INTERNATIONAL STANDARDS FOR CORD BLOOD COLLECTION, BANKING, AND RELEASE FOR ADMINISTRATION

Fifth Edition
DRAFT
September 2012

NOTICE
These Standards are designed to provide minimum guidelines for Cord Blood Banks, facilities, and individuals performing cord blood donor management, collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution, or providing support services for such procedures. These Standards are not intended to establish best practices or include all procedures and practices that a Cord Blood Bank, facility, or individual should implement if the standard of practice in the community or applicable law establishes additional requirements. Each Cord Blood Bank, facility, and individual should analyze its practices and procedures to determine whether additional standards apply. The Foundation for the Accreditation of Cellular Therapy and NetCord disclaim any responsibility for setting maximum standards and expressly do not represent or warrant that compliance with these Standards is an exclusive means of complying with the standard of care in the industry or community. Further, the Foundation for Accreditation of Cellular Therapy and NetCord expressly disclaim any responsibility, liability or duty to member programs, directors, staff, or program donors or patients for any such liability arising out of injury or loss to any person by the failure of member programs, directors, or staff to adhere to these Standards or related guidance.
PART A: TERMINOLOGY, ABBREVIATIONS, AND DEFINITIONS

A1 TERMINOLOGY

For purposes of these Standards, the term *shall* means that the Standard is to be complied with at all times. The term *should* indicates an activity that is recommended or advised, but for which there may be effective alternatives. The term *may* is permissive, indicating that the practice is acceptable, but not necessarily recommended.

A2 ABBREVIATIONS

The following abbreviations are used in these Cord Blood Standards:

- **ABO**: Major human blood group including erythrocyte antigens, A, B, O
- **C**: Accompany
- **F**: Affix
- **ASHI**: American Society for Histocompatibility and Immunogenetics
- **T**: Attach
- **°C**: Degree Celsius
- **CB**: Cord blood
- **CBB**: Cord blood bank
- **CBC**: Complete blood count (Full blood count)
- **CB unit**: Cord blood unit
- **CFU**: Colony forming unit
- **DNA**: Deoxyribonucleic acid
- **EFI**: European Federation for Immunogenetics
- **FACT**: Foundation for the Accreditation of Cellular Therapy
- **FDA**: United States Food and Drug Administration
- **GVHD**: Graft-versus-host disease
- **HLA**: Human leukocyte antigen
- **HPC**: Hematopoietic progenitor cell
- **HTA**: United Kingdom Human Tissue Authority
- **IRB**: Institutional Review Board
- **ISBT**: International Society of Blood Transfusion
- **µg**: Microgram
- **mL**: Milliliter
- **QM**: Quality Management
- **Rh**: Human erythrocyte antigen, Rhesus
- **TGA**: Australia Therapeutic Goods Administration
- **TNC**: Total nucleated cell
- **USDA**: United States Department of Agriculture
- **WMDA**: World Marrow Donor Association

A3 DEFINITIONS

The definitions in this section are descriptive only. In the event of a conflict with the Standards, the Standards shall prevail.

*Accompany (C)*: To go or be together with, but not attached. Information that must accompany the cord blood unit in a sealed package may alternatively be attached or affixed.
Adventitious agent: Any extraneous microbiological, chemical, or radiobiological substance introduced into the cord blood unit during collection, processing, or administration.

Adverse event: Any unintended and unfavorable sign, symptom, abnormality, or condition temporarily associated with an intervention, medical treatment, or procedure that may or may not have a causal relationship with the intervention, medical treatment, or procedure. Adverse reaction is a type of adverse event.

Adverse reaction: A noxious and unintended response to the collection or infusion of any cord blood unit for which there is a reasonable possibility that the cord blood unit caused the response.

Affix (F): To adhere in physical contact with the cord blood unit container.

Allogeneic: Obtained from an infant donor and intended for infusion into a genetically distinct related or unrelated recipient.

 Directed allogeneic: Collected and stored for use by an individual or family that is genetically related to the infant donor.

 Unrelated allogeneic: Obtained from an infant donor and intended for administration into another individual who is not genetically related to the infant donor.

Applicable Law: Any local, national, or international statute, regulation, or other governmental law that is applicable to cord blood donor management including recruitment or eligibility, or to cord blood collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, or distribution that is relevant to the location or activities of the Cord Blood Bank, Cord Blood Collection Site, or Cord Blood Processing Facility.

Aseptic technique: Practices designed to reduce the risk of microbial contamination of products, reagents, specimens, patients, or donors.

Associated sample: Aliquot of biological material (e.g., blood, serum, plasma, tissue, Wharton’s jelly, etc.) derived from the infant donor or maternal donor of the CB unit.

Attach (T): To fasten securely to the cord blood unit container by means of a tie tag or comparable alternative. Any information required to be attached to a container may alternatively be affixed.

Audit: Documented, systematic evaluation to determine whether approved policies, Standard Operating Procedures, or operations have been properly implemented and are being followed.

Autologous: Derived from and intended for the same individual.

Available for distribution: The time at which the cord blood unit may leave the control of the facility.

Biohazard legend: The universal biohazard symbol.
**Biological product deviation:** A deviation from Applicable Law, standards, or other established specifications that relate to the prevention of communicable disease transmission or cord blood unit contamination; or an unexpected or unforeseeable event that may relate to the transmission or potential transmission of a communicable disease or may lead to cord blood unit contamination.

**Calibrate:** To set measurement equipment against a known standard.

**Calibration:** Periodic scheduled activity to check and maintain the accuracy against a known standard.

**CD34:** The 115 kD glycoprotein antigen, expressed by a small portion of cord blood cells, that is defined by a specific monoclonal antibody (anti-CD34) using the standardized cluster of differentiation (CD) terminology. Hematopoietic progenitor cells are largely contained within the CD34 cell population of cord blood units.

**Cellular therapy product:** A somatic cell-based product, including cord blood, that is procured from a donor and intended for processing and administration.

**Circular of Information:** An extension of container labels. The Circular of Information for Cellular Therapy Products is a jointly prepared document containing definitions; descriptions; the cord blood unit; indications and contraindications; side effects and instructions for hazards, dosage, and administration; storage, labeling, and documentation of cellular therapy products such as hematopoietic progenitor cells and other leukocytes that are minimally manipulated. The current Circular of Information can be found at www.factwebsite.org recommendations.

**Clinical Program:** An integrated medical team that administers cord blood units.

**Colony forming unit (CFU):** A clonogeneic cell able to produce hematopoietic colonies in vitro under specific conditions in the presence of appropriate colony stimulating factors and defined by the type of mature progeny that develop.

**Collection:** Any procedure for procuring and labeling cellular therapy products, regardless of technique or source.

**Collection kit:** Package of all materials required to collect a single CB unit. Usually intended for collection at a non-fixed CB Collection Site.

**Communicable disease:** A disease or disease agent for which there may be a risk of transmission by a cord blood unit either to a recipient or to the people who may handle or otherwise come in contact with the cord blood unit.

**Competency:** Ability to adequately perform a specific procedure or task according to directions.

**Complaint:** Any written, oral, or electronic communication about a problem associated with a distributed cord blood unit or with a service related to donor management or the collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, distribution, or infusion administration of a cord blood unit.
Confirmatory typing: A test performed on a second sample of a specific CB donation at the request of a Clinical Program to confirm the original typing and/or to reaffirm the identity of the CB donation.

Contiguous segment: A sealed length of tubing integrally attached to the cord blood unit that contains a sample representative of the cord blood unit that may be used for testing.

Cord blood (CB): The infant’s blood remaining in the placenta and umbilical cord after the umbilical cord has been clamped.

Cord Blood Bank (CBB): An integrated team under a single Cord Blood Bank Director responsible for donor management and the collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution of cord blood units.

Cord blood banking (CB banking): The processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution of cord blood units intended for administration.

Cord blood collection: The procurement of cord blood for banking and administration before and/or after the placenta is delivered.

Ex utero: The collection of cord blood cells from the placental and/or umbilical cord vessels after the placenta has been delivered.

In utero: The collection of cord blood cells from the placental and/or umbilical cord vessels after the infant donor has been delivered and separated from the umbilical cord, but before the placenta has been delivered.

Cord Blood Collection Site: The site location where the infant donor is delivered and the cord blood unit is collected.

Fixed Cord Blood Collection Site: A collection site where there is a written agreement between the collection site and the Cord Blood Bank for the collection of cord blood units over time. The agreement shall describe the interaction between the Cord Blood Collection Site and the Cord Blood Bank for all aspects of the collection process including, at a minimum, personnel training, record keeping, collection, storage, and transportation or shipping of a cord blood unit.

Non-fixed Cord Blood Collection Site: A collection site without an ongoing documented where there is a written agreement with a Cord Blood Bank where one or more for the collection of a single cord blood units may be collected unit at the initiation of the infant donor’s mother and/or family and with documentation that a licensed health care professional has agreed to perform the collection and has training that covers each aspect of the collection process. A non-fixed Cord Blood Collection Site may collect more than one cord blood unit for the Cord Blood Bank with a written agreement for each unit.
**Cord Blood Processing Facility:** The location where cord blood processing activities are performed in support of the Cord Blood Bank. A Cord Blood Processing Facility may be part of the same institution as the Cord Blood Bank or may be part of another institution and performs these functions through contractual agreement.

**Cord blood unit (CB unit):** The nucleated cells including stem and hematopoietic progenitor cells harvested from placental and umbilical cord blood vessels from a single placenta after the umbilical cord has been clamped. HPC, Cord Blood is the proper name of a cord blood unit. Unless otherwise specified, the term cord blood unit in this document refers to any cord blood unit regardless of method of collection or intended use.

**Corrective action:** Action taken to eliminate the causes of an existing discrepancy or other undesirable situation to prevent recurrence.

**Cryopreservation:** The processing of viable cells or tissues that consists of cooling the product to a very low temperature where viability is maintained.

**Designee:** An individual with appropriate experience or expertise who is given the authority to assume a specific responsibility. The person appointing the designee retains ultimate responsibility.

**Disposition:** The current status, location, or use of a cord blood unit.

**Distribution:** Any transportation or shipment (including importation and exportation) of a cord blood unit that has been determined to meet all applicable release criteria or urgent medical need requirements.

**Donor:** A person who is the source of cells or tissue for a cellular therapy product.

**Infant donor:** The infant from whose placenta and/or umbilical cord the cord blood is obtained.

**Maternal donor:** The mother who carries the infant donor to delivery. This may be the genetic or surrogate mother.

**Unrelated donor:** The infant donor whose cord blood is collected and stored for use anonymously by a person with no known genetic relationship.

**Directed/Related donor:** The infant donor whose cord blood is collected and stored for autologous use by an individual or family that is genetically related to the donor. Directed donors can be related or for allogeneic or autologous donors.

**Related donor:** The infant whose cord blood is collected and stored for use by an individual or family that is genetically related to the donor.

**Autologous donor:** The infant whose cord blood is collected and stored for use by the donor.

**Electronic record:** Any record or document consisting of any combination of text, graphics, or other data that is created, stored, modified, or transmitted in digital form by a computer.
**Eligible:** An infant donor and/or mother who meet(s) all donor screening and testing requirements related to transmission of communicable disease as defined by Applicable Law.

**Engraftment:** The reconstitution of hematopoiesis or other cellular functions with cells from a donor.

**Errors and accidents:** Any unforeseen or unexpected deviations from Applicable Law, these Standards, or other established specifications that may affect the safety, purity, or potency of a cord blood unit.

**Establish and maintain:** A process to define, document in writing or electronically, implement, follow, review, and, as needed, revise on an ongoing basis.

**Hematopoietic progenitor cells (HPC):** Self-renewing and/or multi-potent stem cells capable of maturation into any of the hematopoietic lineages, lineage-restricted pluripotent progenitor cells, and committed progenitor cells, regardless of tissue source (bone marrow, umbilical cord blood, peripheral blood, or other tissue source).

**High resolution typing:** A high resolution typing result is defined as a set of alleles that encode the same protein sequence for the region of the HLA molecule called the antigen binding site and that excludes alleles that are not expressed as cell-surface proteins. The antigen binding site includes domain 1 and domain 2 of the class I α polypeptides, and domain 1 of the class II α and domain 1 of the class II β polypeptide chains.

**Identifier:** A numeric or alphanumeric sequence used to differentiate one item from another like item.

**Indefinitely:** A timeframe without a fixed or specified limit.

**Ineligible:** An infant donor and/or mother who does not meet all donor screening and testing requirements related to transmission of communicable disease as defined by Applicable Law.

**Institutional Review Board or Ethics Committee:** A Board or Committee established by an institution in accordance with Applicable Law to review biomedical and behavioral research involving human subjects conducted at or supported by that institution.

**ISBT 128:** The international information technology standard for transfusion medicine and transplantation. ICCBBA, Inc. ([www.iccbba.org](http://www.iccbba.org)) is the organization charged with the international maintenance of this database.

**Key personnel:** Personnel with responsibilities that significantly affect the provision, safety, and/or quality of a service or product.

**Labeling:** Steps taken to identify the original cord blood unit collection and any products or product modifications, to complete the required reviews, and to attach the appropriate labels.
Licensed health care professional: An individual certified by the applicable governmental agency to be competent for the duties performed.

