under that contract. Some of the banks with HRSA contracts are engaged only in cord blood banking while others are subsidiaries of larger organizations such as a university, hospital, or community blood center. Eleven of the 13 banks under contract with HRSA are nonprofit organizations. As a part of their banking activities, the cord blood banks recruit donors, collect cord blood, process and store units, and distribute the units for transplant and research.<sup>24</sup>

Initial education about cord blood donation may be provided by the mother's obstetrician, or from communications from radio, TV, or print sources. Recruitment of a potential donor mother is often done by cord blood banking staff at the hospital upon her arrival to deliver her baby but prior to active labor.<sup>25</sup> Recruitment includes informing the mother about cord blood donation and the benefits of public donation, conducting eligibility screening by administering a maternal questionnaire and a family medical history, and obtaining the donor mother's informed consent.<sup>26</sup> Under NCBI requirements, donor mothers may not give informed consent during active labor.

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<sup>23</sup>Thirteen other banks have contributed to the inventory of domestic cord blood units listed on the NMDP registry but 7 of the 13 have stopped contributing new units, while the other 6 banks are still contributing units.

<sup>24</sup>The Stem Cell Act requires banks to make units that are not appropriate for clinical use available for research.

<sup>25</sup>The active phase of labor begins after the cervix has dilated to a certain diameter and ends when it becomes fully dilated and the presenting part of the baby descends into the mid-pelvis.

<sup>26</sup>Since the cord blood unit will be used for transplant or in clinical research, potential donor mothers must give informed consent consistent with federal regulations. No identifying information about the mother or the baby is provided to the transplant centers or to researchers. Informed consent must be obtained prior to initiation of the collection process. Some of the eligibility screening activities may be completed after the baby has been delivered.

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The 13 banks under contract with HRSA collect cord blood at 114 hospitals—referred to as collection sites—in 24 states.<sup>27</sup> NCBI banks have written agreements with collection sites permitting bank staff, hospital staff, obstetricians, or midwives to collect the cord blood. The collection methods vary by site and can include an obstetrician collecting during a cesarean section; an obstetrician, midwife, or nurse collecting during a vaginal delivery in the second stage of labor; a member of the bank’s staff collecting after the placenta has been delivered; or any combination of these practices. Once collected, the cord blood is placed into a tamper-proof, temperature-monitored container for ground or air transport from the collection site to the cord blood bank.

Upon receipt at the bank, lab personnel check the paperwork and integrity of the cord blood unit. The cord blood is weighed and evaluated for any exposure to extreme temperature changes since collection and then processed. Processing includes various steps such as separating the stem cells from the cord blood; testing the stem cells for potency, viability, and for infectious disease; identifying their genetic characteristics; and freezing and storing the unit.<sup>28</sup> The bank enters data about the cord blood unit, the mother, and the family medical history into an NMDP database for inclusion in NMDP’s national registry. The unit will be searchable on the NMDP registry after its sterility is confirmed. If the unit meets HRSA’s criteria for the inventory and the bank has not yet met its collection goals under its contract, the unit becomes part of the NCBI.<sup>29</sup>

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## HRSA Pilot Project for Remote Collections

In 2009, HRSA initiated a pilot project for remote collections—that is, collections at sites other than those with which a bank has a written agreement. Remote collections through the pilot are performed by physicians or midwives using a cord blood unit collection kit that was provided to eligible mothers by one of the banks participating in the pilot.

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<sup>27</sup>There are 6 other U.S. cord blood banks that contribute cord blood units to the NMDP registry, but do not currently have HRSA contracts. In total, there are 175 hospital collection sites for public cord blood donation in 27 states.

<sup>28</sup>Freezing consists of transferring the cells into bags suitable for freezing in liquid or vapor nitrogen and beginning a controlled cooling of the cells. Once frozen, the stem cells are placed into a special freezer for future retrieval.

<sup>29</sup>If the bank has met its HRSA contract goals, it may continue to collect cord blood units and register them on the NMDP registry or other registries.

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The pilot provides HRSA with data to evaluate the feasibility and utility of the remote collections and inform future decisions to potentially expand the program as a national model for remote collections. It might also provide opportunities to donors who otherwise would be unable to donate because there is no collection site in their area; however, units that are remotely collected cannot currently be added to the NCBI. HRSA officials have said that they are uncertain about whether these units will meet FDA requirements for licensure. In commenting on a draft of this report, HHS noted that HRSA would be willing to revisit the exclusion of these units from the NCBI if they are able to be licensed.

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## HRSA Contracts with Cord Blood Banks

HRSA has awarded contracts to the cord blood banks, based on requirements set out in the Stem Cell Act, through a competitive request-for-proposal process. The act required that the contracts be for 10 years and required HRSA to ensure that no funds would be obligated under the contracts 3 years after the contracts were entered into.<sup>30</sup> HRSA requires banks to make NCBI cord blood units available for transplant indefinitely, or for as long as they are determined viable by HHS.<sup>31</sup> The Reauthorization Act authorized HRSA to obligate funds under new contracts for up to 5 years and to extend the contract period to 10 years past the last date the bank received funds under the contract.<sup>32</sup> HRSA incorporated these changes into its most recent request-for-proposals for new contracts issued on June 15, 2011. HRSA officials said that they are modifying their existing contracts to reflect this change.

