improve patient outcomes. Over the past 18 months, the commit-
tee established common standards for donor recruitment and
screening, cord blood collection, processing, cryopreservation
and storage. Eligible cord blood units are listed on the
NMDP donor registry which provides search management, patient
advocacy, confirmatory typing and donor reservations. The Reg-
distry also facilitates distribution of the cord blood units to the
transplant centers, acquires post transplant follow-up data and
provides this data back to the banks for their internal quality
assurance and regulatory reporting requirements. The NMDP also
holds contracts with over 130 transplant centers performing unre-
lated donor transplants, oversees quality and manages billing for
donor procurement. The initial goals of the NMDP banking pro-
gram were to standardize banking practices among member banks.
Five subcommittees were established to address Collections, Qual-
ity Standards, Research, IS/IT, Research and Economics. These
committees established uniform standards for donor selection, col-
lection, processing, testing and banking; criteria for assessing con-
genital anomalies and infant health; an inter-bank proficiency pro-
gram; an eye-friendly search report through TRANS Link and
cord blood unit report through CORD Link; improved data out-
comes reporting system and incorporated FDA requirements for
eligibility determination and GCTPs into screening documentation
and labeling. A preliminary research agenda was also developed.
A commitment to apply for mandatory accreditation by 12/05 was
adopted by all member banks. Criteria were established for a cord
blood unit to qualify for listing in the NMDP registry and included
a minimum total nucleated cell count of $9 \times 10^9$ cells with minimal
post processing viability of 90%, enumeration of NRBC and CD34
content, negative bacterial cultures, CFU growth, high resolution
HLA typing for DRB1, testing for hemoglobinopathies and a
minimum of 2 attached segments on the bag in which the unit was
cryopreserved. Collection criteria were standardized to exclude
multiple births; gestational age <34 weeks; a history of cancer,
immune or blood disorders in a first degree relative; and the
presence of congenital anomalies associated with congenital blood
disorders on the newborn physical examination. The NMDP in-
ventory now contains approximately 40,000 cord blood units.
Thirty-six percent of the donors represent ethnic minority back-
grounds. Approximately 500 units have been shipped for transplant
to date. Current barriers to collection and banking were reviewed
with their potential solutions. In conclusion, the NMDP banking
network functions as a program within the NMDP employing
common standards for cord blood donors, collection, processing and
storage listing on a single registry in combination with volun-
tary oversight is provided by HBSA. The recent affiliation with the CIBMTR will enable the collection.
Efforts over the next years will focus on increasing collections,
establishing protocols for clinical research and obtaining accredi-
tation for all participating banks.

### 17 QUALITY ISSUES IN CORD BLOOD BANKING

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As the frequency of umbilical cord blood (UCB) stem cell trans-
plantation has increased, the quality of UCB available in banks is
an important part of the success of the transplants. The AABB and
the Foundation for Accreditation of Cellular Therapy (FACT-
NETCORD) have promulgated standards and regulatory requi-
ting to collection, testing, processing, and banking of UCB for
transplantation. These standards are founded upon quality system
elements very similar to that of the current Good Manufacturing
Practices (GMPs) and GTPs promulgated by the FDA. For the
most part, the requirements of the standards are similar and pro-
vide a basis for consistency of UCB bank operations. However,
there are some differences that would allow UCB units to be
determined suitable for transplantation in some banks but not
others depending on the source of standards used by that bank.
Also, the requirements have changed over time and so some units
that were suitable for banking at one time may not meet more con-
temporary requirements. We used a quality assurance moni-
toring system to evaluate UCB units provided to us for transplant
by UCB banks in the United States and Europe. Of 268 units of
UCB shipped to us for transplantation during a three year period,
151 (56%) had one or more issues potentially related to quality
that required evaluation before final decision regarding their suitabil-
ity for use. There were a total of 246 specific issues in the 151 units.
The issues involved quality control (54%), medical history (40%),
and labels and documentation (6%). Risks to patients from these
issues were arbitrarily judged to be likely in 10%, potential in 35%,
and unlikely in 55%. The 10% of issues thought likely to affect the
quality of the unit were primarily due to quality control issue such
as transmissible disease test results, potential bacterial contamina-
 tion, storage conditions during shipping, and processing methods.
Some of these quality issues such as units with incomplete or
positive tests for transmissible diseases, misleading statements
about the status of testing, tests not done on proper blood samples,
improper UCB unit labels, records and documents lacking proper
unique identifying numbers, or important data related to the UCB
and positive bacterial culture results are examples of failure to use
or follow clear expectations of quality assurance programs. Some
of these units should never have been placed in the useable inventory,
which suggests that despite available standards, some UCB banks
are not operating in conformance with published standards. Con-
siderable variation can also occur even when banks follow applica-
table standards and quality control programs. This is due to four
factors. First, there are some differences between standards (AABB
and FACT-NETCORD) that would allow UCB units to be de-
termined suitable for transplantation by some banks but not others
depending on which set of standards is being followed. Secondly,
standards promulgated by AABB/FACT-NETCORD, and FDA are not specific and therefore leave it to the
bank's discretion to establish criteria for donor acceptance and
quality control test results. Thirdly, standards have changed over
time such that units placed appropriately into the bank in the past
may not meet contemporary standards. Fourthly, each bank may
decide to place individual units into their useable inventory despite
failure to meet that bank's own criteria as long as the medical
director takes responsibility and documents the reason for deviat-
ing from the banks standard procedures or policies. If standards
are established to assure quality, these four factors mean that different
units within a UCB bank or units from different banks may have
different degrees of quality and, thus, presumably safety. Our
findings indicate that despite quality programs for UCB promul-
gated by the AABB and FACT-NETCORD, there is considerable
variation in how banks select, process, and control the quality of
units they place into the bank. Some CBU's in banks' inventory
available for patients do not meet AABB/FACT-NETCORD stan-
dards. Some standards are simply specific and lack of consensus
about a number of issues related to quality. Communication
between banks and transplant centers may not sufficiently
timely or effective to allow thoughtful decision-making regarding
the suitability of a specific CBU for a specific patient. Our expe-
rience indicates that it is likely that some UCB units presently
searching in banks in the United States and Europe may not
meet current requirements and/or our desired levels of quality.
Effective and timely communication between the UCB and the
transplant center clinical cell engineering laboratory and transplant
team is essential; present interactions between the banks and trans-
plant centers may not be effective in identifying units that might
pose extra risks and require more unique decision-making. Decisions
about the use of particular units should involve both the transplant
physicians and physicians with expertise in donor suitability.