Linkage: The maintenance of basic demographic information, including name, that would allow tracing of a cord blood unit to the identification of the infant donor and/or the mother.

Listing: The process of transferring information about a cord blood unit to be available for search.

Low resolution typing: A DNA-based typing result at the level of the digits comprising the first field in the DNA-based nomenclature. Examples include A*01; A*02. If the resolution corresponds to a serologic equivalent, this typing result should also be called low resolution.

Manipulation: Ex vivo procedure(s) that selectively removes, enriches, expands, or functionally alters hematopoietic progenitor cells.

Materials management: An integrated process for planning and controlling all steps in the acquisition and use of goods or supply items (materials) used for the collection or processing of cellular therapy products to determine whether these materials are of adequate quality and quantity and available when needed. The materials management system combines and integrates the material selection, vendor evaluation, purchasing, expediting, storage, distribution, and disposition of materials.

Maternal samples: Aliquots of cells, plasma, serum, or cellular material from the blood of the mother that can be used for testing.

May: Acceptable but not necessarily recommended.

Microbial: Related to infectious agents including bacterial and fungal organisms.

Monitoring: Recording quality parameters or indicators on a regular basis.

Mother: Any of the following:

Birth mother: The woman who carries the infant donor to its delivery; may be the genetic mother or a surrogate mother.

Genetic mother: The woman from whose egg the infant donor develops; the egg donor.

Mother: When used unmodified, the term mother refers to the mother who is both the genetic and birth mother.

Surrogate mother: The woman who carries an infant donor not genetically her own from an embryo to delivery. Under circumstances of a surrogate mother carrying the infant donor to term and the cord blood unit being collected, both the surrogate and the genetic mother shall be considered for purposes of communicable disease screening and testing; the genetic mother shall be considered for purposes of genetic information.
**Negative selection**: The manipulation of cord blood such that a specific cell population(s) is depleted.

**NetCord**: The international organization of cord blood banks that meet defined membership requirements of the International NetCord Foundation, established to promote high quality cord blood banking and clinical use of umbilical cord blood for allogeneic stem cell transplantation.

**Nonconforming cord blood unit**: Any cord blood unit that does not completely meet the requirements specified by these Standards, the Cord Blood Bank, and/or the requirements for donor eligibility as defined by Applicable Law.

**Outcome analysis**: The process by which the results of a therapeutic or technical procedure are formally assessed.

**Partial label**: The minimum essential elements that must be affixed at all times to all cord blood unit containers.

**Policy**: Document that defines the scope of an organization, explains how the goals of the organization will be achieved, and/or serves as a means by which authority can be delegated.

**Positive selection**: The manipulation of cord blood such that a specific cell population(s) is enriched.

**Potency**: The therapeutic activity of a cord blood unit as indicated by appropriate laboratory tests or adequately developed and controlled clinical data.

**Procedure**: A document that describes in detail the process or chronological steps taken to accomplish a specific task. A procedure is more specific than a policy.

**Process**: A goal-directed, interrelated series of actions, events, or steps.

**Process control**: The standardization of processes in order to produce predictable output.

**Process development**: The series of procedures performed in order to develop a final process that achieves the required results.

**Processing**: All aspects of manipulation, packaging, and labeling cord blood units, including microbial testing, preparation for storage, and removal from storage. Processing does not include collection, donor screening, donor testing, cryopreservation, storage, or distribution.

**Products**: The proper name for each class (broad descriptions of product) is as follows:*

- **HPC, Cord Blood**: Umbilical cord blood and/or placental blood collected as a source of hematopoietic progenitor cells.

- **TC, Cord Blood**: Umbilical cord blood and/or placental blood collected as a source of nucleated cells. The product is intended for therapeutic use other than as HPCs.
**Proficiency test:** A test to ensure evaluate the adequacy of testing methods and equipment and the competency of personnel performing testing.

**Protocol:** A written document describing steps of a treatment or experimental procedure in sufficient detail such that the treatment or procedure can be reproduced repeatedly without variation.

**Purity:** Relative freedom from extraneous matter in the finished product, whether or not harmful to the recipient or deleterious to the product.

**Qualification:** The establishment of confidence that equipment, supplies, and reagents function consistently within established limits.

**Quality:** Conformance of a product or process to pre-established specifications or standards.

**Quality assessment:** The actions, planned and performed, to evaluate all systems and elements that influence the quality of the product or service.

**Quality assurance:** The actions, planned and performed, to provide confidence that all systems and elements that influence the quality of the product or service are working as expected individually and collectively.

**Quality audit:** A documented, independent inspection and review of a facility’s activities. The purpose of a quality audit is to verify, by examination and evaluation of objective evidence, the degree of compliance with those aspects of the quality program under review.

**Quality control (QC):** A component of a quality program that includes the activities and controls used to determine the accuracy and reliability of the establishment’s personnel, equipment, reagents, and operations in the manufacturing of cord blood units, including testing and product release.

**Quality improvement:** The actions, planned and performed, to develop a system to review and improve the quality of a product or process.

**Quality Management (QM):** An integrated program of quality assessment, assurance, control, and improvement.

**Quality Management Plan:** A written document that describes the systems in place to implement the Quality Management Program.

**Quality Management Program:** An organization’s comprehensive system of quality assessment, assurance, control, and improvement. A Quality Management Program is designed to prevent, detect, and correct deficiencies that may adversely affect the quality of the cord blood unit or increase the risk of communicable disease introduction or transmission.
**Quality Management Supervisor:** A qualified individual approved by the Cord Blood Bank Director to establish methods to review, modify, approve, and implement all Standard Operating Procedures related to Quality Management and to monitor compliance with these Standards.

**Quarantine:** The segregation of a cord blood unit to prevent cross-contamination or improper release. Quarantine can be temporal, physical, or a designation within the cord blood unit record.

**Recipient:** The individual into whom the cord blood unit was transplanted.

**Reference samples:** Aliquots of cells, plasma, serum, or cellular material from the cord blood unit, the umbilical cord, or the placenta that can be used to confirm the identity, HLA typing, or genetic or communicable disease information associated with a single cord blood unit. Such samples may or may not be contiguous segments.

**Registry:** An organization that publishes or makes available the description of cord blood units available for administration and may conduct searches of the available cord blood units, either exclusively or in conjunction with the Cord Blood Bank as defined in their agreement.

**Release:** The removal of a cord blood unit from quarantine or in-process status when it meets specified criteria.

**Reservation:** A temporary allocation of a cord blood unit to a specific recipient to prevent consideration of that cord blood unit for another recipient.

**Retention sample:** An aliquot replicate of the final cord blood unit.

**Rh:** The abbreviation for the Rhesus system of human red cell antigens; is used in this document to refer to the Rh (D) antigen only unless otherwise specified.

**Safety:** Relative freedom from harmful effects to persons or products.

**Search:** The process used to produce a report of cord blood units that are potential matches for a recipient.

**Selection:** The process of identification of a donor or cord blood unit according to defined criteria.

**Shall:** To be complied with at all times.

**Shipping:** The physical act of transferring a cord blood unit within or between facilities during which the unit leaves the control of trained personnel at the distributing or receiving facility.

**Should:** Recommended or advised, but effective alternatives may exist.

**Significant warming event:** Any event when a cryopreserved cord blood unit reaches -120°C or warmer during the life of the cryopreserved cord blood unit.
Standard Operating Procedure: Written detailed instructions required to perform a procedure.


Sterility testing: The processes used to screen for the presence of microbial agents.

Storage: Holding cord blood units for future processing and/or distribution.

Suitability: The maternal and infant donor’s medical fitness to undergo the cord blood collection procedure.

Time of collection: The time of day that the cord blood collection is completed.

Total nucleated cell (TNC) count: The number of cells with a nucleus or nuclei in a cord blood unit.

Trace: To follow the history of a process, product, or service by review of documents.

Track: To follow a process or product from beginning to end.

Transplantation: The infusion of allogeneic or autologous cord blood cells with the intent of providing transient or permanent engraftment in support of therapy for disease.

Transport: The physical act of transferring a cord blood unit within or between facilities. During transportation the product does not leave the control of trained personnel at the transporting or receiving facility.

Unique: Being the only one of its kind or having only one use or purpose.

Unique Identifier: A numeric or alphanumeric sequence used to designate a specific cord blood unit with reasonable confidence that the identifier will not be used for another purpose, including for another cord blood unit.

Urgent medical need: A situation in which no comparable cord blood unit is available and the recipient is likely to suffer death or serious morbidity without the cord blood unit.

Validation: Confirmation by examination and provision of objective evidence that particular requirements can consistently be fulfilled. A process is validated by establishing, by objective evidence, that the process consistently produces a cord blood unit meeting its predetermined specifications.

Variance: A deviation from recommended practice or Standard Operating Procedure.

Verification: The confirmation of the accuracy of something or that specified characteristics have been fulfilled.
Verification typing: HLA typing performed on an independent sample (or, for a cord blood unit, from an attached segment or from the unit itself) with the purpose of verifying concordance of that typing assignment with the initial HLA typing assignment. Concordance does not require identical levels of resolution for the two sets of typing but requires the two assignments to be consistent with one another.

Viability: Living cells as defined by dye exclusion, flow cytometry, or progenitor cell culture.

Written: Documentation in human readable form.

PART B: CORD BLOOD BANK OPERATIONAL STANDARDS

B1 GENERAL REQUIREMENTS

B1.1 The Cord Blood Bank (CBB) shall consist of an integrated team, under a single CBB Director, responsible for donor management; collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution of cord blood (CB) units; and recipient follow-up.

B1.2 The CBB, each CB Collection Site, and each CB Processing Facility shall operate in compliance with Applicable Law and these Standards.

B1.2.1 The CBB shall be licensed, registered, and/or accredited with as required by the appropriate governmental authorities for the activities performed.

B1.3 The CBB shall have a mechanism to list and distribute CB units for clinical use.

B1.3.1 If the CBB utilizes a registry to deliver services related to the listing, search, selection, reservation, release, and/or distribution of a CB unit:

B1.3.1.1 The responsibilities of the registry shall be clearly documented.

B1.3.1.2 The registry shall comply with these Standards as applicable to its responsibilities.

B1.3.1.3 The registry should be accredited by the WMDA.

B1.4 If the CBB contracts with any other entity for services related to CB unit donor management, collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, distribution, and/or any other aspect of banking, the responsibility of each entity shall be clearly documented.

B1.4.1 Each participating entity shall meet these Standards with respect to its interactions with the CBB.

B1.5 There shall be a CBB Director, a CBB Medical Director, a CB Collection Site Director, a CB Processing Facility Director, and a Quality Management (QM) Supervisor.

B1.5.1 The CBB Director shall have an earned doctoral degree in medicine or in a related scientific field, with training and a minimum of two (2) years of experience in immunogenetics of transplantation, basic or clinical immunology, immunohematology, basic or clinical hematology,
transfusion medicine, blood or tissue banking, or cryobiology. The CBB Director has final responsibility for the CBB operations and its overall compliance with these Standards, including all components of the CBB’s policies and Standard Operating Procedures. The CBB Director shall participate regularly in educational activities related to the field of CB banking and/or cellular therapy product collection, processing, and transplantation.

B1.5.1.1 If the CBB Director does not have specific training and expertise in HLA, the CBB shall ensure HLA expertise is available and utilized by the CBB.

B1.5.2 The CBB Medical Director shall be a licensed physician with training in hematopoietic cell transplantation or blood or tissue banking. This individual is responsible for donor recruitment, donor eligibility, the medical aspects of the CB collection procedures, and the CB Processing Facilities CB processing procedures, and review of the release and administration of the CB unit; and compliance of the CB Collection Sites and CB Processing Facilities with these Standards. The CBB Medical Director shall participate regularly in educational activities related to the field of donor safety, CB banking, and/or cellular therapy product collection, processing, and transplantation.

B1.5.2.1 The CBB Medical Director may also serve as the CBB Director, CB Collection Site Director, and/or CB Processing Facility Director if appropriately credentialed.

B1.5.3 The CB Collection Site Director shall be a licensed health care professional who is responsible for communicating with the CBB Medical Director regarding operations at an individual CB Collection Site. The CB Collection Site Director shall participate regularly in educational activities related to the field of donor safety, CB banking, and/or cellular therapy product collection, processing, and transplantation.

B1.5.3.1 The CBB Medical Director may serve the function of the CB Collection Site Director and need not be licensed in the jurisdiction of the CB collection or be on the staff of the CB Collection Site.

B1.5.4 The CB Processing Facility Director shall be an individual with a relevant doctoral degree, qualified by training or experience for the scope of activities carried out in the CB Processing Facility. The CB Processing Facility Director is responsible for all operational aspects of all procedures related to receipt, testing, processing, cryopreservation, storage, release, and distribution of CB units and administrative operations of the CB Processing Facility, including compliance with these Standards. The CB Processing Facility Director shall participate regularly in educational activities related to the field of...
CB banking and/or cellular therapy product collection, processing, and transplantation.

B1.5.4.1 The CB Processing Facility Director may also serve as the CBB Director and/or CBB Medical Director if appropriately credentialed.

