

## Recommended Structure of a National Program

The committee's central charge was to advise the Health Resources and Services Administration (HRSA) on how a National Cord Blood Stem Cell Bank Program should be structured. The committee believes that the primary goal of any program structure created should be able to provide transplant physicians the assurance that when they determine that a hematopoietic progenitor cell (HPC) transplant from an unrelated donor is appropriate, the process for locating the best available cells is accurate and timely; that the procured cells are of high quality; and that information on the clinical experience of the transplant recipient is subsequently collected for ongoing research, quality assurance, and clinical improvement. It is clear to the committee that, at present, umbilical cord blood banks operate under various standards, that the outcomes of a significant proportion of cord blood transplants are not reported either to the bank from which the unit was obtained or to the transplant community in general, and that the economic status of cord blood banking is fragile. The structure that is ultimately identified should address all three of these issues.

Throughout its discussion the committee was aware that current participants in cord blood collection, banking, and transplantation hold strong views about the ideal structure of a national program (summarized in Chapter 1). In addition, the committee recognized that some activities and components of a comprehensive structure already exist, such as a good patient education and advocacy system; however, what is in place is not sufficient to meet for present needs and any structure identified now should be responsive to emerging knowledge about HPC transplantation and should have the capacity to adjust its procedures and structure as necessary and appropriate to incorporate that emerging knowledge.

The committee also considered lessons learned in the process of building a network for facilitating solid transplantation, which are well documented and the subject of a previous Institute of Medicine (IOM) report, *Organ Procurement and Transplantation: Assessing Current Policies and the Potential of the DHHS Final Rule* (IOM, 1999). The committee attempted to learn from this history, to build on existing strengths and to avoid the previously identified pitfalls.

A single national network for access to all sources of HPCs (whether they be adult bone marrow, peripheral blood, or cord blood) would simplify some aspects of the transplantation process, including search efforts, outcomes data collection and analysis, research, and policy making. In fact, for adult donors (of either bone marrow or peripheral blood stem cells), a national network of donor registries and a process for efficient searches already exists and has been regularly strengthened. The National Marrow Donor Program (NMDP) receives substantial federal funding, maintains an informative website, provides access to adult donors (both in the United States and internationally), provides extensive patient and clinician support, and maintains a database to track transplant outcomes. It operates an extensive program and also provides statistical support for making these data, as well as statistical support, available for research. Furthermore, participation in this national network is predicated upon adherence to standards of data quality, clinical performance, and responsiveness to inquiries. This network has also extended its activity into the cord blood transplant process.

However, the NMDP, as currently configured, is not a simple solution for cord blood banking. While many aspects to be performed by the proposed National Cord Blood Stem Cell Bank Network have analogs in the NMDP (e.g. searching, outcomes tracking, patient support) not all US and few non-US cord blood banks participate in the NMDP network,<sup>1</sup> and the procurement and banking of donated cord blood are processes very different from those used to recruit and track potential adult donors.

The committee also heard anecdotal evidence that the NMDP's infrastructure, while comprehensive, can also be unwieldy. Of particular concern to the committee were the reported delays some banks encountered when trying to get their inventory listed in the NMDP's registry, both because of lack of compatibility from system to system, and because of lack of bank personnel to do the data entry and provide the information in a manner specific to the NMDP's search system. This means that in spite of a centralized search, many transplant centers may have to still search banks specifically to get the most up-to-date information on units.

Furthermore, the committee has heard concerns that the NMDP's focus on adult donors would prevent it from paying adequate attention to cord blood's development, though others felt that such concerns were overstated given evidence of substantial investment by NMDP in its cord blood program in recent years.

Even without a national cord blood program, there has been movement toward the use of more uniform methods of reporting of search results, which allows transplant center personnel to more easily evaluate and choose among the available units. However, the lack of a complete, coordinated network for assessing the national inventory and evaluating the outcome of transplants using units from various banks have made it difficult for the committee to accurately assess the status and quality of the available cord blood units and their current use in transplantation.

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<sup>1</sup>Among the domestic cord blood banks that remain independent are the New York Blood Center, Michigan Community Blood Centers, and the University of Colorado Cord Blood Bank.