As part of the competitive award process, each bank proposes the number of units, by racial and ethnic group, that it will place into the NCBI annually. HRSA uses collection and banking of cord blood units within these racial and ethnic groups as a means of increasing the genetic

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<sup>30</sup>The Stem Cell Act required HRSA to ensure that no funds would be obligated under the contracts after the earlier of 3 years after the contracts were entered into or September 30, 2010. The Stem Cell Act provided for extensions of funding beyond the 3-year limit under certain conditions.

<sup>31</sup>At the May 2011 Advisory Council meeting, a council member presented a summary of research on expiration dates that showed no signs of deterioration of a frozen cord blood unit that is used within 10 years of collection. At a prior meeting, a cord bank official noted that the official's bank has units that have been stable for 18 years.

<sup>32</sup>The Reauthorization Act also provided for extensions in funding beyond the 5 years under a slightly different set of conditions than those specified in the 2005 act.

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diversity of the NCBI. The banks' proposed racial and ethnic targets are then subject to negotiations with HRSA and become part of the contract between HRSA and the bank. Since HRSA began contracting for cord blood units for the NCBI, it has indicated to prospective banks that when awarding contracts, special consideration would be given to banks that demonstrated a superior ability to collect and bank large numbers of cord blood units from underrepresented populations, especially African Americans. In addition, in 2009, HRSA began to negotiate reimbursement rates that varied depending on the racial and ethnic status of the unit. HRSA now pays banks higher rates for units collected from minority groups compared to the rates HRSA pays for units collected from the non-Hispanic Caucasian group.

HRSA's reimbursement rate for each cord blood unit banked for the NCBI is negotiated with each bank. HRSA and NMDP estimate that a bank's cost for each cord blood unit placed on the registry is between \$1,500 and \$2,500. Once awarded a contract, a bank submits invoices to HRSA for payment for units placed on NMDP's registry during the invoice period. Only cord blood units that meet HRSA requirements may be reimbursed by HRSA and placed in the NCBI. HRSA requirements include having a minimum blood cell count per unit of 900 million, a special procedure for wrapping the unit prior to freezing, and a 48-hour deadline for collection, processing, and freezing.<sup>33</sup>

Since the first contract became effective in November 2006, per unit reimbursement rates negotiated by HRSA have ranged from \$648 to \$1,637 with an average payment of \$1,110 per unit.<sup>34</sup> HRSA does not pay the complete costs of banking the unit in order to encourage the bank to seek out other sources of revenue. The largest source of revenue for the banks comes from the sale of cord blood units for transplantation. According to a limited financial analysis<sup>35</sup> of the public cord blood banking

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<sup>33</sup>HRSA also requires that cord blood banks and cord blood units meet all applicable FDA requirements, adhere to selected requirements set forth by NMDP, and that the bank have and maintain cord blood accreditation from either one of the two cord blood banking accrediting bodies—the American Association of Blood Banks or the Foundation for the Accreditation of Cellular Therapy.

<sup>34</sup>The average payment is based on the total number of dollars reimbursed to banks contributing to the NCBI divided by the total number of units on invoices submitted to HRSA between March 2007 and June 6, 2011.

<sup>35</sup>The analysis was based on the costs reported to NMDP by four banks.

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industry conducted by NMDP in 2010, 81 percent of the industry's operating costs are covered by sales of cord blood units for transplantation.<sup>36</sup> As of August 2011, banks received payments ranging from \$22,800 to \$35,000 for cord blood units used for transplantation, with a median payment of \$30,000. Other sources of revenue include charitable contributions, excess revenues from other lines of business engaged in by the bank or its parent organization, and HRSA reimbursement for units banked for the NCBI.

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### Advisory Council on Blood Stem Cell Transplantation

The Advisory Council was created by the 2005 Stem Cell Act and advises the Secretary of HHS and the Administrator of HRSA on how to carry out activities associated with managing the NCBI. The council consists of up to 25 members, including cord blood and bone marrow donor centers, banks, transplant centers, and recipients. The members participate in workgroups that cover specific topics related to stem cell transplantation, such as cord blood collection. The workgroups then develop and present the entire Advisory Council with recommendations that could be made to the Secretary of HHS and HRSA about how the NCBI should function.

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### The Food and Drug Administration's Regulation of Cord Blood

The FDA regulates cord blood for use in transplants when the patient is not related to the donor. FDA requires, among other things, that public cord blood banks register with FDA, screen potential donors for certain diseases according to FDA eligibility criteria, and comply with Current Good Manufacturing Practice, Current Good Tissue Practice, and applicable regulations. Until October 20, 2011, banks can voluntarily distribute cord blood units<sup>37</sup> for use in transplants—when the patient is not related to the cord blood donor—as an investigational new drug (IND).<sup>38</sup>

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<sup>36</sup>For the purposes of our report, public cord blood banking refers to banking cord blood units for use by the general public.

<sup>37</sup>This applies to cord blood units that have been minimally manipulated. FDA regulations further define "minimal manipulation" for structural tissue as "processing that does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement." 21 CFR 1271.3 (2011).

<sup>38</sup>An investigational new drug is a drug that has not been approved for general use by the FDA but is under investigation in clinical trials to evaluate its safety and efficacy by clinical investigators using patients who have consented to participate. The application that is submitted and approved by FDA for a drug to be used as an investigational new drug is referred to as an IND.