B1.5.5 The QM Supervisor shall be an individual with relevant training in quality management and approved by the CBB Director to establish and maintain systems to review, modify as necessary, approve, and implement all policies and Standard Operating Procedures related to QM and Procedures intended to monitor performance of the CBB, the quality of the CB units, and compliance with these Standards.

B1.5.5.1 The QM Supervisor shall be a different individual from the CBB Director, CBB Medical Director, CB Collection Site Director, and the CB Processing Facility Director.

B1.5.5.2 The QM Supervisor shall not have oversight of his/her own work if this person also performs other tasks in the CBB.

B1.5.5.3 The QM Supervisor shall participate regularly in educational activities related to the field of quality management, CB banking, and/or cellular therapy product collection, processing, and transplantation.

B1.5.6 The CBB shall have an adequate number of qualified staff for its operations.

B1.5.6.1 Qualifications, training, continuing education, and continued competency for the performance of all assigned operations shall be documented for all staff.

B2 QUALITY MANAGEMENT

B2.1 The CBB shall establish and maintain a QM Program that includes all key CBB functions including donor management, collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution, and outcome analysis.

B2.1.1 The CBB shall establish and maintain a written QM Plan that describes the QM Program.

B2.1.2 The CBB Director and the QM Supervisor shall be responsible for participate in the establishment and maintenance of the QM Plan.
B2.1.2.1 The QM Supervisor shall have authority over and responsibility for ensuring the QM Program is effectively established and maintained.

B2.1.3 The QM Supervisor shall report on quality management activities, at a minimum, quarterly.

B2.1.4 The QM Supervisor shall report on the performance of the QM Program on an annual basis, at a minimum.

B2.2 The QM Plan shall document, include, or summarize and reference, documentation of the relationship and interaction among all participating facilities and services, including, at a minimum, CB Collection Sites, CB Processing Facilities, IT services, testing laboratories, storage facilities, and registries, and outcomes databases.

B2.2.1 The QM Plan shall include, or summarize and reference, an organizational chart of key personnel positions, functions, and interactions within the CBB, the CB Collection Sites, and the CB Processing Facility.

B2.3 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for development, establishment and implementation, maintenance of written agreements with external parties whose services impact the CB unit.

B2.3.1 Agreements shall include the responsibility of the external party performing any relevant aspect of CB collection, testing, banking, or release, distribution for administration to comply with Applicable Law, these Standards, and the requirements of other applicable accrediting agencies.

B2.3.2 Agreements shall be dated and reviewed on a regular basis.

B2.4 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for personnel education, experience, and training requirements for each key position in the CBB. Personnel requirements shall include at a minimum:

B2.4.1 Current position description for each staff member.

B2.4.2 A system to document for each staff member:

B2.4.2.1 Initial qualifications.

B2.4.2.2 Orientation.

B2.4.2.3 Initial training, training on each procedure performed, and retraining as necessary.
B2.4.2.4 Competency for each function performed.
B2.4.2.5 Continued competency at least annually.
B2.4.2.6 Annual performance review.
B2.4.2.7 Continued education.

B2.4.3 Trainer and training requirements for each position in the CBB, including at a minimum:

B2.4.3.1 A policy and/or Standard Operating Procedure for personnel training and competency assessment.
B2.4.3.2 A system to ensure consistent training programs.
B2.4.3.3 A description of minimal trainer qualifications.

B2.4.4 Records of identification codes of personnel including methods to link the name and/or signature, to the initials, and inclusive or other codes used to identify the responsible staff member. These records shall include dates of employment.

B2.5 The QM Plan shall include, or summarize and reference, a system for change control that includes at a minimum:

B2.5.1 A description of the proposed change and who is affected.
B2.5.2 Analysis of the change for compliance with these Standards and Applicable Law.
B2.5.3 Identification of risks of the change to the donor, CB unit, or recipient.
B2.5.4 Determination of impact on existing processes, policies, and Standard Operating Procedures.
B2.5.5 System for change approval, effective date, and implementation.
B2.5.6 Methods for communication of the change and training, if applicable.

B2.6 The QM Plan shall include, or summarize and reference, a system for document control. The document control system shall include the following elements at a minimum:

B2.6.1 Definition and Current listing of all critical documents that shall comply with the document control system requirements. Controlled documents shall include at a minimum:

B2.6.1.2 Worksheets.

B2.6.1.3 Forms.

B2.6.1.4 Labels.

B2.6.1.5 Educational, promotional, and recruitment materials.

B2.6.2 Assignment of a numeric or alphanumeric identifier and title to each document and document version regulated within the system.

B2.6.3 A procedure for document approval, including the approval date, signature of approving individual(s), and the effective date.

B2.6.4 A procedure for document distribution to relevant personnel, including written confirmation that relevant personnel have received and read the document.

B2.6.5 A system for document change control that includes description of the change, signature of approving individual(s), approval date, and effective date.

B2.6.5.1 There shall be a system to ensure that controlled documents cannot undergo accidental or unauthorized modification.

B2.6.6 A system for document creation, assembly, review, storage, archival, retention, and retrieval.

B2.6.6.1 There shall be a standardized system for denoting the date each document became effective and when it was archived, if applicable.

B2.6.6.2 There shall be a system for the retraction of obsolete documents to prevent unintended use.

B2.6.6.3 Records of archived Standard Operating Procedures, protocols, and labels, in their historical sequence including inclusive dates of use, shall be maintained indefinitely.

B2.6 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for establishing and maintaining clearly written policies and Standard Operating Procedures that are precise and unambiguous and address all aspects of the operation.
B2.6.7 A Standard Operating Procedure for preparation, approval, implementation, and review, revision, and archival of all policies and Standard Operating Procedures.

B2.7 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures to support management of electronic record systems and electronic records and to maintain pertinent electronic records, if applicable.

B2.8 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures to ensure continuous operations in the event that the electronic record system ceases to function, including a plan for data backup and to ensure compliance with Applicable Law. CBB’s operations are interrupted.

B2.9 The QM Plan shall include, or summarize and reference, a system to maintain confidentiality.

B2.10 The QM Plan shall include, or summarize and reference, policies, Standard Operating Procedures, and a schedule for conducting audits of key CBB functions annually at a minimum to verify compliance with elements of the Quality Management Program and operational policies and procedures.

B2.10.1 Key functions shall include donor management, collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution, and outcome analysis.

B2.10.2 There shall be a written procedure for the management of external audits and inspections.

B2.10.2.1 Documentation of results of inspection and accreditation visits shall be maintained indefinitely.

B2.10.3 Quality audits shall be conducted by an individual with sufficient expertise to identify problems, but who is not directly solely responsible for the process being audited.

B2.10.4 Collection and analysis of data related to the audit shall be reviewed, reported, and documented, at a minimum, on an annual basis.

B2.10.5 The results of audits shall be used to recognize problems, detect trends, and identify improvement opportunities, and determine the effectiveness of corrective and preventive actions when necessary.

B2.10.6 Audit results shall be shared with the appropriate Director and/or Medical Director, supervisor of the area audited, and other relevant staff.
B2.10.7 Audits shall include documentation that external facilities performing critical contracted services have met the requirements of the written agreements.

B2.11 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures to address errors, accidents, biological product deviations, adverse events, variances, and complaints, including the following activities at a minimum:

B2.11.1 Detection.

B2.11.1.1 There shall be a defined process improvement plan that includes policies or procedures for the recognition of all issues that require corrective action.

B2.11.2 Investigation.

B2.11.2.1 A thorough investigation shall be conducted by the CBB in collaboration with the CB Collection Site, CB Processing Facility, registry, and/or Clinical Program, as appropriate.

B2.11.3 Documentation.

B2.11.3.1 Cumulative files of errors, accidents, biological product deviations, adverse events, variances, and complaints shall be maintained.

B2.11.3.2 A written report of the investigation including conclusions, follow-up, and corrective action, if applicable, shall be prepared and maintained as part of the record for that final CB unit and maintained in the applicable cumulative file.

B2.11.3.3 Investigation reports shall be reviewed and signed by the CBB Director or designee.

B2.11.3.4 Records of all severe or unexpected adverse events or adverse reactions during CB collection and infusion shall be maintained.

B2.11.4 Tracking.

B2.11.4.1 Errors, accidents, biological product deviations, adverse events, variances, and complaints shall be tracked and trended in order to categorize and identify system problems and initiate corrective action.

B2.11.4.2 Investigation reports shall be utilized in quality monitoring and tracking in order to analyze trends.

B2.11.5 Evaluation.
B2.11.5.1 Planned variances shall be pre-approved by the appropriate CBB Director and/or Medical Director, representatives from the QM Program, and other staff as appropriate.

B2.11.5.2 Unplanned variances and associated corrective action, if necessary, shall be reviewed by the appropriate CBB Director and/or Medical Director, representatives from the QM Program, and other staff as appropriate.

B2.11.5.3 The CBB Director or designee shall review all errors, accidents, biological product deviations, adverse events, variances, and complaints in a timely manner. This review shall be documented.

B2.11.5.4 Each complaint shall be evaluated to determine if the complaint is related to a product deviation or adverse reaction. Corrective action shall be initiated when appropriate.

B2.11.6 Reporting.

B2.11.6.1 When it is determined that the CB unit was responsible for an adverse reaction, the reaction and results of the investigation shall be reported to the Clinical Program, other facilities participating in the manufacturing of the CB unit, registries, and governmental agencies as required by Applicable Law or these Standards.

B2.11.6.2 Errors, accidents, biological product deviations, variances, and complaints shall be reported to other facilities performing CBB functions on the affected CB unit and to the appropriate regulatory and accrediting agencies, registries, grant agencies, and IRBs or Ethics Committees as necessary.

B2.11.7 Corrective action.

B2.11.7.1 Corrective action shall be implemented and documented as indicated, including both short-term action to address the immediate problem and long-term action to prevent the problem from recurring.

B2.11.7.2 Corrective actions shall include the initiation of retraining and/or re-education of employees and performing follow-up audits of deficiencies, as appropriate.

B2.11.7.3 Documentation of the corrective action shall include the nature of the problem requiring corrective action and the identity and disposition of the affected CB unit, if indicated.
B2.11.7.4 Documentation of the corrective action shall be maintained, including the dates of corrective action and a designated timeframe at which the outcome of the corrective action shall be evaluated.

B2.11.7.5 Corrective actions shall be evaluated by the appropriate Director and/or Medical Director, or designee, representatives from the QM Program, and other appropriate staff.

B2.12 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for qualification of critical vendors, equipment, supplies, and reagents, and facilities.

B2.12.1 Qualification studies shall be reviewed and approved by the CBB Director or designee from the QM Program.

B2.12.2 Suppliers of critical supplies, reagents, services, and equipment shall be qualified by a method that ensures they are compliant with applicable laws and regulations and these Standards.

B2.13 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for validation of significant critical procedures of the CBB functions.

B2.13.1 Determination of which critical procedures to be validated shall be made by the CBB Director or CBB Medical Director in collaboration with representatives of the QM Program.

B2.13.2 Validation studies Each validation shall include:

B2.13.2.1 A validation plan, including conditions to be validated.

B2.13.2.2 Acceptance criteria.

B2.13.2.3 Data collection.

B2.13.2.4 Evaluation of data.

B2.13.2.5 Summary of results.

B2.13.2.6 Documentation of review and approved acceptance of the methodology by representatives of the QM Program.

B2.13.2.7 Review and approval by the CBB Director or designee from the QM Program of the validation results and conclusions.

B2.13.3 Changes to a process shall be verified or validated to ensure that they do not create an adverse impact anywhere in the operation.
B2.13.4 Records shall be maintained to document that procedures have been validated to achieve the expected end-points, including viability of CB cells and product characteristics.

B2.14 The QM Plan shall include, or summarize and reference, processes, policies and procedures for CB unit tracking, tracing, and linkage that allow tracking and tracing of the CB unit from the infant donor to the recipient or final disposition and tracing from the recipient or final disposition to the infant donor.

B2.14.1 Linkage of the CB unit to the infant donor and mother shall be retained confidentially and indefinitely.

B2.14.2 Documentation of all facilities involved in each stage of CB unit manufacturing shall be established and maintained.

B2.15 The QM Plan shall include, or summarize and reference, processes, policies and procedures to track, trend, investigate, and evaluate details of clinical outcome data and CB unit characteristics.

B2.15.1 The CBB shall define expected clinical outcomes and CB unit characteristics.

B2.15.2 Both individual CB unit data and aggregate data shall be evaluated.

B2.15.3 There shall be a written stability program that annually evaluates a minimum of three CB units.

B2.15.3.1 There shall be a plan for defining an expiration date.

B3 POLICIES AND STANDARD OPERATING PROCEDURES

B3.1 The CBB shall establish and maintain policies and/or Standard Operating Procedures addressing critical aspects of operations and management in addition to those required in B2. These documents shall include all elements required by these Standards and shall address at a minimum:

B3.1.1 Donor recruitment.

B3.1.2 Maternal screening and testing (including interpretation and acceptable results).

B3.1.3 Informed consent.

B3.1.4 Donor eligibility criteria and determination.