### 18 A COMPARISON OF PRE- AND POST-CRYOPRESERVATION CD34+ COUNTS FROM CORD BLOOD UNITS

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The identification of CB units with maximum engraftment po-
tential is an essential issue in CB transplantation. University of
Minnesota (UM) data have shown a high probability of survival in
recipients of 4-6/6 HLA match grafts when at least 1.7 $\times 10^5$ CD34$^+$ cells/kg are infused. This association was based on the CD34$^+$ counts assessed on thawed products. But the question to be addressed is whether indeed whether we can predict the thawed CD34$^+$ cell dose based on an analysis of the pre-freeze CD34$^+$ enumeration and the reliability of a CD34$^+$ assessment using an associated aliquot. Therefore, we evaluated fifty duplicate cryopreserved CB aliquots (1.5 ml cryovials) from CB units stored according to the standard banking procedures at the Madrid CBB (MCBB). After shipment using a transport liquid nitrogen container, the aliquots were thawed and processed by the same protocol at both the UM and MCBB. Total pre-freezing NC/ml was 8.21 $\pm$ 3.36 $\times 10^5$. Post-thaw counts at UM (6.77 $\pm$ 2.92 $\times 10^5$) and Madrid (6.49 $\pm$ 3.0 $\times 10^5$) indicated equivalent NC recoveries (83 $\pm$ 15% and 79 $\pm$ 15%, respectively). Cell viability by trypan blue before freezing was 90 $\pm$ 8%. However, there was a large difference between the post-thaw viabilities at the UM (52 $\pm$ 10%) and MCBB (81 $\pm$ 11%), indicating this technique is far from normalization. Similarly, different CFU-GM scoring criteria at the UM and MCBB (counting all CFU-GM colonies made up of greater than 40 or 20 cells, respectively) gave a lower CFU-GM number at UM vs. MCBB (7.6 $\pm$ 5.6 vs. 20.3 $\pm$ 13.6/600000 cells plated). Despite this variable readout, a significant correlation between these values ($r = 0.7$) was probably related to the consistency of the method and the same culture media used in this study. The CD34$^+$ frequencies (analyzed according to the ISHAGE dual-platform protocol) were also discrepant. While the post-thaw %CD34 was 98 $\pm$ 0.66 at the UM, it was 97 $\pm$ 0.39 at the MCBB (with the pre-thaw %CD34 being 0.35 $\pm$ 0.22). Bland-Altman and Intra-class Correlation tests displayed considerable lack of agreement and no consistent bias was observed between post-thaw CD34$^+$ at UM and either pre-freeze or post-thaw CD34$^+$ values at MCBB. Thus, the CD34$^+$ cell analysis at the UM and MCBB could not be used interchangeably. However, linear regression showed a significant relationship ($p < 0.001$). The linear equations estimated for each prediction model were: i) $y = 2.758x + 0.0121$ (post-thaw [pt] UM from pre-freeze [pf] MCBB counts); ii) $y = 1.534x + 0.111$ (pt UM from pt MCBB counts); and iii) $y = 1.684x + 0.00567$ (pt MCBB from pf MCBB counts). The coefficient of determination ($R^2$) for each model was 0.85, 0.82 and 0.80 respectively. Therefore, as high as 85% and 82% of the total variance of post-thaw CD34$^+$ values at the UM was explained respectively by the variation in pre-freeze (first model) or post-thaw (second model) CD34$^+$ values at the MCBB. Importantly, all but one of the observed CD34$^+$ counts were above the lower 90% individual prediction limits. In summary, regardless the variability of CD34$^+$ cell enumeration from UM and MCBB, it is impossible to foresee, based on a confidence of 95% the CD34$^+$ cell dose that would be infused to CB transplantation patients at the UM, either from the pre-freeze MCBB data or from the CD34$^+$ assessment using a cryopreserved aliquot. Whereas this regression model is only valid between the transplantation outcomes from CD34$^+$ data provided by all CB banks. Finally, on examination of the flow cytometry data files, the CD34 enumeration discrepancy was seemingly due to differences in the initial cell acquisition performed at the UM and MCBB. This discrepancy could be minimized by adopting uniform operating procedures.