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Effective October 20, 2011, all cord blood units, including those currently in cord blood bank inventories, will have to be approved for use by the FDA as an IND or under an FDA-approved license.<sup>39</sup> As of August 2011, none of the banks had an approved license for cord blood, though many were using their own or NMDP's existing IND approvals. Two cord blood banks have submitted license applications, and eleven banks have either completed or scheduled meetings with FDA to discuss the license application process.

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## Banks Reported a Number of Practices and Challenges Related to Increasing Units Banked

Banks reported practices that they believe could increase collections at existing sites, but noted that increased expenditures and other factors could present challenges to banking cord blood. Expanding the number of collection sites could also increase the number and diversity of cord blood units in the NCBI, but banks reported funding challenges related to establishing new sites. Banks also reported additional practices to increase the genetic diversity of the NCBI, but certain characteristics of the cord blood units collected from various racial groups may limit the number of units banked. Remote collection of cord blood units is under consideration. Finally, sales of cord blood units have slowed and could challenge banks' efforts to increase the NCBI.

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<sup>39</sup>On January 20, 1998, FDA issued a notice in the *Federal Register* stating that it was requesting comments on the development of product standards and physical facility and processing controls for certain products, including cord blood. To allow sufficient time for the development of data and standards for these products, the notice also announced the agency's intention to phase in implementation of IND and license application requirements for these products. 63 Fed. Reg. 2985 (Jan. 20, 1998). In 2007, FDA published draft guidance regarding these standards and processing controls and in 2009 FDA published the final guidance. In the October 20, 2009, *Federal Register* notice announcing the final guidance, FDA announced that the phase-in implementation period would end October 20, 2011. 74 Fed. Reg. 53753 (Oct. 20, 2009).

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**Banks Reported Practices That Could Increase Collections at Existing Sites, but Increased Expenditures and Other Factors Could Present Challenges**

Ten of the 13 banks that we interviewed told us that the following practices could increase the number of cord blood units collected at existing collection sites:

- **Adding more staff at collection sites during more hours of the day and/or more days of the week.** For example, one bank said that they are currently losing the opportunity to collect from 25 percent of the women who deliver on the weekends because they do not have staff working 24 hours a day on weekends.
- **Providing recognition or feedback to motivate medical staff about their cord blood collections.** Eight banks told us that they use this practice, and several of these banks noted that this has resulted in increased collections or improved the quality of collection practices, which results in better cord blood units with high volumes and cell counts. Such feedback can also include letting collectors know if the units that they collected did not meet the bank's standards.
- **Lowering the age of consent for donating cord blood.** For example, one bank said it could collect more cord blood units if the age of consent was lowered, particularly at one hospital that serves many women under the age of 18, which is HRSA's current age requirement. In May 2011, the Advisory Council recommended that HRSA broaden the definition of the minimal eligible maternal age for consenting to donate cord blood to reflect the law in each state. As a result, the age of maternal emancipation could be used, which in some states is lower than 18. HRSA officials told us that they are implementing this change in their fiscal year 2011 contracts and in modifications to existing contracts.

Resource limitations, as well as competition from private cord blood banks, could make increasing collections at existing sites challenging.<sup>40</sup> Three of the five banks who discussed adding staff to increase collections noted that they have limited ability to address the increase in expenditures associated with hiring additional staff to cover more hours of collection. Some banks said that they receive additional funds from donations and financial support from parent organizations—in addition to

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<sup>40</sup>Private cord blood banks store cord blood units only for use by a family member. These banks generally charge a fee for banking of the cord blood and leave any decisions regarding the use of the unit to the donor or the donor's family.

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HRSA's reimbursement and cord blood sales—to cover their total cost of operations. Four banks also reported that competition from private banking at the hospital where they are collecting reduces their opportunity for collections as some mothers choose to privately bank their cord blood. For example, one bank said that at hospitals with more affluent patients, the loss of available cord blood units to private banking can exceed 20 percent of the deliveries.

Another challenge reported by four banks was that bank staff must provide continuous opportunities for hospital staff to learn how to collect cord blood due, in part, to turnover of the medical staff collecting cord blood units. For example, residents who are trained to collect cord blood may later move to their next medical rotation or to another hospital. Additionally, one bank said having bank staff routinely conduct training about cord blood collection at the hospital helps ensure the proficiency levels of trained collectors in collecting high quality units by reinforcing proper methods. However, these continuous training requirements force banks to dedicate staff hours to training and reduce their ability to use them to expand hours to support cord blood collections.

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### Expanding the Number of Collection Sites Could Increase the Size and the Diversity of the NCBI, but Banks Reported Challenges Funding New Sites

Another way to increase the number of units in the NCBI, and the inventory's diversity, is to expand the number of collection sites, especially if banks can identify collection sites that will add to the racial and ethnic diversity of their collections. When considering new collection sites, most of the banks we interviewed reported focusing on those sites with a large number of deliveries or those with significant racial and ethnic diversity among their deliveries. Eight of the 13 banks reported using one of the following practices related to expanding collections to sites with a high number of minority births. These include:

- **Using hospital census data to target hospitals with a high number of minority births.** Some banks try to ascertain the ethnic composition of the deliveries at a hospital before approaching the hospital as a potential collection site.
- **Building on existing relationships with collection sites served by the bank's parent organization.** For example, some banks are also part of a community blood center. Hospitals that use the community blood center's services may be encouraged to also operate as a cord blood collection site.