B3.1.5 Interaction between the CB Collection Site and the CBB.

B3.1.6 Documentation of infant donor health at birth.
B3.1.7 Collector training.
B3.1.8 Collection of CB units, associated samples, and maternal samples.
B3.1.9 Completion of records at the CB Collection Site.
B3.1.10 Storage of CB units, associated samples, maternal samples, and documentation at the CB Collection Site.
B3.1.11 Transport and shipping of the CB unit, associated samples, maternal samples, and documentation to the CB Processing Facility.
B3.1.12 Labeling of the CB unit, associated samples, reference samples, retention samples, maternal samples, and associated documents at the CB Collection Site, at the CB Processing Facility, and at release for administration.
B3.1.13 CB unit acceptance criteria for receipt, processing, cryopreservation, and storage.
B3.1.14 Process control, including product specifications and nonconforming products.
B3.1.15 Storage of reference samples, retention samples, and maternal samples for testing.
B3.1.16 Communicable disease testing, microbial cultures, hemoglobinopathy testing, and other testing. Acceptance criteria for test results shall be described.
B3.1.17 Notification of mothers or their responsible physicians and/or governmental agencies, when required, of positive or indeterminate communicable disease and/or genetic test results.
B3.1.18 Criteria for qualification and listing of CB units available for search and administration.
B3.1.19 Listing, search, selection, reservation, release, and distribution of CB units.
B3.1.20 HLA typing to include requirements for resolution, loci, timing, and verification.
B3.1.21 Verification that the infant donor and recipient are different individuals in the case of complete HLA matches.
B3.1.22 Collection and analysis of transplant outcome data.
B3.1.23 Electronic record entry, verification, and revision.
B3.1.2 Data management.
B3.1.25 CB unit records.
B3.1.26 CB unit disposition.
B3.1.27 Facility management and environmental monitoring.
B3.1.28 Materials management, maintenance and monitoring of equipment, cleaning and sanitation procedures, and disposal of medical and biohazardous waste.
B3.1.29 Emergency and safety procedures.
B3.1.30 Biological, chemical, and, if applicable, radiation safety.
B3.1.31 Disaster plan, including CBB-specific issues.

B3.2 The CBB shall maintain a detailed Standard Operating Procedures Manual.
The Standard Operating Procedures Manual shall include at a minimum:

B3.2.1 A table of contents.
B3.2.2 A standardized format for policies, procedures, worksheets, forms, and labels.

B3.3 Standard Operating Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to follow and complete the procedures successfully. Each individual Standard Operating Procedure shall include:

B3.3.1 A clearly written description of the objectives.
B3.3.2 The personnel responsible for its execution.
B3.3.3 A description of the facility, equipment, and supplies required.
B3.3.4 A stepwise description of the procedure.
B3.3.5 Acceptable end-points and the expected range of results, if applicable.
B3.3.6 Reference to other Standard Operating Procedures or policies required to perform the procedure.
B3.3.7 A reference section listing appropriate literature, if applicable.
B3.3.8 A current version of worksheets, forms, reports, and labels, where applicable.
B3.3.9 The date(s) and the approval signature of the CBB Director, the QM Supervisor, and relevant key personnel prior to implementation.

B3.3.10 The date of review or revision and the approval signature of the CBB Director or designee, the QM Supervisor, and relevant key personnel upon procedural modifications and at least every two years after implementation.

B3.4 All policies and Standard Operating Procedures shall comply with these Standards.

B3.5 Copies of policies and Standard Operating Procedures of the CBB relevant to the processes being performed shall be readily available to the CBB personnel.

B3.6 All personnel at the CBB, CB Collection Sites, and CB Processing Facilities shall follow the applicable policies and Standard Operating Procedures established by the CBB.

B3.7 Review and/or training by a staff member shall be documented before the staff member is allowed to perform new and revised policies and procedures.

B4 FACILITIES AND SAFETY

B4.1 All CBB facilities and sites shall be safe, sanitary, and secure.

B4.1.1 The CBB space shall be of adequate size, construction, and location to maintain safe operations, prevent contamination, and ensure orderly handling.

B4.1.2 The CBB space shall be maintained in a clean, sanitary, and orderly manner to prevent introduction, transmission, or spread of communicable disease.

B4.1.3 Separate areas shall be identified and maintained for processing and storage of CB units to prevent mislabeling, mix-ups, product contamination, and cross-contamination of CB units.

B4.1.4 The CBB shall be secure to prevent the admittance of unauthorized individuals.

B4.2 There shall be policies and Standard Operating Procedures for biological, chemical, and radiation safety as appropriate, including:

B4.2.1 Communicable disease agents.

B4.2.2 Chemical hygiene.

B4.2.3 Hand washing.
B4.2.4 Fire safety.
B4.2.5 Radiation safety, if applicable.
B4.2.6 Latex allergy.
B4.2.7 Power failures.
B4.2.8 Liquid nitrogen.
B4.2.9 Discard of medical biological waste.

B5 CORD BLOOD BANK OPERATIONS

B5.1 The responsibilities of each CB Collection Site, CB Processing Facility, collecting licensed health care professional, and registry as they relate to the CBB shall be clearly defined and documented.

B5.1.1 A CBB that includes multiple CB Collection Sites and/or CB Processing Facilities shall employ coordinated policies and Standard Operating Procedures, protocols, staff training and competency evaluation procedures, and quality management systems.

B5.1.2 A CBB that includes multiple CB Collection Sites and/or CB Processing Facilities shall demonstrate evidence of regular interaction between these CB Collection Sites and/or CB Processing Facilities and the CBB.

B5.2 The CBB shall be responsible for all components of CB unit manufacturing, including at a minimum:

B5.2.1 Donor recruitment and consent processes.
B5.2.2 Infant donor and maternal screening and testing.
B5.2.3 Donor eligibility determination.
B5.2.4 Documentation of infant donor health at birth.
B5.2.5 Collection.
B5.2.6 Testing.
B5.2.7 Processing.
B5.2.8 Labeling.
B5.2.9 Cryopreservation.
B5.2.10 Storage.
B5.2.11 Release for listing.
B5.2.12 Listing CB units available for search.
B5.2.13 Selection and reservation.
B5.2.14 Release of the CB unit for administration.
B5.2.15 Transportation and shipping.
B5.2.16 CB unit records.
B5.2.17 CB unit disposition
B5.2.18 **Recipient** follow-up and outcome analysis.

B5.3 Records of each CB unit shall be made concurrently with each stage of donor management and CB unit collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, distribution, and/or disposal **in such a way that all steps may be accurately traced.**

B5.3.1 Records shall identify the person immediately responsible for each step **from collection to final disposition of the CB unit** and include appropriate dates and times to provide a complete history of the work performed and to relate the records to a particular CB unit.

B5.3.2 Records shall be as detailed as necessary for a clear understanding by a person experienced in CBB procedures.

B5.4 The CBB shall have an established relationship with each fixed CB Collection Site to ensure implementation of and compliance with the CBB QM Program and Standard Operating Procedures.

B4.6 For collection of CB units at non-fixed CB Collection Sites, the CBB shall have a written agreement with and informed consent from the infant donor family and shall have communicated with the collecting licensed health care professional.

B4.6.1 The CBB shall provide the appropriate policies, Standard Operating Procedures, and materials for the collection, labeling, storage, packing, and transport or shipment of the CB unit, reference samples, and maternal samples.

B4.6.2 The CBB shall monitor the quality of the CB unit collections through its QM Program.
B5.5 The CBB shall incorporate CB collection activities at fixed and nonfixed CB Collection Sites into its Quality Management program.

B5.6 The CBB shall utilize an HLA testing laboratory appropriately accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), the European Federation for Immunogenetics (EFI), or equivalent accrediting organization outside North America and Europe, with the capability of carrying out deoxyribonucleic acid (DNA)-based HLA typing.

B5.7 All laboratories utilized by the CBB for testing of reference samples and maternal samples shall be accredited, certified, or licensed to perform such testing in accordance with Applicable Law.

B5.7.1 The CBB shall maintain documentation of the accreditation, certification, or licensure of these laboratories to perform this testing.

B5.7.2 When external laboratories are used for any aspect of reference sample or maternal sample testing, the CBB shall maintain a record of all samples sent to such laboratories, including the identifiers, results, date sent, and date results are received.

B5.8 Confidentiality.

B5.8.1 There shall be a process for maintenance of confidentiality of all records and communications among the CBB, the CB Collection Sites, the CB Processing Facility, testing laboratories, registries, and Clinical Programs according to Applicable Law.

B5.8.2 The CBB shall have written policies and Standard Operating Procedures for circumstances where the infant donor’s mother or legal guardian and/or her physician could be contacted.

B5.8.3 Employee records shall be maintained in a confidential manner as required by Applicable Law.

B5.9 Quality control procedures shall be developed to monitor the continuing adequacy of the procedures, reagents, equipment, and supplies as used under routine operating conditions by the CBB personnel.

B5.9.1 The results of ongoing internal monitoring shall be documented and checked, and trends shall be analyzed on a regular basis.

B5.10 There shall be a process for the regular review of records and for the assessment of record review to identify recurring problems, potential points of failure, or need for process improvement.
B5.11 The CBB shall obtain, maintain, and analyze sufficient critical outcome data to ensure that the procedures in use in the CBB consistently provide a safe and effective product.

B5.12 Institutional Review Board or Ethics Committee Requirements.

B5.12.1 In compliance with Applicable Law, the CBB shall have formal review of investigational protocols and maternal consent for CB banking and related activities by a mechanism that is approved by the Office of Human Research Protections under the United States Department of Health and Human Services (HHS), the United States Food and Drug Administration (FDA), or non-U.S. equivalent governmental authority.

B5.12.2 The CBB shall maintain documentation of all its research protocols, Institutional Review Board or Ethics Committee approvals or equivalent, correspondence with regulatory agencies, investigational new drug or device exemptions, annual reports, and any adverse events.

B6 CODING AND LABELING OF CORD BLOOD UNITS

B6.1 ISBT 128 Coding and Labeling.

B6.1.1 CB units shall be identified according to the proper name of the unit, including appropriate modifiers and attributes, as defined in ISBT 128 Standard Terminology for Blood, Cellular Therapy, and Tissue Product Descriptions.

B6.1.2 If the CBB has not fully implemented ISBT 128 technology, an implementation plan for the usage of ISBT 128 coding and labeling shall be in place.

B6.2 Label Controls.

B6.2.1 Pre-printed labels.

B6.2.1.1 Labels shall be held upon receipt from the manufacturer pending review and proofing against a copy or template approved by the CBB Director or designee to ensure accuracy regarding identity, content, and conformity.

B6.2.1.2 Stocks of unused labels representing different products shall be stored and maintained in a controlled manner to prevent errors.

B6.2.1.3 Unused obsolete labels shall be destroyed.
B6.2.2 Print-on-demand label systems shall be validated to ensure accuracy regarding identity, content, and conformity of labels to templates approved by the CBB Director or designee.

B6.2.3 A system for label version control shall be employed.

B6.2.4 Representative obsolete labels shall be archived indefinitely.

B6.2.5 The label shall be validated as reliable for storage under the conditions in use.

B6.3 Labeling Operations.

B6.3.1 Labeling operations shall be conducted in a manner adequate to prevent mislabeling or misidentification of CB units, associated samples, reference samples, maternal samples, and associated documents.

B6.3.2 There shall be processes to verify that all labels in use are accurate, legible, and maintain physical integrity.

B6.3.2.1 A system of checks in labeling procedures shall be used to prevent errors in transferring information to labels.

B6.3.2.2 A controlled labeling procedure consistent with applicable law shall be defined and followed if container label information is transmitted electronically during a labeling process. This procedure shall include a verification step.

B6.3.2.3 When the label has been affixed to the CB unit bag, a sufficient area of the bag shall remain uncovered to permit inspection of the contents.

B6.3.2.4 The information entered manually on the CB unit bag label shall be verified by at least two (2) staff members prior to allowing the CB unit to progress to the next stage of processing, storage, or distribution.

B6.3.2.5 All data fields on labels shall be completed.

B6.3.2.6 All labeling shall be clear, legible, and printed using ink that is indelible to all relevant agents.

B6.3.2.7 Labels affixed directly to a CB unit bag shall be applied using appropriate materials as defined by the applicable regulatory authority.

B6.3.3 CB units that are subsequently re-packaged into new containers shall be labeled with new labels before they are detached from the original container.
B6.3.3.1 The process to establish linkage between original and new labels shall be validated.

B6.3.3.2 This linkage shall be maintained as a permanent part of the CB unit record.

B6.4 Identification.

B6.4.1 There shall be a human-readable system and a machine-readable system of in operation for identification for the CB unit, associated samples, reference samples, maternal samples, and associated documents.

B6.4.2 Each CB unit shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to trace any CB unit to its maternal and infant donor data, delivery information, family history, test results, and to all records describing the handling and final disposition of the CB unit.

B6.4.2.1 There shall be processes to ensure that the CB unit identifier is unique to prevent errors in identification.

B6.4.2.2 If a single CB collection is stored in multiple portions more than one fraction, there shall be a system to identify each portion fraction.