Given all of these considerations, the committee sought to incorporate the following elements into the final structure of the network:

- assured clinical access through substantial increases in the current inventory,
- maximal efficiency of processes,
- minimal redundancy of systems and investment,
- guaranteed cord blood unit quality,
- protected patient and donor confidentiality,
- timely data collection and outcome reporting,
- transparent policies and procedures,
- the long-term financial viability of cord blood banks,
- enhanced communication among all parties, and
- adherence to ethical standards.

In moving toward the structure described below, the U.S. Department of Health and Human Services (DHHS) is urged to make transparent to the transplant community, banks, patients, and the public the process for establishing, implementing, and evaluating a national program.

Table 1-1 in Chapter 1 compares two perspectives on what an ideal national cord blood program would look like. Table 7-1 reviews the elements presented in that table and briefly describes how these might be developed if the structure recommended in this chapter is adopted. The committee did not choose elements from either of the two main parties, but rather created its own ideal. For this reason, it is important for readers of this report to refrain from any attempt to develop a scorecard on the relative strengths of either reported perspective.

**TABLE 7-1** Key Functions of a National Cord Blood Program, as Envisioned by the Institute of Medicine Committee

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Governance:	A National Cord Blood Policy Board (the National Board) should establish policies and regularly monitor all issues related to cord blood uses. Day-to-day management should be done by a National Cord Blood Center, identified by HRSA through a competitive process.
Search Database:	Data on both cord blood units available for transplantation and patient outcomes after the transplant are needed. As these two types of data serve different purposes, it is not necessary for them to be available in a single integrated database.
Unit Selection:	The National Cord Blood Center should facilitate coordinated searches while allowing transplant centers to customize reports according to local selection practices, and to work directly with cord blood banks. Search support should provide guidance or information on the selection of adult donor versus cord blood graft sources.
Source of Transplanted Material:	The choice of the source for HPCs must be driven by the patients' needs and the best available evidence about the different sources of material for transplantation. This evidence about uses of all sources of material for transplantation must be regularly updated and made available.
Finances:	Federal funds for support of cord blood banking should be allocated to the expansion of the inventory of banked units with some funds reserved for the national infrastructure that will be needed.
Cord Blood Bank Selection:	Banks wishing to participate in the National Cord Blood Program should meet the standards to be established by the National Board and must meet all data requirements of the national program.
Standards:	Quality standards for banks, donor centers, and transplant centers will be set by an accrediting agency that is independent of the National Cord Blood Center. The accrediting agency will be chosen by a competitive mechanism.
Outcomes Data:	The National Board should have ready access to comprehensive data that allow for analysis of all transplants in which HPCs are used and that can be used to establish the desired inventory size and readily update the policies of the National Cord Blood Program.

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## NATIONAL OVERSIGHT

**Recommendation 7.1: The Secretary of U.S. Department of Health and Human Services (DHHS) should establish a National Cord Blood Policy Board (National Board) to set policy and advise the Secretary of DHHS and the Health Resources and Services Administration on policy regarding the donation, collection, and uses of umbilical cord blood, as well as on research needed to improve and augment the uses of the cells in cord blood. The National Board should routinely review outcomes data for all clinical uses of umbilical cord blood and develop policy on changes in inventory size, procedures, and standards, as experience and emerging science indicate. The National Board should ensure active interactions among the various organizations involved in adult donor peripheral blood and bone marrow transplantation and umbilical cord blood transplantation.**

Relating directly to the earlier mentioned goal of transparent policies and procedures, this new National Board should be established by the Secretary of DHHS. As a chartered body subject to the Federal Advisory Committee Act (96 Stat. 1822), the charter and all appointments should be publicly announced in the *Federal Register*, and meetings of the National Board should be open to interested parties. The National Board should include experts in cord blood transplantation; cord blood collection, storage, and distribution; clinical transplantation; ethics; epidemiology; statistics; informatics; health care services; and other relevant areas. In addition, the National Board should have representation from the public. The members of the National Board should be objective and free of financial and professional conflicts of interest.