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- **Working with advocacy groups that support cord blood banking to encourage collection sites to participate.** One cord blood bank said that it has added collection sites as a result of their relationships and networking with advocacy groups and foundations.

Twelve of the banks we interviewed identified at least one of the following challenges to adding new collection sites. First, banks reported that they must finance the costs for new collection sites, including bank and hospital staff salaries, supplies, and expenses associated with transporting cord blood, because HRSA does not provide specific funding to defray these costs. Some banks reported being contacted by hospitals that are interested in becoming cord blood collection sites, but the banks say they are limited in the number of sites they can add because of the expense of adding new sites. HRSA officials agreed that it is expensive to add new collection sites. They reported that the agency is encouraging efforts to increase collections in the most efficient manner, consistent with available resources. HRSA officials also said that as long as capacity for additional cord blood collections remains at current collection sites, the agency believes that increasing activity at those sites may be the most efficient means of increasing annual collections. HRSA officials said they do not plan to estimate the number of collection sites to meet the NCBI goal of at least 150,000 units because there are multiple variables to consider when trying to estimate the number of collection sites needed. Instead, the agency is encouraging efforts to increase collections at existing sites. The 13 banks providing cord blood units to the NCBI have agreements with between 2 and 33 collection sites, depending on the bank, for a total of 114 collection sites. A second challenge banks reported was the amount of time they spend developing agreements to collect at sites because of multiple reviews, such as the site's agreement having to be approved by different departments within a hospital.

Finally, one bank reported that a challenge that is specific to expanding to a new collection site with a large number of racial and ethnic deliveries is that these sites are more likely to be understaffed; therefore, nurses and physicians have less time to participate in cord blood collection. The bank reported that when they approach the administration of such hospitals the administration is less likely to agree to participate in cord blood collection because of the additional workload collecting cord blood will place on their staff.

Whether the bank is trying to increase cord blood collection at an existing site or by adding a new site, the banks reported the following practices: identifying a "champion" associated with the collection site, such as a

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doctor or administrator, to support the site's collection efforts and to motivate staff to collect cord blood; providing bank staff or paying the salaries of hospital staff to carry out some or all of the collection activities at each site; contributing to the nurses' education fund at the site; or paying for space to use for collection activities.

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**Banks Reported Additional Practices for Increasing the Genetic Diversity of the NCBI, but Characteristics Associated with Some Units Pose Challenges**

In addition to adding new collection sites with diverse populations, 6 of the 13 banks that we interviewed reported specific practices to recruit donors and bank cord blood from various racial and ethnic groups in order to increase collections that enhance the genetic diversity of the NCBI. For example, some of the banks have tried to reach more African American donors through outreach to community groups such as churches, health fairs, schools, and support groups, such as Mocha Moms, Inc., rather than through events that are conducted in concert with medical practices. As another example, some banks use bilingual recruiters and educational materials to recruit Hispanic donors. One bank reported that the use of bilingual cord blood collectors combined with a targeted public relations effort that included radio advertising and a telethon decreased their refusal rate among the predominantly Spanish-speaking patient population at one hospital from 25 percent to 2 percent within a 48-hour period.

While a few of the banks reported challenges related to the willingness of mothers from racial and ethnic groups to donate cord blood, most banks reported that certain characteristics of the cord blood collected from various racial groups present challenges to banking units that meet HRSA standards for inclusion in the NCBI. Specifically, four banks said issues of medical mistrust, including concern about how units may be used for research, could present a barrier to increasing the number of donors from certain groups. Seven of the banks reported that the cord blood they collected from certain groups, such as African American donors, has a

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lower volume and total cell count especially when compared to units collected from Caucasian donors.<sup>41</sup>

Of the seven banks that reported differences in collections from African Americans compared to others, two of the banks reported collecting more units from African American donors in order to collect one unit that can meet their banking standards relative to the number of units collected and banked from Caucasian donors.<sup>42</sup> In addition, some banks use different volume or cell count thresholds when deciding whether to process cord blood collected from different racial and ethnic groups. One cord blood bank reported that it was able to establish a higher volume threshold to process cord blood from Caucasian donors than cord blood from African American donors because it is easier to collect large-volume units from Caucasian donors. For this bank, cord blood collected from Caucasian donors must contain at least 80 milliliters to be processed further, while cord blood collected from African American donors must contain at least 60 milliliters of blood. Another bank reported that it raised the cell count threshold for units from Caucasian donors to 1.25 billion cells while holding the cell count threshold for units from African American donors at 900 million cells, while for a second bank its cell count threshold to process cord blood from Caucasian donors is 1.5 billion and 1.1 billion cells for other groups. According to some of the banks, this allows them to add cord blood units with higher cell counts, while increasing the number of units from African American donors in the inventory. While some banks reported difficulty in collecting and banking cord blood units with at least 900 million cells from African Americans, the median cell count of such units in NMDP's registry is 1.05 billion cells per unit.

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<sup>41</sup>A 2007 study conducted by one of the banks comparing the characteristics of 556 stored units from African American and Caucasian donors showed that the median total nucleated cells for African American and Caucasian units was 956.5 million and 1.0367 billion, respectively. This difference was found to be statistically significant. See J. Wofford, J. Kemp, D. Regan and M. Creer, "Ethnically mismatched cord blood transplants in African Americans: the Saint Louis Cord Blood Bank experience," *Cytotherapy*, vol. 9, no. 7 (2007), 660-6.