B6.4.3 Facilities may designate an additional or supplementary numeric or alphanumeric identifier to the CB unit, associated samples, reference samples, or maternal samples.

B6.4.3.1 Supplementary identifiers shall not obscure the original identifier.

B6.4.3.2 No more than one supplementary identifier shall be visible on a CB unit bag.

B6.4.3.3 The facility associated with each identifier shall be documented.

B6.5 The information provided on the label by the CB Collection Site shall be maintained indefinitely as part of the CB unit record.

B6.6 Label Content.
B6.6.1 There shall be processes to ensure the content of each label is compliant with Applicable Law and the requirements of these Standards.

B6.6.2 Each label shall include at least the required information detailed in Appendix I, the Cord Blood Unit Labeling table in Appendix I and in the Modified Circular of Information Biohazard and Warning Labels table in Appendix II.

B6.6.3 A CB unit bag with a partial label shall be accompanied by the required information detailed in Appendix I, the Cord Blood Unit Labeling table in Appendix I attached securely to the CB unit on a tie tag or enclosed in a sealed package to accompany the CB unit.

B6.6.4 A partial label at a minimum shall be present on the CB unit during all stages of processing.

B6.7 Elements detailed in Appendix III, the Accompanying Documents at Distribution to a Clinical Program, table in Appendix III shall accompany the CB unit at distribution to a Clinical Program, according to Applicable Law.

B5.6 If required by Applicable Law, the CB unit label shall include:

B5.6.1 For products under Investigational New Drug Application the statement “Caution: New Drug—Limited by Federal (or United States) law to investigational use.”

B5.6.2 For licensed products, the statement “Rx Only.”

B7 EQUIPMENT

B7.1 All critical equipment shall be defined, qualified, and validated for the intended use.

B7.1.1 Equipment shall be used in accordance with the manufacturer’s instructions.

B7.2 Equipment used shall not adversely affect the viability of the CB units and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease, mix-ups, contamination, and cross-contamination, and that does not compromise unit function and integrity.

B7.3 Equipment shall conform to Applicable Law.

B7.4 Equipment records shall include the manufacturer’s name, serial number or other identifier, manufacturer’s instructions, equipment location, and use of each piece of equipment, including the identification of each CB unit for which the equipment was used.
B7.4.1 Equipment records shall be maintained for a minimum of 10 years after distribution of the CB unit.

B7.5 Calibration.

B7.5.1 Equipment shall be observed, tested, and calibrated on a regularly scheduled basis as recommended by the manufacturer, after a critical repair or move, or and, at a minimum, annually.

B6.4.2 Calibration acceptance criteria shall be defined.

B7.5.2 All equipment with a critical measuring function shall be calibrated against a traceable standard, if available. Where no traceable standard is available, the basis for calibration shall be described and documented.

B7.5.3 When equipment is found to be out of calibration or specification, there shall be a defined process for action required for CB units manufactured during the period of uncertainty.

B7.5.4 Records of the dates and copies of calibration results shall be maintained.

B7.6 Maintenance and repairs.

B7.6.1 Equipment shall be maintained in a clean and orderly manner and located so as to facilitate cleaning, disinfection, calibration, and maintenance according to established schedules.

B7.6.2 Records of the maintenance schedule; maintenance performed; and damage, malfunction, modification, or repair to equipment shall be maintained.

B6B7.6.3 There shall be a procedure that addresses the actions to take in the event of equipment malfunction or failure.

B7.7 Cleaning and sanitation.

B7.7.1 Equipment shall be cleaned and sanitized according to established schedules.

B7.7.2 Records of equipment cleaning and sanitation shall be maintained.

B7.8 Equipment shall be routinely inspected for cleanliness, sanitation, and calibration and to ensure adherence to applicable equipment maintenance schedules.
B7.8.1 Equipment shall be routinely inspected for compliance to cleaning and maintenance schedules.

B7.9 Records of recent maintenance, cleaning, sanitizing, calibration, and other activities shall be displayed on or near each piece of equipment.

B8 SUPPLIES AND REAGENTS

B8.1 Vendors for all critical reagents and supplies shall be qualified.

B8.2 Critical reagents and supplies shall be defined and qualified to function as expected.

B8.3 Supplies and reagents shall not adversely affect the viability of the CB units and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease.

B8.4 Supplies and reagents that come into contact with the CB unit shall be sterile.

B8.4.1 Sterilization of supplies and reagents prepared within the facility shall be documented.

B8.5 Supplies and reagents should be used in a manner consistent with instructions provided by the manufacturer.

B8.6 Supplies and reagents used for CB collection, processing, or cryopreservation, whenever possible, shall be approved for human use.

B8.6.1 Supplies and reagents shall be of the appropriate grade for the intended use.

B8.7 Certificates of analysis shall be obtained and maintained indefinitely on file for all critical reagents.

B8.8 Receipt, inspection, verification, acceptance, and storage of supplies and reagents shall be documented.

B8.8.1 The disposition of rejected supplies and reagents shall be documented.

B8.9 The lot number, expiration date, and manufacturer of supplies and reagents used for the collection and processing of each CB unit shall be documented.

B9 INVENTORY MANAGEMENT
The inventory management system shall clearly distinguish directed-related CB units from unrelated CB units.

The inventory management system for CB units shall ensure-allow each CB unit and its associated samples, reference samples, maternal samples, and records related to be located in a timely way. The inventory records shall include:

- B9.2.1 CB unit unique identifier.
- B9.2.2 Maternal donor identifier.
- B9.2.3 Storage device identifier.
- B9.2.4 Location within the storage device.

The inventory management system shall be designed to prevent mix-ups, contamination of the CB units during storage, and the improper release of quarantined CB units.

The inventory management system shall be designed to address the duration of storage for cryopreserved CB units, including assigning an expiration date to CB units where appropriate.

The CBB shall have policies related to the return of CB units to the CBB inventory.

- B9.5.1 Unrelated allogeneic CB units shall not be returned to the CBB inventory after they have left the CBB premises.
- B9.5.2 If related CB units are returned to the CBB inventory, there shall be documentation of appropriate storage and transportation.

INVENTORY TRANSFER

If all or part of a CB unit inventory is to be transferred to another CBB:

- B10.1 The CBB shall have policies and Standard Operating Procedures describing the transfer of inventory.
- B10.2 There shall be a written agreement between the transferring and accepting CBBs that describes the responsibilities of each CBB, including the elements in B9B10, at a minimum.
- B10.3 There should be a mechanism to contact the transferring CBB Director or designee for future reference, as defined in the contract or agreement.
Inventory transferred to another CBB shall be accompanied by the following at a minimum:

All collection and processing records, including at a minimum:

- Medical and genetic history
- Identity and results of all maternal and CB unit testing
- A summary of records used to make the donor eligibility determination
- Cryopreservation records, including freezing curve.

All associated samples, reference samples, and maternal samples.

The complete storage history of each CB unit inventory in a way that the history of individual CB units can be traced, including the storage temperature records and records of any transfer of a CB unit to a different storage location.

The transferring and accepting CBBs shall collaborate to ensure that:

- The inventory is transferred in a manner that maintains proper storage temperature and prevents mix-ups and contamination.
- Transport and shipping does not adversely affect the integrity of the CB units.
- The safety of transporting and shipping personnel is ensured.
- The accepting CBB is notified of the manufacturer and dimensions of the storage bag and canister to properly store the CB unit.

There shall be policies to maintain confidentiality.

Responsibilities of the accepting CBB.

Records shall be in a language and form that can be understood by the accepting CBB personnel.

There shall be documentation of review of records and of transferred inventory to ensure that:

- The CB units were stored in appropriate storage bags at appropriate storage temperatures.
B9.5.2.2 Maintenance of appropriate storage conditions throughout the period of storage can be documented.

B9.5.2.3 Integrais attached segments and other reference samples and maternal samples CB units meet the requirements of the written agreement for each CB unit are included in the transferred transfer of inventory.

B9.5.2.4 Records are available to link each CB unit to its infant donor, its reference samples and maternal samples; and all relevant history, collection, processing, cryopreservation, and testing records.

B9.5.3 Records received shall include at a minimum:

B10.5.3 Transferred records shall include at a minimum:

B10.5.3.1 Maternal consent.

B10.5.3.2 Medical and genetic history.

B10.5.3.3 Identity and results of all maternal and CB unit communicable disease tests, and, if performed, the identity and results of all CB unit communicable disease tests.

B10.5.3.4 All results from testing performed on the CB unit, including CB unit cell counts and sterility testing.

B10.5.3.5 Processing methods Processing information.

B10.5.3.6 Cryopreservation records, including freezing curve.

B10.5.3.7 The manufacturer and approximate dimensions of the storage bag and canister.

B10.5.3.8 EnumerationNumber of attached segments and other reference samples.

B9.5.4 There shall be access to all records described in B10.

B10.5.3.9 Other records as required to allow the receiving CBB to meet these Standards.

B10.5.4 There shall be a process for inspecting incoming CB units for damage and contamination.
B10.5.5 After the CB units have been transferred, but before the transferred inventory is made available for search:

B10.5.5.1 The integrity and viability of thawed CB units shall be verified to ensure confirm the transport or shipping method did not compromise CB unit viability.

B10.5.5.2 There shall be confirmation of the completeness of the records including donor identity and HLA as described in B10.5.3, typing results.

B10.5.5.3 The accepting CBB shall determine whether to accept, reject, or place in quarantine incoming CB units based on established criteria designed to prevent the transmission of communicable diseases.

B11 DOCUMENTS AND RECORDS REQUIREMENTS

B11.1 A record management system shall be established and maintained to ensure allow for protection, preservation, integrity, and ready retrieval of records.

B11.1.1 Records shall be available for inspection by authorized individuals upon request from a regulatory or accrediting agency.

B11.2 If records are maintained in more than one location and/or format, there shall be a system to ensure for prompt identification, location, and retrieval of all records.

B11.3 Identity and medical records of the infant donor and family shall be in a language understood by the CBB personnel, registry, and/or Clinical Program.

B11.3.1 Records of CB units manufactured in or exported to the U.S. shall be in English or, if in another language, shall be translated to English and accompanied by a statement of authenticity by the translator prior to release of the CB unit.

B11.4 The following CBB records shall be maintained indefinitely:

B11.4.1 Infant donor and parental records.

B11.4.2 CB unit records related to collection, processing, storage, and distribution.

B11.4.3 QM records.

B11.4.4 Personnel records.
B11.5 Facility cleaning and sanitation records shall be retained for three (3) years at a minimum.

B11.6 Equipment maintenance, inspection, calibration, and sterilization records shall be retained indefinitely.

B11.7 Records in case of divided responsibility.

B11.7.1 If two (2) or more facilities participate in donor management or the collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, or distribution of the CB unit, the records of each facility shall plainly show the extent of its responsibility.

B11.7.2 The CBB shall maintain a listing of the names, addresses, and responsibilities of other facilities that perform manufacturing steps on a CB unit.

B11.7.3 There shall be a system to allow the CBB access to information that tracks all manufacturing steps performed by other facilities.

B11.7.4 Each participating facility shall furnish to the facility of final disposition a copy of CB collection and processing records related to the safety of the CB unit.

B11.8 Electronic Records Requirements.

B11.8.1 The CBB shall establish and maintain a current listing of all critical electronic record systems. Critical electronic record systems shall include at a minimum systems under the control of the CBB that are used:

B11.8.1.1 In lieu of paper.

B11.8.1.2 To make decisions.

B11.8.1.3 To perform calculations.

B11.8.1.4 To create and/or store information used in critical procedures.

B11.8.2 For all critical electronic record systems, there shall be policies, procedures, and system elements to ensure the authenticity, accuracy, integrity, identity, and confidentiality of all records.

B11.8.2.1 There shall be a means by which access to electronic records is limited to authorized individuals.
B11.8.2.2 There shall be protection of the records to enable their accurate and ready retrieval throughout the period of record retention.

B11.8.2.3 All critical electronic record systems shall ensure that all donor and CB unit identifiers are unique.

B11.8.3 For all critical electronic record systems, there shall be an alternative system for all electronic records that ensures to allow for continuous operation of the CBB in the event that critical electronic record systems are not available. The alternative system shall be validated and CBB staff shall be trained in its use.

B11.8.4 For all critical electronic record systems, there shall be written procedures for record entry, verification, and revision.

B11.8.4.1 A system method shall be established or the system shall provide for review of data before final acceptance.

B11.8.4.2 A method shall be established or the system shall provide for the unambiguous identification of the individual responsible for each record entry.

B11.8.5 For all critical electronic record systems, there shall be the ability to generate true copies of the records in both paper and electronic format suitable for inspection and review.

B11.8.6 For all critical electronic record systems, there shall be a validated procedures for and documentation of:

B11.8.6.1 Systems development.

B11.8.6.2 Numerical designation of system versions, if applicable.

B11.8.6.3 Prospective validation of system, including hardware, software, and databases.

B11.8.6.4 Installation of the system.

B11.8.6.5 Training and continued competency of personnel in systems use.

B11.8.6.6 Monitoring of data integrity.