The committee urges the National Board to play an active role in ensuring that the lessons learned during the development and growth of NMDP, COBLT, and solid-organ transplant program are appropriately applied to all funding and policy decisions regarding the National Cord Blood Program. For example, all policy-setting activities should be the purview of the National Board and not the coordinating center, as described below. This arrangement contrasts with the blending of policy and day-to-day management within the Organ Procurement Transplantation Network, in which the role of the DHHS Scientific Advisory Committee for Organ Transplantation is solely advisory; that committee has no policy-making function.

The National Board should meet no less frequently than three times a year to remain abreast of the developments in the fields of cord blood transplantation and banking and to set policy accordingly. The IOM committee assumes that more frequent meetings may be essential during the formative period to develop a clear perspective on the field of HPC transplantation and to establish the initial policies.

## STRUCTURE AND GOVERNANCE

**Recommendation 7.2: The Health Resources and Services Administration should use an open, competitive process to establish and fund a National Cord Blood Coordinating Center (the Cord Blood Center). The Cord Blood Center would have day-to-day responsibility for carrying out the policies promulgated by the National Board, including:**

- **managing a national network linking participating transplant centers with participating cord blood banks;**
- **collecting data on the outcomes of subsequent cord blood transplants; and**
- **ensuring that data regarding banked cord blood units and the outcomes of cord blood transplants are available to policy makers (including the National Board) for decision making, the participating banks and transplant centers for quality assurance purposes, and researchers seeking to better understand and expand the uses of cord blood.**

In soliciting proposals for the Cord Blood Center, there should be no requirement that all of the program components be centrally managed, provided that satisfactory mechanisms for coordination are proposed, nor should the central management of all program components be prohibited. The request for proposal (RFP) should require that applicants specify a mechanism that ensures efficient access to the available units and that also fosters the evolution of best practices. In line with the above mentioned goal of efficiency, members of the IOM committee are concerned that a requirement to force all aspects of cord blood activity into a single, central organization might slow the matching process and might stifle the creativity of the participating banks and transplant centers and their ability to search for improved practices; responses to the RFP should specifically address this concern. In line with the goal of enhanced communication between the parties, proposals should describe mechanisms for fostering meaningful links between and among transplant centers and banks, a means for achieving appropriate standardization, and methods that provide clinicians with access to the information needed for clinical decision making.

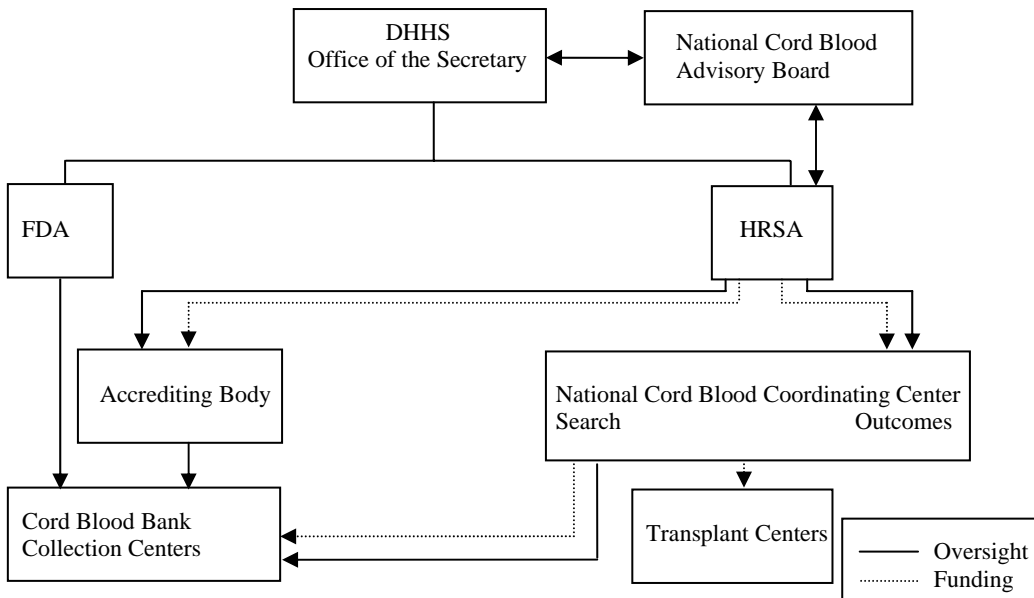
With regard to the goal of minimal redundancy, the committee envisions not the creation of something new, but rather the development of an appropriate mechanism for coordinating the elements that already exist. While the committee does not believe that any single party is currently doing all the elements that coordinating center would perform, the committee does hold the opinion that the elements exist and need a means by which they can be brought together, or conversely, that a single party could develop

the mechanisms necessary to support the bank program – bearing in mind the aforementioned goals of efficiency and the need to support cord blood in its infancy.