<sup>42</sup>At the May 2011 Advisory Council meeting, a work group's report on the impact of raising the cell count standards for inclusion in the NCBI noted that if the cell count threshold for African American units was raised from 900 million cells to 1.25 billion cells, the percentage of units collected and then banked from this group would decrease from between 20 to 24 percent to 5 percent or less.

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Those banks whose HRSA contracts were effective September 2010 are paid more for cord blood units collected from some minority groups who have historically had difficulty finding a cord blood or adult donor match.<sup>43</sup> HRSA identifies alternative ways federal funds could be distributed to cord blood banks, in part to encourage the collection of diverse cord blood units, in its *Interim Report on How Federal Funds are Distributed to Cord Blood Banks Participating in the National Cord Blood Inventory*, which was provided to Congress on August 11, 2011. The report describes options for modifying the existing methods for distributing funds to cord blood banks, including providing a small amount of up-front funding to cord blood banks to defray start-up costs associated with initiating collections at new sites, providing payment for cord blood units collected remotely at hospitals in which the cord blood bank does not have a written agreement, or providing higher per unit reimbursement rates for cord blood units contracted by HRSA. The report notes that specific recommendations relating to NCBI funding will be included in HHS' next annual Report to Congress on stem cell issues.

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### Remote Collection Is under Consideration for Increasing Cord Blood Units in the NCBI

Another potential approach for increasing the NCBI is to use remote collections. Remote collections involve sending a cord blood collection kit to a mother who plans to deliver her child at a site that does not have a written agreement with a public cord blood bank to routinely allow collections. The kit is then used by the mother's physician or midwife to collect the cord blood unit, which is then transported to the sponsoring cord blood bank. Currently, cord blood units collected remotely cannot be added to the NCBI because HRSA requires banks to have a written agreement with the collection site in order for units collected at the site to be included in the NCBI. Additionally, HRSA officials have said that they are uncertain about whether these units will meet FDA requirements for licensure.

HRSA, through a contract with NMDP, has begun a pilot program with three of its contracted cord blood banks to remotely collect and bank 500 cord blood units to determine whether cord blood donation using a kit-based model can increase the opportunities for public cord blood donation. As of March 2011, the three banks had collected 758 units. Of

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<sup>43</sup>In the summer of 2009, HRSA extended several of the NCBI contracts and included this same differential reimbursement for cord blood units collected from minority donors.

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the 758 units, 68 had been banked—that is, processed and stored; the major reasons that units were discarded and not banked were units arriving at the lab after the allowed time for processing, low volume of cord blood collected, and required labels or documents associated with units being missing.

Two of the three banks participating in the HRSA pilot identified some practices to address challenges identified during the pilot. Some of the lessons learned by one cord blood bank included (1) only initiating remote collections with mothers who start the process no later than 35 weeks gestation;<sup>44</sup> (2) screening mothers for eligibility before sending out a collection kit; and (3) obtaining the doctors' agreement to participate and complete training on cord blood collection. Another bank reported working to develop a web-based training program targeting the physician collectors participating in remote collections that emphasizes the importance of collecting a large-volume cord blood unit. This pilot is scheduled to end September 2011 and the results will be analyzed by HRSA and NMDP at that time.

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### Increase in Demand of U.S. Cord Blood Units Has Slowed and Could Challenge Banks' Efforts to Increase the NCBI

Worldwide demand for U.S. cord blood units has slowed compared to the demand that existed when the NCBI was created. According to a GAO analysis of data from the World Marrow Donor Association, worldwide sales of cord blood units by U.S. banks rose 13.6 percent between 2005 and 2006 and 38.4 percent between 2006 and 2007. In contrast, sales rose only 0.2 percent between 2007 and 2008, 10.4 percent between 2008 and 2009, and only 0.4 percent between 2009 and 2010. According to the Advisory Council and HRSA, the slowing increase in demand for cord blood units may reflect factors that affect the demand for cord blood specifically, or stem cells in general. These factors include the medical community's questions about what diseases are best treated using stem cell transplantation, coverage limitations by health insurers for stem cell transplants, and alternative types of treatment for blood-related cancers that stem cell transplants are used to treat. Because banks rely heavily on cord blood unit sales to finance their operations, slowdowns in demand could adversely affect the banks' ability to finance efforts to expand collections at current collection sites or to expand the number of sites.

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<sup>44</sup>Gestation is the period of time between conception and birth, and is measured in weeks. A normal pregnancy can range from 38 to 42 weeks.

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According to presentations at Advisory Council meetings, stem cell transplantation is an evolving area of medicine in which questions exist about the diseases that are best treated by blood stem cell transplantation or about treatment protocols. Questions related to the practice of stem cell transplantation that are still under active clinical investigation include criteria for stem cell source selection,<sup>45</sup> patient pretransplant preparation regimens, and ways to treat acute and chronic graft versus host disease. In May 2010, the Advisory Council recommended that the Secretary of HHS convene an expert panel to develop consensus regarding an evidence-based list of diagnoses for which stem cell transplantation is an accepted standard of care. The panel has been formed and is in the process of conducting its work.

