Model Criteria for Regulation of Cord Blood Banks and Cord Blood Banking

Adopted by the Cord Blood Association
Board of Directors
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A substantial volume of the umbilical cord blood used in clinical therapies around the world is transported between countries. The unit of cord blood that is the best biological match for a particular patient frequently has been collected, processed and stored in another country.

Unfortunately, the laws and regulations for cord blood banking vary greatly from country to country, thus complicating the movement of critically needed cells. For this reason, the Cord Blood Association has developed "model criteria" for banking rules and regulations. The purpose of the Model Criteria is to (1) harmonize regulations among countries where regulations currently exist, (2) guide the development of regulations in countries where few exist, and (3) assist cord blood banks that are not accredited.

These criteria should not be viewed as optimal standards, such as those developed and promulgated by accrediting agencies such as AABB and the Foundation for the Accreditation of Cellular Therapy (FACT.) Rather, the Model Criteria are minimum requirements for national-level laws and regulations that govern cord blood banks and cord blood banking.

The Model Criteria were developed by the CBA Government & Global Affairs Committee, with representatives from 15 countries. No gap analysis was performed to compare the Model Criteria to existing laws and regulations of any country. Rather, the committee's process has been driven by evidence and consensus to establish criteria that can be updated in the future as laboratory and clinical advances occur in cord blood banking and in cord blood-based therapies. The draft Model Criteria were circulated to association members for comment, and then published for public comment. The committee considered all submitted comments and finalized the draft that was then adopted as association policy by the CBA Board of Directors.

Except where specified in the text, these Model Criteria are applicable to both unrelated and related cord blood banking.

Model Criteria for Regulation of Cord Blood Banking

Provided below are recommended criteria for government regulation of cord blood banks and cord blood banking.

1. QUALITY MANAGEMENT

The regulations should address the policies and standard operating procedures of all critical aspects of cord blood bank operations and management, including:

- Organizational structure and personnel requirements
- Safety
- Validation of critical procedures
- Proficiency testing
- Agreements with external parties
- Donor (i.e., parental) consent
- Maternal and infant donor evaluation
- Confidentiality
- Labeling and tracking
- Change control and process

- Documents and records handling, control and storage
- Electronic record systems
- Errors, non-conformance, deviations and adverse events
- Equipment, critical supplies and reagents
- Inventory management and storage stability
- Clinical outcome data collection and management
- Regular quality review, internal audits and reporting

2. CONTENT OF CONSENT OR CONTRACT WITH THE FAMILY FOR BANKING

The required components of parental consent or contract should include:

- A statement of consent (i.e., consent for use in transplant, research, commercialization or quality control)
- Who can sign the consent or contract
- Testing to be performed on the cord blood and maternal blood
- Storage and discard
- Potential benefits
- Potential risks and discomforts
- Alternatives to banking
- Storage of donor's personal information
- Future contact (for test results and follow up on baby's health status)
- Cost and reimbursements
- Criteria for withdrawal of consent or termination of contract
- Consent to collection only (i.e., pre-consent, mini-consent, if applicable, should include permission for use in research or commercialization if identity is anonymized, or information about how the family will be approached for additional consent for other uses of the collected cord blood.

Regulations for cord blood bank marketing and education should:

- Assure fair, balanced and evidence-based information for parents and health care providers
- Prohibit misrepresentations, omissions, unsubstantiated claims and emotional appeals that are likely to mislead parents or health care providers

3. DONOR SCREENING AND TESTING

The required components of donor screening should include:

- Personal information – lifestyle (e.g., drug abuse, prostitution)
- Medical history, including family history, obstetric and delivery history, and health of the baby
- Travel history as it could relate to contagious diseases (e.g. malaria, Zika, T-cruzi)[1]
- Testing of maternal blood for a minimum of the following infectious agents[2]:

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[1] The World Marrow Donor Association/NetCord Working Group is developing a summary document to describe parameters from a global perspective for determining cord blood donor suitability. This will be a helpful reference tool.

[2] Other screening should be considered based on local incidence of endemic blood borne infections. (See Laboratory Tests table)

Hepatitis B Surface Antigen and NAT
Hepatitis C antibody and NAT
CMV antibody
HIV 1, 2 +/- O antibody and NAT
Syphilis Antibody

4. COLLECTION

Cord blood collection must be performed by a trained, qualified health care professional into an approved or validated container, containing an anticoagulant. The requirements for collection should address:

- Method of cord blood collection (e.g., in utero vs. ex-utero)
- Type of delivery (Vaginal or C-Section)
- Singleton or multiple delivery
- Time lapse between cord blood collection and cryopreservation
- Maternal blood collection for donor screening tests within 7 days of collection/delivery
- Shipment of cord blood and/or maternal blood in a container with temperature monitoring or validation that the container can maintain intended temperature during shipment

5. MANUFACTURING

The regulations for manufacturing should address:

- Supplies, reagents and other consumables that come into contact with the cord blood product, including a requirement that they must be approved for use in human patients
  DMSO, or other non-approved reagents for processing or cryopreservation, are the exception to this requirement. Use of DMSO or other non-approved reagents must be validated by the bank for clinical use.
- Critical materials (supplies and reagents) management, storage, validation, verification and supplier audits
- Labeling, including donor and product identification from collection to cryopreservation and product release
- Cord blood and maternal blood storage requirements, including temperature and time
- Processing facility SOPs, environment, classification, cleaning, equipment, monitoring, safety, and back-up systems
- Specifications for banking for potential clinical use, including minimum criteria for total nucleated cell count and viability
- Validated processing platform
- Validated cryopreservation process and containers
  The CBA strongly recommends storage of final product in bags, with availability of attached segments for ancillary testing (e.g. identity, potency~~, infectious disease~~)
- Product testing (see table). NB: Maternal and cord blood plasma or serum samples should be stored under appropriate conditions
  Total nucleated cell count (TNCC)
  Sterility (If culture positive, identity and sensitivity of organisms must be performed.)
  Viability
  CD34
  CFUs (recommended