Figure 7-1 illustrates the relationships that the committee envisions under the governance structure described in these recommendations.

### Source of Transplanted Material

The National Board should set policy and the Cord Blood Center should perform its functions with full recognition that cord blood, peripheral blood, and bone marrow are complementary, alternative sources of HPCs. The source chosen must be driven by the patients’ needs and anticipated outcomes on the basis of the best available evidence rather than on an a priori selection of the source. Thus, every effort should be made to collaborate, as appropriate, with NMDP and other bone marrow donor registries. However, IOM committee members heard a number of expressions of anxiety that NMDP might, because of its resources, unduly influence national decisions about HPC transplantation. For that reason, it is essential that the National Board should assure all parties that policy decisions are made in a fair and unbiased way and that cord blood transplantation is supported in its emergence as a therapeutic option in the complicated world of HPC transplantation.



**FIGURE 7-1** The relationships that the IOM committee envisions under the governance structure described in its recommendations.

### Inventory Database and Unit Selection

The Cord Blood Center should work to explore the best possible methods for transplant physicians to search the database of the cord blood inventory, obtain confirmatory human leukocyte antigen (HLA) typing, and reserve and select cord blood units for transplantation on the basis of the best available evidence. These protocols will need regular review, as the field is changing rapidly. These methods should include a format for reporting search results that provides a coherent summary of all units available through the national program and that incorporates flexibility to allow transplant centers to customize reports to meet the needs of local selection practices. For clinical purposes, a central database of all available units is not essential (but also not precluded), as long as current information on the inventory in all participating banks is accessible at the time of a search. The data system and policies should allow individual participating transplant centers to work directly with participating banks to locate a unit, if desired. In addition, the Cord Blood Center should work to facilitate efficient access to units collected internationally, as long as they fulfill the quality requirements set by the national system and are compliant with Food and Drug Administration (FDA) regulations.

The committee heard from many sources regarding the desirability of ‘one-stop-shopping’ for all sources of HPC. As mentioned in Chapter 1, this is not currently a realistic goal. However, upon the development of a comprehensive outcomes database (see Recommendation 7.3), and evaluation of the data therein, the National Cord Blood Policy Board should consider working toward the development of a mechanism by which all sources of HPCs can be concurrently searched.

### Outcomes Data

**Recommendation 7.3: The National Board should support the development of an outcomes database that can guide decisions on inventory size and track cord blood bank quality and other policies as well as assist with the assessment of outcomes from *all* sources of hematopoietic progenitor cells.**

This recommendation is directly linked to the goal of timely data and outcomes reporting. Collection of outcomes data by the Cord Blood Center should follow a standardized format and capture the appropriate clinical information that is required by cord blood banks to meet their quality assurance, accreditation, and regulatory requirements. This might be achieved internally by the new Cord Blood Center or, perhaps more economically, by contracting with an existing organization having appropriate capacity. Any transplant center desiring to participate in the national program should agree to supply timely data on the immediate and long-term outcomes for patients receiving cord blood units supplied by the national program. The format for this data-reporting process should be consistent with that used for adult donor transplantation and, as mentioned earlier, to

foster the development of algorithms to identify the optimal graft source for diverse patient groups, a single outcomes database for adult donor and cord blood HPC transplants should be considered, building on existing efforts if possible. This information would not only ensure that complete data on the clinical outcomes following transplantation are collected, but would also provide data to qualified researchers as well as policy makers and clinicians interested in overall analysis of both national adult donor and cord blood resources. Because these data requirements will impose a burden on the participating organizations, and because the collection and submission of high-quality data are time-consuming activities, some financial support will be needed to assist transplant centers with their data collection and data transfer activities.