Insurance coverage for treatment for stem cell transplantation varies. According to an Advisory Council working group, coverage varies because the use of stem cell transplantation as an effective treatment against certain diseases is not well understood by physicians, the insurance industry, or the public. The working group found that public and private insurers may not cover blood stem cell transplantation and if they do, they may cover the procedure only under limited circumstances or may exclude ancillary costs such as costs associated with searching for a donor. For example, the Medicare program covers stem cell transplants from donors for the treatment of certain diseases, and, in some cases, only if the beneficiary receives the transplant as part of a clinical trial.<sup>46</sup>

Alternative treatments to cord blood transplantation may also affect the demand for cord blood. Alternative treatments can include chemotherapy or stem cell transplants from sources other than cord blood. According to HRSA, advances in a drug used in the treatment of some types of leukemia have been successful in achieving remission for some patients, who might otherwise have been treated with a transplant, thereby reducing the demand for cord blood units for this particular group. However, according to at least three banks, it is too early to know whether

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<sup>45</sup>Stem cell sources include bone marrow and the bloodstream from the patient, as well as donors, and cord blood.

<sup>46</sup>This is a description of Medicare's national coverage policy. All other indications for stem cell transplantation not otherwise noted by Medicare as covered or noncovered nationally remain at local Medicare administrative contractor discretion.

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advances in other types of treatments will reduce the future demand for cord blood.

Alternatively, other potential factors might increase the demand for cord blood. In 2010, a clinical researcher at the Fred Hutchinson Cancer Research Center successfully expanded the number of blood stem cells in cord blood units up to 164-fold. This could be beneficial because a higher number of stem cells in a cord blood unit could more quickly reconstitute a patient's immune system with new stem cells, thereby lowering the risk that a patient would acquire life-threatening infections during this recovery period. Researchers are also examining other types of stem cells contained in cord blood for possible future clinical applications including tissue regeneration. If such advancements lead to future increases in demand, it would also increase banks' ability to finance their efforts to expand collections and more quickly reach the NCBI goal.

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## Most Banks Have Adopted Practices to Reduce Costs, but Are Uncertain about the Effect of Regulations on Costs and Revenues

Most banks reported that they had adopted practices to reduce the costs of cord blood banking, but some expressed concern that one proposed practice could reduce the genetic diversity of the NCBI. Some banks also reported uncertainty about the effect of FDA regulations on costs and revenues.

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## Banks Reported Practices to Lower Costs, but Also Concerns that One Practice Could Adversely Affect the Genetic Diversity of the NCBI

Banks reported using a variety of practices to reduce the costs or to improve the efficiency of some of the activities associated with cord blood banking. One cost-saving practice reported by 11 of the 13 banks we interviewed is to use an early screening process to identify units that do not meet the NCBI cell count threshold of 900 million cells or the bank's own volume or weight requirements before incurring the costs of processing these units. This practice of establishing a preprocessing threshold eliminates the costs of processing units unlikely to be reimbursed by HRSA or to be desirable for use in stem cell

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transplantation.<sup>47</sup> Preprocessing thresholds reported by the banks ranged from 900 million to 1.5 billion cells.<sup>48</sup> Some of these banks reported lower thresholds for units from African American donors and other donor groups.

However, a proposed practice could reduce the genetic diversity of collections, including those for the NCBI. A limited financial analysis of public cord blood banking conducted by NMDP in 2010 found that raising the preprocessing threshold for all public cord blood units to at least 1.25 billion cells would allow the cord blood banking industry (but not necessarily individual banks) to gain enough excess revenue within 2 years to cover their annual operating costs.<sup>49</sup> According to NMDP's analysis, increasing the percentage of higher cell count cord blood units in the public inventory, including those units in the NCBI, would respond to the increasing demand for higher cell count cord blood units. However, some of the cord blood banks have expressed concerns about NMDP's analysis, including that the industry averages used did not adequately account for bank variations in overhead and operating costs, that the model's assumptions about future demand were too high, and that NMDP did not take into account the potential effect of raising the cell count threshold on some groups' access to transplants. An official from NMDP acknowledged that, at higher thresholds, banks would process fewer units, particularly in some minority populations, which could reduce the genetic diversity of cord blood inventories, including the NCBI. According to HRSA, the Center for International Blood and Marrow Transplant Research is currently analyzing whether matching cord blood across ethnicities is as effective as matching cord blood between donors and recipients of the same groups.

Some banks reported other practices for reducing their costs by increasing collaboration with organizations that have activities that are related to those of the bank.

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<sup>47</sup>In 2010, 82 percent of all NMDP cord blood units chosen for transplantation had cell counts equal to or greater than 1.25 billion cells.

<sup>48</sup>The 11 banks reported preprocessing thresholds based on cell count only (6 banks), both cell count and volume (3 banks), volume only (1 bank), and weight only (1 bank).

<sup>49</sup>NMDP's analysis included HRSA reimbursement as one of the industry's revenue sources.

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- To lower the cost of transportation, two banks rely on their local community blood bank to transport cord blood units collected at regional hospitals.
  - To lower its costs of donor recruitment and ongoing staff support to collection sites, one bank has developed partnerships with two nonprofit organizations dedicated to increasing patients' access to cord blood transplants. The two organizations have assumed some of the responsibilities normally assigned to bank staff, including monitoring collection activity at the site, ensuring an adequate supply of collection kits, and answering questions from site staff about cord blood collection. One of the organizations also pays for the collection kits at a collection site.
  - To lower the per unit cost of processing and storing cord blood units, two banks reported that they also process and store units for companies that market cord blood collection to expectant mothers for future use by the baby or other family members.
  - To lower the bank's costs of donor recruitment, one bank reported that it has entered into an arrangement with a neighboring state. The state is paying for staff to screen potential donor mothers and to obtain their informed consent, to pack and transport cord blood collected by physicians, and to administratively support the program. Upon receipt of the cord blood, the bank will then process and store the units. If a unit is sold for transplant, the bank will share the revenue with the state.