19 STANDARDIZATION OF CFU ASSAYS
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The advantages of using cord blood derived cells for the treatment of leukemia and other hematological malignancies are now well recognized. A recent regulatory ruling has mandated that a functional test (e.g. a colony forming cell (CFC) assay) evaluating the proliferative potential of the cells within the product following cell processing and freezing must be performed if the sample is to be used for transplantation. This highlights the need for a standardized assay. Previously published data have reported significant variability in the quantification of the hematopoietic progenitors using the CFC assay. Originally, recognition and enumeration of the colonies was believed to parallel the variation in CFC quantification. However, several media formulations or technical errors in sample preparation, cell counting and dilution. Two distinct proficiency testing programs were designed to assess the contribution of these various parameters to the variability. The preliminary program, with 54 participants within North America, sought to determine the variability in the recognition and enumeration of CFC. This was achieved by determining the coefficient of variation (CV) for CFU-GM and total CFC enumeration when sample preparation events were controlled. The second program was global, and also assessed the contribution of the cell preparation steps to the overall variability of the CFC assay. Participants ($n = 134$) were provided with identical vials of frozen bone marrow cells and were instructed to thaw, wash, count, assess viability and dilute the cells prior to their addition to a standardized formulation of MethoCult™. Fourteen days later, participants quantified myeloid and erythroid colonies as in the original tests. The considerable increase in the CVs in this second test confirmed that sample preparation steps contribute significantly to the variability in this assay. Standardized protocols for cell preparation and training will decrease this variability and facilitate global applicability of data generated from various laboratories.

20 UNRELATED CORD BLOOD TRANSPLANTATION IN PEDIATRIC PATIENTS WITH NON-MALIGNANT DISEASES

The COLBT or Cord Blood Transplantation Study was a multi-institutional study sponsored by the National Heart Lung and Blood Institute. It was comprised of a banking and transplantation study. The banking study established 3 banks which employed common standards for donor screening and recruitment and cord blood collection, processing, testing, cryopreservation and storage. Screening of 34,700 women candidates 24,200 eligible for the study who were approached for consent to participate. Eighty-five percent (20,710 women) were consented and 17,207 were collected, 47% of which were discarded for low cell count, infectious disease or maternal history exclusion or problems with processing. Of note, a lower percentage of African American donations were eligible for banking because they tended to have lower cell counts per unit volume. Approximately 9112 units were moved to long term storage and available for transplantation. The transplantation study employed common protocols for preparative regimens, GVHD prophylaxis and supportive care. Uniform definitions of engraftment, GVHD and toxicity scoring, graft failure, causes of death and relapse were employed. Strata were developed for children and adults with malignant and non-malignant conditions. This report focuses on outcomes in 69 patients with inborn errors of metabolism transplanted between August of 1999 and June of 2004. The median age of the patients was 1.8 years (range 0.1-11.7 years). There was a predominance of males (55%) and Caucasians (74%). The patients were diagnosed with MPS syndromes (57%), ALD (12%), MLD (6%), Krabbe Disease (23%) and Tay Sachs Disease (4%). Only 25% of patients were CMV seropositive before transplant. A significant portion of the patients (35%) had a performance status defined by a Lansky score $\leq$80%. The COLBT banks provided 70% of the donor units used in the study. The median total nucleated cell dose and CD34$^+$ cell dose selected were 8.7 $\times 10^5$/kg and 2.4 $\times 10^5$/kg, respectively. HLA matching was performed using molecular typing at an intermediate resolution for HLA Class I and high resolution for DRB1. High resolution matching was scored retrospectively. The majority of patients received grafts mismatched at 1 (45%) or 2 (48%) HLA loci. After high resolution typing, 23% of patient/donor pairs were demoted to lesser matches. Patients were prepared for transplant with busulfan (16 doses with first dose pharmacokinetics targeting a steady state of 600-900 ng/ml), cyclophosphamide 200 mg/kg and equine ATG 90 mg/kg. GVHD prophylaxis was delivered with methylprednisolone and cyclosporine. The cumulative incidence

Abstracts

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