### Finances

**Recommendation 7.4: The national program should provide the participating banks with the financial support that they need to achieve an inventory sufficient to provide as many potential recipients as possible with a high probability of a therapeutically effective cord blood unit when one is clinically indicated.**

**Finding 7.1: At present, if it is assumed that an effective cord blood unit should have a minimum cell dose of  $>2.5 \times 10^7$  nucleated cells per kilogram of recipient body weight with two or fewer human leukocyte antigen (HLA) mismatches at HLA-A, HLA-B (intermediate resolution), and HLA-DRB1 (high resolution), the committee estimates that at least 100,000 new, high-quality units need to be added to the current inventory to achieve the inventory size recommended in Recommendation 7.4.**

The committee believes that expansion of the current inventory with units that meet the established standards should receive the highest priority in the near future to facilitate enhanced patient access. As discussed in Chapter 6, the National Board should offer support to participating banks that are designing expansion plans for their inventories to include racially and ethnically diverse sources of cord blood, thus enhancing access to cord blood by individuals in racial and ethnic minority groups. Participating banks should be reimbursed for the unit that they supply for transplantation through health care payment systems in a manner that allows them to become more self-sufficient by the end of the period of federal funding.

**Recommendation 7.5: Some portion of the funds dedicated to the establishment of the national program should be reserved to support the infrastructure described in this chapter.**

The national program will require an infrastructure that supports the outcomes database, as well as the Cord Blood Center and the National Board. The ongoing program of accreditation of participating centers should be supported by the common method of participant fees. To ensure that the available cord blood units are used to the greatest advantage for patient care, federal funds should be provided for start-up and ongoing costs for the development of mechanisms for the sharing and publication of outcomes data; verification that the participating banks and transplant centers meet quality assurance standards; and encouragement of innovation and improvement in banking, matching, and related processes.

Though as mentioned earlier, the committee does not envision the necessity of creating completely new components for the national program, the means to coordinate the program will require support initially.

#### **Cord Blood Bank Selection**

**Recommendation 7.6: The National Board should establish minimum criteria for quality standards and data sharing for banks participating in the national program. The Cord Blood Center should monitor and manage the implementation of those standards and coordinate a competitive process for the distribution of funds to qualifying banks for inventory growth.**

In order to support the goal of guaranteed quality, banks should be selected on the basis of published criteria and demonstration of the quality of their operations (e.g., accreditation and licensure) by their responses to a formal RFP issued by HRSA and subsequent selection by a specially appointed, independent expert panel. Public cord blood banks not receiving funds directly for inventory growth may be linked to transplant centers via the Cord Blood Center search mechanism, should they meet the other participation standards. Although accredited foreign cord blood banks should not be eligible to receive federal funds for inventory expansion, they should be encouraged to participate in other aspects of the program, including provision of access to their cord blood units, data sharing, and the provision of clinician and patient support. Although the committee did not expect that participation in this network to be a requirement for all public banks, given the financial and logistical advantages network participation will bring, the committee believes that most banks will choose to take part in the program.

### **Standards**

Quality standards for participating banks, collection sites and centers, and transplant centers should be established and overseen by an accreditation body. The specifics of the quality standards are more fully discussed in Chapter 4. This independent accreditation body should be independent of the Cord Blood Coordinating Center and should be identified through a competitive process open to the several existing groups, as well as any other group(s) that may emerge. The final decision on the body to be recognized by the national program should be made by an expert panel. Only those banks and transplant centers accredited by this body should be able to participate in the National Cord Blood Stem Cell Bank Program. Furthermore, as recommended in Chapter 4, FDA should move quickly to license all blood banks units. At this point, FDA licensure of units would be required of any bank participating in the national program.

### **Patient Support**

Support services, in the form of counseling and assistance with insurance and financial matters, are needed for patients searching for either an adult donor or a cord blood unit, as are educational activities to increase understanding of the transplant process. These elements are essential to a national program and are suggested as a part of the structure. These activities are being conducted well by NMDP and should be adapted and built on as part of the national program. The committee encourages the NMDP to continue their efforts at minority outreach and in making this information about transplantation and the search process available in multiple formats and languages.

### **REFERENCE**

IOM (Institute of Medicine). 1999. *Organ Procurement and Transplantation: Assessing Current Policies and the Potential Impact of the DHHS Final Rule*. Washington, DC: National Academy Press.