In other efforts to reduce costs, one bank shifted recruiters' time that was spent obtaining informed consent from nonhospital settings to the hospital. Initially, bank staff obtained consent from potential donor mothers at clinics, health fairs, and birthing classes weeks and months prior to delivery. However, the bank noticed that many of these women, upon arrival at the hospital to deliver their babies, forgot their paperwork or did not inform the hospital staff of their desire to donate. To increase the effectiveness of the staff's efforts, the bank shifted the informed consent process to the hospital where the time spent in this process could ensure a greater number of mothers actually donating. Finally, to improve the efficiency of processing cord blood, two banks reported moving from manual to automated cord blood processing systems. According to one of the banks, the new system will allow the bank to increase the number of units processed threefold without changing the number of laboratory technicians.

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## Some Banks Reported Uncertainty about the Effect of Complying with FDA Licensure Regulations on Costs and Revenues

Five of the 13 banks reported that their efforts to apply for FDA licensure have already increased their costs or noted that the total cost burden of operating as an FDA licensed bank is unclear. For example, two banks reported having to hire external consultants or reorganize staff duties to complete the application for licensure. Two banks reported that they have already incurred significant expenditures to make building renovations, buy new equipment, or hire additional staff in attempts to comply with FDA regulations.

Further, banks reported uncertainty in how to meet some of FDA's regulatory and administrative requirements for licensure, which could result in increased expenditures to meet these requirements. Nine of the 13 banks reported that these concerns related to whether the spaces and equipment currently used by banks to collect and process cord blood will satisfy FDA licensure requirements or whether the banks will lose collection sites if licensure requirements force collection sites to register with the FDA. Some banks questioned whether FDA would require a "clean room" for processing units, which not all banks currently have. Banks also expressed concern that collection sites will no longer want to participate in public cord blood collection if FDA requires the sites to register with FDA. According to FDA officials, establishments that manufacture certain products, which include cord blood, are required to register and list their products with the FDA.<sup>50</sup> These establishments are subject to FDA inspection. Some banks are concerned about the additional burdens that this will impose. If banks lose collection sites because of concerns about possible FDA inspection, the banks would be subject to the additional costs of adding new sites, which would include training site staff, providing collection materials, and transporting the units from the site to the bank. However, FDA officials told GAO in a July 2011 interview that they are taking the approach that neither individuals nor hospitals that have agreements with banks to collect cord blood will be required to register separately with FDA. FDA officials said that such entities are required to comply with product requirements applicable to their collecting activities, and the cord blood bank is responsible for ensuring that these entities under contract with the bank comply with FDA regulations.

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<sup>50</sup>These products include human cells, tissues, or cellular- and tissue-based products.

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FDA officials have said that the benefits of cord blood licensure include greater assurance among doctors and patients of the quality and efficacy of cord blood units. Additionally, with licensure, cord blood banks will be able to sell cord blood units without IND pricing restrictions. However, some banks also reported that they were uncertain whether potential increased revenue from licensed units will offset their costs. In addition, the Advisory Council has expressed concerns about the potential for FDA's licensure requirements to result in increased cost and decreased availability of public cord blood units without necessarily increasing the safety, stability, potency, or purity of the units. In November 2010, the Advisory Council recommended that the FDA meet with the banks applying for licensure to share and resolve specific concerns regarding licensure. FDA officials have been meeting individually with cord blood banks to discuss the specifics of each bank's licensure application and circumstances. While FDA officials have stated that they could not confirm, for example, that a certain facility design would be acceptable in all situations, they said that they could provide clarification of the manufacturing regulations for individual banks.

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## Concluding Observations

Since 2005, HRSA has contracted for about 30 percent of the minimum statutory goal of at least 150,000 new units of high quality cord blood. While not yet meeting the statutory goal, the NCBI has increased the number of high quality, genetically diverse units available for transplantation in the United States. This inventory, along with other sources of cord blood stem cells, contributed to making nearly 135,000 U.S. cord blood units available in the NMDP registry. In 2010, about 1,200 patients had received cord blood transplants from units identified in the registry. However, although there are nearly 135,000 cord blood units in the registry, members of certain racial and ethnic groups will continue to have more difficulty finding a closely matched unit than other groups. This disparity would be reduced, though not completely eliminated, if the number of units available were expanded.

Cord blood banks contracting with HRSA are taking steps to increase collections and make their operations more efficient and cost-effective, but continuing advances in medical science make it difficult to predict future demand for cord blood stem cells and the resulting level of collections that should be undertaken. Based on current science, cord blood appears to present some advantages over other stem cell sources—such as bone marrow—both in terms of health benefits and in being already collected and readily available for use when listed in public registries. These advantages may increase in future years if factors that

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could increase the quality of cord blood units are realized or they may diminish if alternatives to cord blood are developed or improved.