B11.8.6.7 Back-up or alternative system for all of the electronic records that ensures continuous operation in the event that primary electronic data are not available. System on a regular schedule.
B10.6.4.1 Documentation of periodic testing of the alternative system shall be maintained.

B10.6.5 There shall be a system that limits access to the electronic records to only authorized individuals.

B10.6.6 B11.8.6.8 System maintenance and operations.

B11.8.7 All system modifications shall be authorized, documented, and validated prior to implementation.

B12 INTERRUPTION OF OPERATIONS AT ESTABLISHED SITES

B12.1 In the event that any CB collection or processing function is discontinued for a period exceeding six months, there shall be documentation of the training and continued competency of all staff to perform the duties assigned upon resumption of activities.

B12.2 If CB collection activity is discontinued at any fixed CB Collection Site for a period exceeding six months, the CBB Director or designee shall review and renew the CB collection contract with that site.

B12.3 If a CBB discontinues processing of new CB units:

   B12.3.1 There shall be competent staff to oversee, maintain, and distribute the inventory.

   B12.3.1.1 The staff shall maintain communication with all relevant registries and Clinical Programs, if applicable.

   B12.3.2 A process to distribute CB unit contiguous segments and samples for testing shall be maintained.

   B12.3.3 All records of the entire inventory in storage shall be maintained.

B12.4 Prior to the reestablishment of either CB collection or processing, as applicable, the following at a minimum shall be documented:

   B12.4.1 Review of all procedures to ensure that methods are consistent with current practices.

   B12.4.2 Inspection of all reagents and supplies to ensure none will be used past its expiration date.
B12.4.3 Validation, calibration, and maintenance of all equipment have been completed within the time periods specified in the Standard Operating Procedures and manufacturer’s instructions.

B12.5 Cessation of operations.

B12.5.1 The CBB shall follow all contractual obligations that are specified in written agreements with the directed infant CB Collection Sites, donor families.
PART C: CORD BLOOD DONOR MANAGEMENT AND COLLECTION STANDARDS

C1 GENERAL REQUIREMENTS

C1.1 These Standards shall apply to all CB donor management and collection procedures.

C1.2 Written Agreements.

C1.2.1 There shall be a written agreement specifying the relationship between the CBB and the CB Collection Site and outlining responsibilities for complying with CBB policies and Standard Operating Procedures.

C1.2.2 There shall be documentation that a health care professional has agreed to perform the collection.

C1.3 CB Collection Sites.

C1.3.1 The CB Collection Site shall have processes to prevent the introduction, transmission, or spread of communicable disease.

C1.3.2 Fixed CB Collection Site.

C1.3.2.1 There shall be a written agreement describing the interaction between the fixed CB Collection Site and the CBB.

C1.3.2.2 There shall be adequate space for the performance of the collection procedure.

C1.3.3 There shall be adequate space for secure storage of the CB unit, associated reference samples and maternal samples, and documents until they are transported or shipped to the CB Processing Facility.

C1.3.4 There shall be a designated area for appropriate and secure storage and preparation of the reagents, supplies, and equipment needed for the collection procedures.

C1.3.4.1 Reagents, supplies, and equipment shall be stored according to the manufacturer’s recommendations and used prior to the expiration dates in an area and manner appropriate to protect their integrity and functionality.

C1.2.5 Records supplied to the CBB shall include the following at a minimum:

C1.2.5.1 Identity of supplies and reagents including manufacturer, lot number, and expiration date.
C1.2.5.2 Documentation of appropriate storage of all supplies, reagents, CB units, reference samples, and maternal samples.

C1.3 Non Fixed CB Collection Site.

C1.3.1 For directed donations, there shall be a written agreement between the infant donor family and the CBB related to CB unit collection and transport or shipping.

C1.3.2 For unrelated donations, there shall be a written agreement between the licensed health care professional and the CBB regarding the CB unit collection and transport or shipping.

C1.3.3 The CBB Medical Director or designee shall be responsible for ensuring that there are policies and Standard Operating Procedures applicable to the non-fixed CB Collection Site that meet the requirements of these Standards and address at least collector training, storage, security of the supplies and reagents, completion of documents, the collection procedure, labeling, storage, and transportation or shipment.

C1.3.4 Reagents, supplies, and equipment needed for the collection procedure shall be stored.

C1.3.4.2 The temperature of reagents and supplies in a CB collection kit shall be continuously monitored from the time it leaves the CBB to the time it is received by the CB Collection Site.

C1.3.4.3 Reagents and supplies shall be used prior to the expiration dates.

C1.4 When a CB collection kit is prepared and sent from the CBB, there shall be adequate instructions and materials provided to collect, label, store, pack, and transport or ship the CB unit, reagents and supplies, CB unit, associated samples, and maternal samples.

C1.3.5.1 The stability of temperature of the kit during transportation or shipment shall be validated or monitored from the time it leaves the CBB to the return of the kit to the CBB.

C1.5 Records supplied to the CBB shall include the following at a minimum:

C1.3.5.1 Identity of supplies and reagents including manufacturer, lot number, and expiration date.
C1 5.2 Documentation of these parameters shall be provided to the CBB and maintained in the CB unit file. Temporary appropriate storage of the all supplies, reagents, CB unit, references, associated samples, and maternal samples, and documents shall be secure until they are transported or shipped to the CB Processing Facility.

C2 CORD BLOOD COLLECTION PERSONNEL REQUIREMENTS

C2.1 All CB collection personnel shall comply with these Standards.

C2.1.1 Where there are CB Collection Sites that are not staffed by CBB personnel, there shall be a designated individual who is responsible for communication with the CBB Medical Director or designee.

C2.2 All CB collection personnel shall have a defined line of communication with relevant CBB personnel.

C2.2.1 At non-fixed CB Collection Sites, the CBB shall provide a mechanism for the collecting licensed health care professional to communicate with the CBB Medical Director or designee for any problems with the collection.

C2.3 Where there are CB Collection Sites that are not staffed by the CBB personnel, there shall be a designated individual who is responsible for the daily operation of the CB Collection Site and communication with the CBB Medical Director or designee.

C2.3.1 Personnel not employed by the CBB shall comply with these Standards.

C2.3.2 At CB Collection Sites where individual licensed health care professionals perform collections, the individual licensed health care professional may be the contact person.

C2.3 All collections shall be performed by personnel trained for the collection procedure.

C2.5 At non-fixed CB Collection Sites:

C2.5.1 There shall be documentation that a licensed health care professional has agreed to perform the collection.

C2.5.2 Training shall cover each aspect of the CB collection process, including and include at a minimum:

C2.3.1.1 The use of the CB-collection supplies and reagents.
C2.3.1.2 Cleaning of the umbilical cord to minimize the risk of microbial contamination with maternal blood.

C2.3.1.3 Use of the CB collection bag to avoid microbial contamination and clotting.

C2.3.1.4 Labeling.

C2.3.1.5 Verification of the identity of the donor.

C2.3.1.6 Packaging, storage, and shipping of the CB unit.

C2.3.1.7 Safety of the donor mother and infant.

C2.3.2 Training shall be documented.

C3 POLICIES AND STANDARD OPERATING PROCEDURES

C3.1 The CB Collection Site shall establish and maintain policies and/or Standard Operating Procedures addressing critical aspects of operations and management in addition to those required in B2. These documents shall include all elements required by these Standards, be consistent with the policies and Standard Operating Procedures of the CBB, and address at a minimum:

C3.1.1 Donor recruitment and education.

C3.1.2 Maternal screening (including interpretation and acceptable results).

C3.1.3 Informed consent.

C3.1.4 Donor eligibility criteria and determination.

C3.1.5 Documentation of infant donor health at birth.

C3.1.6 Infant donor screening (including interpretation and acceptable results).

C3.1.7 Maintenance of linkage of the CB unit to the infant donor and mother.

C3.1.8 Collection of CB, reference associated samples, and maternal samples.

C3.1.9 Labeling of the CB unit, reference associated samples, maternal samples, and associated documents.
C3.1.10 Storage and packaging of CB units, reference associated samples, maternal samples, and documentation at the CB Collection Site.

C3.1.11 Transport and shipping of the CB unit, reference associated samples, maternal samples, and documentation to the CB Processing Facility.

C3.1.12 Personnel and collector training.

C3.1.12.1 Documentation of continued competency, if appropriate, for the procedures performed.

C3.1.13 Ordering, storage, security, and use of supplies and reagents.

C3.1.14 Equipment monitoring, qualification, and maintenance.

C3.1.15 Facility management including supplies, maintenance and monitoring of equipment, cleaning and sanitation procedures, disposal of medical and biohazardous waste, emergency and safety procedures, and a disaster plan.

C3.2 All collection personnel shall follow the policies and Standard Operating Procedures related to their positions established by the CBB and the CB Collection Site.

C3.2.1 Current versions of the policies and Standard Operating Procedures relevant to the processes being performed shall be readily available to the personnel involved in the CB collection procedures at all times.

C3.2.2 Review and training of an individual participating in CB collection shall be documented before the individual is allowed to perform new and revised policies and procedures.

C4 INFORMED CONSENT

C4.1 Informed consent shall be obtained and documented from the mother.

C4.1.1 Informed consent shall be obtained and documented while the mother is able to concentrate on the information and is not distracted by aspects of labor.

C4.1.2 In cases of a surrogate mother, informed consent shall be obtained and documented from both the surrogate mother and the genetic mother.

C4.2 All aspects of participation in CB donation shall be discussed with the mother in a language and with terms that she understands.
C4.3 Informed consent shall be obtained from or confirmed by a trained individual who is not a member of the donor’s family.

C4.4 The CBB shall only perform steps in the CB banking process for which it has informed consent from the mother, including at a minimum:

- **C4.4.1 Collection.**
- **C4.4.2 Processing.**
- **C4.4.3 Long-term storage.**

C4.5 The mother shall have an opportunity to ask questions.

C4.4 Consent for at least the collection procedure shall be obtained and documented prior to delivery, including the following information at a minimum:

- **C4.6** An explanation of the collection procedure in terms the mother can understand.
- **C4.4.2** The possible risks and benefits of CB collection.
- **C4.4.3** The right of the mother to refuse the collection without prejudice at any time.
- **C4.4.4** The mother will be approached at a later time for complete consent, including consent to process, bank, and release the CB unit for administration and all of the elements in Section C4.5 informed consent shall include.
- **C4.4.5** Any services that will be performed prior to obtaining full consent to process, bank, and release the CB unit for administration.

C4.5 Prior to processing, full consent shall be obtained and documented, including

C4.6 The informed consent shall include the following information at a minimum:

- **C4.6.1** The overall purpose and participation of the mother and infant donor.
- **C4.6.2** An explanation of the collection procedure and activities in terms the mother can understand.
- **C4.6.3** The possible risks and benefits to the mother and/or infant donor.
- **C4.6.4** The possible alternatives to participation.
- **C4.6.5** The right of the mother to refuse without prejudice.
C4.6.6 The intent of the donation for either unrelated use or for directed allogeneic or autologousrelated use.

C4.6.6.1 If the CB unit is intended for unrelated allogeneic use, the mother shall be informed that the CB unit is a donation that will be made available to other individuals and will not necessarily be available to the infant donor or the infant donor’s family at a later date.

C4.6.6.2 If the CB unit is intended for directed allogeneic or autologousrelated use, the mother shall be informed that the release of the CB unit will be limited respectively to the family, intended recipient(s), or the infant donor.

C4.6.6.3 If the CB unit is intended for related use but may potentially be used for unrelated use, the mother shall be informed of the process for making the CB unit available for unrelated use.

C4.6.6.4 If the CB unit may potentially be used for reasons other than the primary intent, this shall be fully disclosed in the informed consent.

C4.6.7 The mother will be asked to provide personal and family medical history.

C4.6.8 Personnel will be permitted to review the medical records of the mother and infant donor.

C4.6.9 ReferenceMaternal samples and maternalassociated samples will be collected.

C4.6.9.1 A sample will be collected from the mother for communicable disease testing and other testing, as applicable.

C4.6.9.2 ReferenceAssociated samples and maternal samples will be collected for communicable disease testing, genetic disease testing, HLA typing, and other testing, as applicable.

C4.6.10 ReferenceAssociated samples, reference samples, and maternal samples will be stored for future testing.

C4.6.11 The CBB will indefinitely maintain linkage for the purpose of notifying the infant donor’s mother or family and/or her physician of communicable or genetic diseases, whenever possible, between the donor and the CB unit.

C4.6.11.1 The CBB retains the right to follow up with the mother or her primary physician relevant healthcare provider at a future date.
C4.6.11.2 Information related to the infant donor and the infant donor’s family shall remain confidential and is only available for review by individuals designated by the CBB or by national authorities to evaluate the CBB.

C4.5.11.3 Linkage between the infant donor and mother with the CB unit shall be maintained indefinitely.

C4.6.12 The CB unit will be processed, stored, and made available for use.

C4.6.12.1 Information regarding the CB unit, including donor eligibility, will be shared with registries nationally and/or internationally, as applicable, and with other individuals as appropriate.

C4.6.13 Possible uses of the CB unit for purposes other than clinical transplantation administration.

C4.6.14 The CBB’s policies for disposal of CB units, including at a minimum:

C4.6.14.1 Nonconforming CB units.