ABO Rh (recommended)
HLA typing (before release)

6. POTENCY AND RELEASE

The regulations for cord blood unit release should include:

- Confirmation of identity through HLA confirmatory typing
- A validated potency assay on a representative cryopreserved testing sample (e.g., viability of the CD34 population, CFU assay, ALDHbr content or other)
- Determination of cord blood unit donor eligibility

7. SHIPPING AND TRANSPORTATION

The regulations for cord blood unit shipping and transportation should address:

- Documentation that accompanies the cord blood unit
- Method of transport (must be shipped in a validated dry shipper)
- Shipping conditions, including data loggers, GPS tracking, and security of the shipper

8. OUTCOMES MONITORING

The regulations for clinical outcome monitoring should include:

- Cord blood banks requests for post thaw TNCC, CD34, CFU (if performed) and sterility from the treatment center
- Cord blood banks requests for treatment outcome and safety data from all facilities to which units are released for clinical use. Data should include:
  - Administered cell dose
  - Detection of microbial infection post-transplant
  - Adverse events associated with administration of the cord blood unit
  - Complaints associated with the cord blood unit
- Analysis of clinical outcomes

Treatment outcome data collected for units of cord blood released for hematopoietic reconstitution should include:

- Time to neutrophil and platelet engraftment
- Chimerism (for allogeneic cord blood units)
- Identity of engrafting cord blood unit (when more than one unit is infused)
- Details of expanded or manipulated cord blood units (or additional cell products)
- Disease status and/or relapse
- Annual or more frequent survival rates
- Annual or more frequent GVHD results

9. REGISTRY PARTICIPATION AND DATA SHARING

Banks that collect and store cord blood for allogeneic unrelated use should participate in appropriate bone marrow donor registries that provide listing, search, selection, reservation, release and distribution. The regulations pertaining to registry participation should include:

- Contractual agreement between the cord blood bank and the registry
- Clearly defined and documented responsibilities of the registry

- Listing of only those cord blood units that are suitable for clinical use
- A validated process for submitting (i.e., uploading) information about cord blood units to the registry
- A validated electronic records system that enables search and match operations and reporting of results within an acceptable timeframe
- Policies and standard operating procedures for the reservation and allocation of cord blood units, to avoid problems such as a unit being reserved for more than one patient at a time, and the listing of units that have already been released
- An agreement between the registry and clinical facilities that treatment outcome data will be provided to the cord blood bank that released the unit for the purpose of monitoring and evaluating safety and efficacy of the unit

It is recommended that cord blood banks submit, and donor registries accept, treatment outcome data for units released for autologous use.

Laboratory Tests

A variety of laboratory tests help assure that cord blood products are safe and effective for clinical use. The table below lists recommended tests, based on the standards of the AABB and NetCord-FACT accrediting agencies and an examination of current regulations within countries represented on the CBA Government and Global Affairs Committee.

Generic tests are listed in recognition that test availability and testing algorithms differ within and between national jurisdictions.

	Comments
Test (IDM) Maternal Blood	
Anti HIV 1 and 2	Required
Anti HCV	Required
Anti CMV Total / IgG / IgM	Required
Syphilis	Required
Anti HTLV I/II	Recommended
HBsAg	Required
Anti HBc	Required
HIV -1 NAT	Required
HCV NAT	Required
HBV NAT	Required

Cord Blood Cell Analysis	
CBC / Differential	Required
TNCC	Required
CD34	Required
Total Viability	Required
Viable CD34	Required
CD34 % Viability	Required
CFU or other potency test	Recommended

HLA	For unrelated units, needed upfront AND confirmatory. For related cord blood, needed at time of release
HLA A,B, DRB1	Required
HLA C	Recommended
High Res A, B, DRB1	Required, with at least 1 test to be high resolution
High Res C	Recommended, with at least 1 test to be high resolution

Other	
Sterility	Required
Aerobic	Required
Anaerobic	Required
Fungi	Required
Isolate microbial identity	Required
Isolate Antibiogram	Required
ABO/Rh group	Required
Hemoglobinopathy (autologous)	Depends on family history
Hemoglobinopathy (unrelated)	Required

Conclusion

These Model Criteria, prepared by the Government & Global Affairs Committee, are recommended minimum requirements for the regulation of cord blood banks and cord blood banking. The purpose is to encourage harmony among national-level laws and regulations, which is important because cord blood frequently must be moved between national jurisdictions.

Government & Global Affairs Committee

Ngaire Elwood (Chair)	Melbourne, Australia
Ed Brindle	Mississauga, Canada
Salmaan Dalvi	Uxbridge, United Kingdom
Carlos de Rivas	Mexico City, Mexico
Ralph Fariello	Cedar Knolls, New Jersey, USA
Andre Gomes	Cantanhede, Portugal
Susana Gomez	Barcelona, Spain
Stem Hung	Hsinchu City, Taiwan
Mamoru Ishii	Tokyo, Japan
Gesine Kögler	Düsseldorf, Germany
Joanne Kurtzberg	Durham, North Carolina, USA
Yijia Li	Kunming, China
Julie Mandel	Jerusalem, Israel
Brian Plummer	San Francisco, California, USA
Elisabeth Semple	Lund, Sweden
Gocha Shatirishvili	Tbilisi, Georgia
Bernie Siegel	Palm Beach, Florida, USA
Roberto Waddington	São Paulo, Brazil