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## Agency Comments

In commenting on a draft of this report, HHS provided additional information concerning several content areas of the report, including demand for U.S. cord blood units, HRSA's pilot project for remote collections of cord blood units, and efforts to increase the diversity of the cord blood units collected for the NCBI. We included that additional information where appropriate. HHS's comments are printed in appendix I. HHS also provided technical comments, which we incorporated as appropriate.

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We are sending copies of this report to the Secretary of Health and Human Services and other interested parties. In addition, the report will be available at no charge on GAO's website at <http://www.gao.gov>.

If you or your staff have any questions about this report, please contact me at (202) 512-7114 or at [crossem@gao.gov](mailto:crossem@gao.gov). Contact points for our Office of Congressional Relations and Office of Public Affairs can be found on the last page of this report. Other major contributors to this report are listed in appendix II.



Marcia Crosse  
Director, Health Care

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# Appendix I: Comments from the Department of Health and Human Services



DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation  
Washington, DC 20201

SEP 27 2011

Marcia Crosse, Director  
HealthCare  
U.S. Government Accountability Office  
441 G Street NW  
Washington, DC 20548

Dear Ms. Crosse:

Attached are comments on the U.S. Government Accountability Office's (GAO) draft report entitled, "NATIONAL CORD BLOOD INVENTORY: Practices for Increasing Availability for Transplants and Related Challenges" (GAO-12-23).

The Department appreciates the opportunity to review this report before its publication.

Sincerely,

A handwritten signature in cursive script that reads "Jim R. Esquea".

Jim R. Esquea  
Assistant Secretary for Legislation

Attachment

GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) TO THE GOVERNMENT ACCOUNTABILITY OFFICE'S DRAFT REPORT ENTITLED, "NATIONAL CORD BLOOD INVENTORY: PRACTICES FOR INCREASING AVAILABILITY FOR TRANSPLANTS AND RELATED CHALLENGES" (GAO-12-23)

Page 7 - HRSA requests that the following sentence be added to the paragraph: "Similarly, 30 percent of NCBI units are from Hispanic donors versus 16 percent for non-NCBI CBUs and 13 percent for adult donors." This will ensure that a comparison is provided for Hispanic donors.

Page 12 - last sentence under the header *HRSA Pilot Project for Remote Collections*. HRSA requests that the report note why units from remote collections are not included in the NCBI. Please add the following sentence: "Banks would need to obtain licensure from FDA for CBU collected using this method. HRSA has expressed its willingness to re-visit the exclusion of such units from the NCBI once licensure is achieved."

Page 13, line 3 - HRSA requests that the agency's rationale for differential reimbursement rates across different racial/ethnic groups be added here. HRSA requests that the challenges associated with obtaining units of qualifying cell counts from certain groups and HRSA's goal of continuing to grow the inventory for patients who have historically had a difficult time finding an adequate adult donor or cord blood unit for transplantation be noted here as this section addresses the difficulty, quality, and costs of the collection and use of cord blood for minority and underserved populations (HRSA's payment for units collected from minority groups is addressed again on page 26).

Page 18, paragraph one, bullet #1 - HRSA requests that the bullet note that the NMDP provided cord blood banks with information on U.S. hospitals that are located in metropolitan areas with large African-American and Asian populations and where there are large numbers of births.

Page 20, last sentence - HRSA requests that GAO underscore the lower nucleated cell counts between African-American donors and other racial groups and ethnicities by stating that no banks reported equivalent cell counts between African-American donors and other groups.

Page 23 - HRSA requests that this section, *Increase in Demand of Cord Blood Units Has Slowed and Could Challenge Banks' Efforts to Increase the NCBI*, be modified.

- HRSA requests that the section start by addressing the U.S. experience and only mentioning briefly worldwide demand. The NCBI and C.W. Bill Young Cell Transplantation Program are intended to increase access to transplant for U.S. patients. GAO's emphasis on decreased/slowed demand for cord blood worldwide may mislead readers about the U.S. issues. In fact, NMDP-facilitated cord blood transplants and CBU shipments continue to increase. Additionally, cord blood continues to play a critical role in minority transplants facilitated by the NMDP. Cord blood transplants are increasing in the U.S., though less rapidly than in years past. Please note the cost pressures on cord blood transplants, as well as cord blood banking, as factors impacting the decreased rate of growth in cord blood transplants.

GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) TO  
THE GOVERNMENT ACCOUNTABILITY OFFICE'S DRAFT REPORT ENTITLED, "NATIONAL CORD  
BLOOD INVENTORY: PRACTICES FOR INCREASING AVAILABILITY FOR TRANSPLANTS AND  
RELATED CHALLENGES" (GAO-12-23)

- CBU shipments continue to increase significantly as more cord blood transplants that use multiple cord blood units are performed for adults. Overall, NMDP cord blood transplants are increasing.

Page 30, paragraph 1, last two sentences under the section, *Concluding Observations* - Although the statement is true, it could be read to imply additional CBU would make no difference. HRSA requests changing the last sentence to read: "This disparity would be reduced, though not completely eliminated, if the number of available units were expanded."

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# Appendix II: GAO Contact and Staff Acknowledgments

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## GAO Contact

Marcia Crosse, (202) 512-7114 or [crossem@gao.gov](mailto:crossem@gao.gov)

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## Staff Acknowledgments

In addition to the contact named above, Karen Doran, Assistant Director; Carrie Davidson; Cathleen Hamann; Toni Harrison; Natalie Herzog; and Monica Perez-Nelson made key contributions to this report.

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