C4.6.14.2 Directed allogeneic or autologous Related CB units, if these units are no longer required.

C4.6.14.3 Agreed-upon duration of storage for related CB units.

C5 MATERNAL AND INFANT DONOR EVALUATION

C5.1 There shall be written criteria for maternal and infant donor evaluation and management.

C5.1.1 There shall be a process for maternal and infant donor identification and linkage.

C5.1.2 There shall be criteria and evaluation procedures in place to protect the safety and confidentiality of the infant donor and mother.

C5.1.3 If a related CB unit may potentially be used for unrelated donation, the evaluation process shall include all evaluation requirements for unrelated CB units at the time of donation.

C5.1.4 Maternal and infant donor evaluation results shall be documented.

C5.1.5 Maternal and infant donor evaluation shall be reviewed by qualified CBB personnel.

C5.1.6 There shall be a policy for follow-up of donors for management of donation-associated adverse events.
C5.2 There shall be infant donor and mother evaluation procedures in place to evaluate the risk of infectious and genetic disease transmission from CB units.

C5.2.1 Maternal and infant donor eligibility shall be determined based upon results of screening and testing in accordance with Applicable Law.

C5.2.2 Risks of genetic disease transmission shall be determined based upon results of the screening questionnaire and testing.

C5.3 There shall be written criteria for maternal screening.

C5.3.1 A medical and genetic history of the infant donor’s family (parents, grandparents, siblings, and parents’ siblings including egg, sperm, or embryo donor, if applicable) shall be obtained from the maternal donor and documented.

C5.3.1.1 The history shall be obtained and documented while the mother is able to concentrate on the information and is not distracted by aspects of labor.

C5.3.1.2 The history shall be obtained in a language the mother understands.

C5.3.1.3 Family members should not serve as interpreters or translators.

C5.3.1.4 The history shall collect information to include at a minimum genetic history, malignant disease, and inherited disorders that are transmissible to the recipient in the mother’s and father’s family including the infant donor’s grandparents, if appropriate known.

C5.3.1.5 The CBB shall have policies to defer assess deferral of a donor or collected CB unit from unrelated allogeneic use if there is a family history of a genetic or malignant disease, according to Applicable Law, that could transmit to a recipient unless testing or follow-up excludes the risks.

C5.3.2 A history for the mother’s communicable disease risk behavior shall be obtained and documented.

C5.3.2.1 The mother’s communicable disease risk behavior shall be obtained in a confidential manner.

C5.3.2.2 The history shall include the mother’s prenatal communicable disease testing, if known, and results of other general medical testing that could influence communicable disease transmission.
C5.3.2.3 Previously obtained—If history for communicable disease transmission risk was obtained in advance of the maternal donor’s presentation for delivery, the history shall be updated to include information up to the time of delivery. This shall be completed within 14 days after delivery.

C5.3.2.4 In the case of a surrogate mother who carries gives birth to an infant donor not genetically hers to delivery, a communicable disease risk history of the surrogate mother shall be obtained and documented.

C5.3.2.5 The mother’s and surrogate mother’s, if applicable, travel history shall be obtained and documented. Travel-related donor eligibility shall be determined according to Applicable Law and documented.

C5.3.2.6 In the case of sperm, egg, or embryo donation from a bank not licensed in accordance with Applicable Law, the communicable disease risk history of the sperm, egg, or embryo donor shall be obtained, reviewed, and documented.

C5.3.2.7 Screening for human transmissible spongiform encephalopathy, including Creutzfeldt-Jakob disease, shall be documented.

C5.3.3 There shall be documentation that the mother and surrogate mother, if applicable, shall confirm affirmed that all the information provided is true accurate to the best of her knowledge.

C5.3.4 The CBB shall have policies regarding the acceptance of nonconforming ineligible CB units for unrelated allogeneic use if there is a communicable disease risk that may adversely affect the recipient.

C5.3.5 When a mother does not meet the established screening criteria, the CBB Medical Director or CB Collection Site Director and a representative from the QM Program shall document and maintain in the permanent record the nature of the variances and the rationale for inclusion of that CB unit.

C5.3.6 The mother shall be provided with information to contact the CBB if the infant donor later develops a serious disease.

C5.5 Infant Donor Screening and Testing.
C5.5.1 History of the current pregnancy and delivery shall be obtained and reviewed.

C5.5.2 The infant donor’s birth data shall be obtained and documented, including gender, gestational age, other results of clinical examination, and if the baby is free of any finding suggestive of disease potentially transmissible through administration of a CB unit.

C5.6 Maternal Samples.

C5.6.1 Blood from the birth mother shall be obtained within seven (7) days before or after collection of the CB unit for communicable disease testing required in D11.1.

C5.6.2 A sufficient volume of blood from the birth mother shall be obtained to meet D5.3.1.

C5.6.3 A sufficient volume of blood from the genetic mother including egg donors, if possible, shall be obtained to meet D5.3.2.

C6 CORD BLOOD COLLECTION PROCEDURES

C6.1 CB collection procedures and practices shall protect the mother and the infant donor and have no impact on obstetric practice or patient care.

C6.1.1 Delivery practices shall not be modified in an attempt to increase CB unit volume.

C6.2 When in utero CB collection is performed, there shall be additional safeguards in place to ensure the safety of the mother and the infant donor.

C6.2.1 In utero CB collections should only be performed in utero from documented singleton deliveries.

C6.2.1.1 If CB collection is performed in utero in a multiple gestation pregnancy, all infants shall be delivered before any CB collection begins.

C6.2.2 In utero CB collections shall only occur in uncomplicated deliveries as determined by the licensed health care professional responsible for the delivery.

C6.2.3 Unrelated CB units collected in utero shall only be obtained from infant donors after a minimum of 34 weeks’ gestation.

C6.2.4 Related CB units collected in utero at less than 34 weeks’ gestation shall be based on an evaluation of infant donor safety by the licensed health care professional responsible for the delivery.
C6.3 CB collection shall be performed according to written policies and Standard Operating Procedures.

C6.3.1 The identity of the mother shall be verified.

C6.3.2 The identity of the collecting licensed health care professional cord blood collector shall be documented.

C6.3.3 CB collection procedures shall be validated to result in acceptable progenitor cell viability, cell recovery, and rate of microbial contamination.

C6.3.4 Methods for CB collection shall employ aseptic techniques.

C6.3.5 The primary CB collection bag shall be approved for use with human blood and shall be used and sealed to prevent leakage and minimize the risk of cell loss and of microbial contamination.

C6.3.6 All reagents and supplies for CB collection that come into contact with the CB unit shall be sterile.

C6.4 There shall be a unique numeric or alphanumeric identifier for the CB unit, reference associated samples, maternal samples, and associated documents.

C6.5 There shall be a written policy at the CB Collection Site for labeling of the CB unit, reference associated samples, maternal samples, and associated documents that permits tracking and tracing among the CB unit, infant donor, infant donor’s mother, reference associated samples, maternal samples, and documentation.

C6.6 At completion of CB collection, the primary collection bag shall bear or be accompanied by the information required in Appendix I, the Cord Blood Unit Labeling table in Appendix I.

C6.7 There shall be a written policy for storage of CB units, reference associated samples, maternal samples, and documents at the CB Collection Site prior to transport or shipping to the CB Processing Facility.

C6.7.1 CB units, reference associated samples, and maternal samples shall be maintained in a secure environment.

C6.7.2 CB units shall be maintained in a temperature range validated to protect cell viability.

C6.8 Records shall be maintained at the CBB of all reports of adverse events that occur during or immediately after CB collection.
TRANSPORTATION AND SHIPPING OF NON-CRYOPRESERVED CORD BLOOD UNITS BETWEEN THE CORD BLOOD COLLECTION SITE AND THE CORD BLOOD PROCESSING FACILITY

C7.1 Transport and shipping of CB units shall be in compliance with Applicable Law.

C7.2 The methods of transport and shipping of the CB unit between the CB Collection Site and the CB Processing Facility shall be designed to protect the integrity of the CB unit and the health and safety of personnel.

C7.3 The primary CB collection bag shall be placed in a sealed secondary plastic bag to contain any leakage from the primary bag.

C7.4 The CB unit shall be transported or shipped with required accompanying records as defined in Standard Operating Procedures.

C7.5 CB units shall be placed in an outer container that maintains qualified and validated to maintain a designated temperature range around the CB unit to protect cell viability during CB unit transportation and shipping as documented by prior validation of the container, a continuous recording of the temperature of the container during transportation or shipping, or another method to document maintenance of temperature within the accepted range, distribution.

C7.5.1 The outer container shall be made of material adequate to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling during transportation or shipping.

C7.6 The temperature of a CB collection kit shall be monitored from the time it leaves the CBB until it is received by the CBB.

C7.6.1 Documentation of these parameters shall be provided to the CBB and maintained in the CB unit file.

C7.7 When a CB unit is shipped, the temperature inside the transport container shall be continuously monitored.

C7.8 The outer container shall be labeled with the information required in the Cord Blood Unit Labeling table in Appendix I.

C7.8.1 The outer container shall be secured.

C7.9 Transportation and Shipping Records.

C7.9.1 A list identifying each CB unit and its associated samples, maternal samples, and documents that are enclosed in a package shall be included.
C7.9.2 Transportation and shipping records shall permit the tracking of the CB unit from the CB Collection Site to its final destination.

C7.5.2 A list identifying each CB unit and its associated reference samples, maternal samples, and documents that are enclosed in a package shall be included.

C7.9.3 Transportation and shipping records shall identify:

C7.9.3.1 The CB Collection Site responsible for transporting or shipping the CB unit.

C7.9.3.2 The date and time of transport or shipment.

C7.9.3.3 The identity of the courier.

C7.9.3.4 The date and time of receipt of the package.

C7.9.3.5 The condition of the package upon receipt.
PART D: CORD BLOOD PROCESSING STANDARDS

D1 CORD BLOOD PROCESSING FACILITY REQUIREMENTS

D1.1 The CB Processing Facility shall be licensed, registered, and/or accredited with as required by the appropriate governmental authorities for the activities performed.

D1.2 There shall be designated facilities with adequate space for design, and location that prevent improper labeling, mix-ups, contamination, or cross-contamination of CB units during the following activities:

D1.2.1 Performance of processing activities and ancillary functions.

D1.2.2 Preparation of, and safe, sanitary, and orderly storage of, the supplies, reagents, and equipment needed for processing, testing, cryopreservation, storage, and release.

D1.2.3 Storage of CB units prior to release or distribution.

D1.2.4 Maintenance of records.

D1.3 The CB Processing Facility shall be secure in order to prevent the entrance of unauthorized personnel and protect daily operations, equipment, and records.

D1.3.1 The CB Processing Facility shall have oversight of non-processing personnel visiting the CB Processing Facility to ensure maintenance compliance with these Standards.

D1.4 The CB Processing Facility shall provide adequate lighting, ventilation, access to hand decontamination, and air quality to ensure adequate conditions for proper operations in compliance with Applicable Law.

D1.5 The CB Processing Facility shall be maintained in a clean, sanitary, and orderly manner to prevent the introduction, transmission, or spread of communicable disease in compliance with Applicable Law.

D1.5.1 There shall be documentation of facility cleaning and sanitation.

D1.6 Environmental conditions, that affect the safety and potency of the CB unit shall be defined, controlled, monitored, and recorded to demonstrate ongoing compliance.

D1.6.1 There shall be inspection of environmental control systems to ensure adequate conditions for proper operations in compliance with Applicable Law.
D1.7 Critical CB Processing Facility parameters that may affect cellular therapy product processing, storage, or distribution shall be defined, controlled, monitored, and recorded to demonstrate ongoing compliance.

D1.8 CB Processing Facility environmental conditions for temperature, humidity, ventilation, and air pressure, filtration and classification shall be defined and, if appropriate, monitored for cell processing.

D1.9 Facility Personnel Safety Requirements.

D1.9.1 The CB Processing Facility shall have programs operating in compliance with Applicable Law procedures that utilize universal precautions and are designed to minimize risks to the health and safety of employees, volunteers, and visitors.

D1.9.2 There shall be procedures for biological, chemical, and radiation safety as appropriate, including at least:

D1.9.1.1 Bloodborne pathogens.
D1.9.1.2 Chemical hygiene.
D1.9.1.3 Hand washing and/or decontamination.
D1.9.1.4 Fire safety.
D1.9.1.5 Radiation safety, if applicable.
D1.9.1.6 Latex allergy.
D1.9.1.7 Power failures.
D1.9.1.8 Liquid nitrogen.

D1.9.2 Gloves and protective clothing shall be worn while handling biological specimens. Such protective clothing shall not be worn outside the work area.

D1.9.3 The CB Processing Facility shall have written policies and procedures for action in case of exposure to communicable disease agents or to chemical, biological, radiological, or liquid nitrogen, or, if applicable, radiological hazards.

D1.9.4 Decontamination and disposal techniques for Medical waste shall be described. decontaminated and—Human tissue shall be disposed of in a manner to minimize hazard to facility personnel and the environment in accordance with Applicable Law.

D2 CORD BLOOD PROCESSING FACILITY PERSONNEL REQUIREMENTS
D2.1 All CB Processing Facility personnel shall comply with these Standards.

D2.2 The CB Processing Facility shall have oversight of non-processing personnel visiting the CB Processing Facility to ensure compliance with these Standards shall be trained and competent as required by B2.4.

D2.3 The CB Processing Facility shall ensure contracted processing services are in compliance with these Standards.

D3 POLICIES AND STANDARD OPERATING PROCEDURES

D3.1 The CB Processing Facility shall have clearly written policies and/or Standard Operating Procedures that are precise and unambiguous. Procedures addressing critical aspects of operations and management in addition to those required in B2. These documents shall include all elements required by these Standards, be consistent with the policies and Standard Operating Procedures of the CBB, and address all aspects of the CB processing operation, including at a minimum:

D3.1.1 CB unit acceptance criteria, processing, cryopreservation, and storage.

D3.1.2 Labeling of the CB unit, reference samples, maternal samples, and associated documents.

D3.1.3 Storage and retrieval of reference samples and maternal samples for testing.

D3.1.4 Communicable disease testing, microbial cultures, HLA typing, hemoglobinopathy testing, and other testing. Acceptance criteria for test results shall be described.

D3.1.5 Criteria for release of CB units from quarantine, including nonconforming CB units.

D3.1.6 Criteria for qualification of CB units available for search and administration, including nonconforming CB units.

D3.1.7 Personnel training and documentation of continued competency for the procedures performed.

D3.1.8 Facility management of supplies, maintenance and monitoring of equipment, cleaning and sanitation procedures, disposal of medical and biohazardous waste, and emergency and safety procedures.

D3.1.9 A disaster plan to ensure continuous safe storage and transport and shipping, if applicable, of the CB units.

D3.1.10 Discard and Disposal of a CB units...
D4.1 Acceptance Criteria.

D4.1.1 Upon receipt of a CB unit package into the CB Processing Facility, there shall be a system to verify the following at a minimum:

D4.1.1.1 The receipt of the package within an acceptable amount of time as defined by the CBB.

D4.1.1.2 The integrity of the outer container and the temperature against validated parameters.

D4.1.1.3 Verification of the contents of the package against the list of enclosed items.

D4.1.1.4 The integrity of the primary and secondary containers.

D4.1.1.5 The CB unit for appropriate appearance, integrity, labeling, and identification.

D4.1.1.6 The reference associated samples and maternal samples, and documents for appropriate labeling and identification, and associated documents.

D4.1.2 For unrelated CB units, an appropriately signed consent authorizing processing, collection, processing, testing, cryopreservation, and storage of the CB unit, associated samples, reference samples, and maternal samples for the intended purpose shall be present before processing is initiated.

D4.1.3 For directed related CB units, there shall be a signed agreement from the requesting family shall be present, including the name of the intended recipient if applicable, for processing, testing, cryopreservation, and storage, for collection, processing, testing, storage, and a name and contact information of the donor family.

D4.1.4 If a CB unit collected for related use may subsequently be released for unrelated use, there shall be informed consent for such release obtained before processing.

D4.2 Processing.
D4.2.1 Only properly labeled and clearly identified cord blood units shall be accepted for processing.

D4.2.2 CB units during all stages of processing shall minimally contain an affixed in-process label with the CB unit unique identifier at a minimum.

D4.2.3 Information regarding processing steps that have been completed on a CB unit shall accompany the CB unit or be available electronically during all stages of processing.

D4.2.4 Processing and cryopreservation of CB units shall be performed according to validated Standard Operating Procedures validated to result in acceptable viability and recovery.

D4.2.4.1 Critical control points and associated assays shall be identified and performed on each CB unit as defined in Standard Operating Procedures.

D4.2.4.2 Failure of the processing procedure to achieve acceptable end-points or specifications shall be evaluated and documented.

D4.2.5 Methods for processing shall employ aseptic technique and CB units shall be processed in a manner that minimizes the risk of mix-ups and cross-contamination.

D4.2.5.1 Where processing of CB units involves exposure to the environment, processing shall take place in an environment with specified air quality and cleanliness.

D4.2.5.2 The effectiveness of measures to avoid contamination and cross-contamination shall be verified and monitored.

D4.2.6 Cryopreservation of unrelated CB units shall be initiated within 48 hours of collection.

D4.2.7 Cryopreservation of directed related CB units shall be initiated within 72 hours of CB collection.

D4.2.8 More than simple dilution and/or volume reduction by depletion minimal manipulation of erythrocytes and/or plasma CB unit shall only be performed according to in accordance with Applicable Law and:

D4.2.8.1 Using reagents and/or devices approved for that manipulation by the appropriate governmental agency or

D4.2.8.2 With an Institutional Review Board or Ethics Committee-approved protocol or
D4.2.8.3 With an Investigational New Drug Protocol, Investigational Device Exemption, or non-U.S. equivalent.

D4.2.9 Equipment, supplies, and reagents shall not adversely affect the viability of the CB units and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease.

D4.3 At the completion of processing prior to cryopreservation, the freezing bag shall be labeled with or be accompanied by the information as required in Appendix I, by the Cord Blood Unit Labeling Table--table in Appendix I.

D4.4 Records pertinent to the CB unit shall be reviewed by the CB Processing Facility Director or designee and found to be acceptable prior to the release from quarantine status.

D5 REFERENCE SAMPLES AND MATERNAL SAMPLES

D5.1 At a minimum, the following reference samples shall be collected from the CB unit prior to cryopreservation:

D5.1.1 A minimum total volume of at least 200 μL divided into at least two segments with each sealed and integrally attached to the freezing bag.

D5.1.1.1 The contents of each reference sample shall be representative of the CB unit.

D5.1.1.2 When a CB unit is initially requested, a minimum of one (1) segment shall be used for confirmatory to confirm the results of HLA typing and should be used for cell viability and/or potency analysis.

D5.1.2 Additional samples of a minimum total of 2 x 10⁶ nucleated cells divided into at least two (2) vials or additional contiguous segments.

D5.1.2.1 Reference samples intended for viability or potency analysis shall be stored at -150°C or colder the same temperature as the CB unit.

D5.1.2.2 When reference samples are stored in liquid nitrogen vapor phase at -150°C or colder, the freezers shall be qualified to show that all reference samples are maintained at appropriate temperatures. Reference samples used for purposes other than viability or potency analysis shall be stored at -70°C or colder.
D5.1.3  A minimum total volume of 3.6 mL of serum or plasma from non-heparinized samples in divided into at least two vials.

D5.1.3.1  The serum or plasma should be stored at -70°C or colder.

D5.1.4  Suitable material for preparation of at least 50 µg genomic DNA.

D5.2  A retention sample from the CB unit should be stored indefinitely.

D5.3  Maternal samples to be maintained shall include:

D5.3.1  From the birth mother, a minimum total volume of 3.6 mL of serum and/or plasma from non-heparinized samples divided into at least two vials.

D5.3.1.1  The serum or plasma shall be stored at -70°C or colder.

D5.3.2  From the genetic mother, including egg donors, if possible, suitable material for preparation of at least 50 µg of genomic DNA with the exception of egg or embryo donors.

D6  CRYOPRESERVATION

D6.1  CB units shall be cryopreserved using controlled rate freezing or an equivalent procedure. If an equivalent procedure is used, it shall be validated to maintain equivalent demonstration of recovery of viable and viability of nucleated cells potent cells.

D6.2  Cryopreservation Standard Operating Procedures shall specify that the following information is recorded for each unit:

D6.2.1  Total nucleated cell concentration within a defined range.

D6.2.2  The cryoprotectant, its final concentration, and the duration of cell exposure prior to freezing.

D6.2.3  Method of freezing and end-point temperature of cooling.

D6.2.4  Cooling rate within a defined range—continuous monitoring of the temperature.

D6.2.5  Freezing curve parameters within a defined range.

D6.2.6  Storage temperature.

D6.3  CB units shall be stored in freezing bags designed and approved for the cryopreservation of human cells and shall be placed into metal canisters to provide protection during freezing, storage, transportation, and shipping.
D6.3.1 Each freezing bag and its satellite container(s), if any, shall be examined visually for damage or possible contamination prior to use.

D6.3.2 Freezing bags shall allow the filling of at least two contiguous segments.

D6.3.2 Reference and retention samples to be used for viability, potency, or stability study assays shall be cryopreserved and stored in the same manner as the CB unit.

D6.4 Processes must minimize the risk of overfilling and underfilling freezing bags.

D6.4.1 After filling, each freezing bag shall be visually examined for possible leaking, overfilling or underfilling of the freezing bag, and breakage of seals. The results of these inspections shall be documented.

D6.5 The duration from addition of cryoprotectant to initiation of freezing shall be minimized and validated by the CBB.

D6.6 The duration from completion of freezing to storage at -150°C or colder shall be minimized and validated by the CBB.

D7 CONDITIONS FOR STORAGE

D7.1 Each CB unit storage device shall be located in a secure area. The device and/or the area shall have locking capability that is used at least when the area is not occupied by the CBB staff.

D7.2 Facilities storing CB units shall validate the duration and conditions of storage.

D7.2 Refrigerators and freezers used for the storage of CB units, blood components, human cells, tissues, specimens, or reagents used in CB unit collection, processing, or cryopreservation shall not be used for any other purpose.

D7.3 Procedures to minimize the risk of microbial cross-contamination of CB units shall be defined and maintained.

D7.4 Processes for storing CB units in quarantine shall be defined in Standard Operating Procedures.

D7.4.1 Quarantined CB units shall be easily distinguishable and stored in a manner that minimizes the risks of cross-contamination and inappropriate distribution.
D7.4.2 Each CB unit shall be maintained in quarantine storage until the CBB Director or designee has approved the release of the CB unit from quarantine status based upon review of maternal communicable disease risk history, other medical history, maternal test results, and CB unit sterility test/microbial culture results as required under Applicable Law.

D7.4.3 Records shall indicate when a CB unit was released from quarantine into permanent storage.

D7.4.4 CB units shall remain quarantined if the reference samples or maternal samples have reactive and/or positive or indeterminate screening test results for communicable disease or increased infectious disease risk obtained through the donor screening process.

D7.5 Temperature.

D7.5.1 CB units shall be stored at -150°C or colder.

D7.5.1.1 If CB units are not fully immersed in liquid nitrogen, the storage freezers shall be qualified to show that all CB units are maintained at appropriate temperatures.

D7.5.1.2 Transfer of cryopreserved CB units shall be validated and monitored.

D7.5.2 Warming events at any time after the process of storage and/or distribution shall be minimized.

D7.5.2.1 The duration of warming events shall be documented, and the impact on the CB unit shall be assessed.

D7.5.2.2 If a warming event may have potentially decreased the potency of an unrelated CB unit, the unit shall not be made available for distribution for administration.

D8 MONITORING AND ALARM SYSTEMS

D8.1 Refrigerators used for storage of CB units before cryopreservation of the CB unit shall have a validated system to monitor the temperature continuously or record the temperature at a minimum every four hours at a minimum.

D8.2 Freezers used for CB unit storage where CB units are not fully immersed in liquid nitrogen shall have a validated system to monitor the temperature continuously or record the temperature every four hours at a minimum.

D8.3 When CB units are stored fully immersed in liquid nitrogen, the level of liquid nitrogen shall be continuously monitored or recorded every four hours at a minimum.
D8.3 There shall be a validated mechanism to consistently maintain levels of liquid nitrogen in liquid nitrogen freezers.

D8.4 Alarm Systems.

D8.4.1 Storage devices for CB units and associated, reference samples, retention samples, and maternal samples shall have validated alarm systems that are continuously active.

D8.4.2 Alarm systems shall have audible and visible signals.

D8.4.3 Alarm systems shall be checked periodically for technical function. The records of such checks shall be maintained.

D8.4.4 The alarm system shall be capable of notifying designated personnel 24 hours a day.

D8.4.4.1 A procedure for notifying designated staff shall be readily accessible.

D8.4.5 Alarm parameters shall be set to allow staff sufficient time to salvage CB units, reference samples, and maternal samples, retention samples, and maternal samples.

D8.4.6 Written instructions to be followed if the storage device fails shall be displayed in the immediate area of the storage device and at each remote alarm location.

D8.4.7 Any alarm event and its resolution shall be documented.

D8.5 Additional Contingency plans or storage devices of appropriate temperature shall be available for CB unit storage if the maintaining CB units, associated samples, reference samples, retention samples, and maternal samples at the storage temperature in the event the primary storage device fails.

D9 DISPOSAL

D9.1 Disposal The CBB shall have a policy regarding the disposition of any CB unit, including at a minimum:

D9.1.1 CB units released for clinical use.

D9.1.2 CB units used for research.

D9.1.3 CB units used for quality assurance activities.

D9.1.4 CB units that are discarded.

D9.2 Nonconforming CB units.
D9.2.1 The CBB shall have a policy for the management of CB units that are not accepted into inventory.

D9.2.2 The CBB shall have a written policy for the management of CB units that do not meet in-process or final unit endpoints and/or specifications.

D9.2.3 The CBB shall have a written policy to address positive or indeterminate results found during the screening process and/or laboratory testing of reference samples or maternal samples.

D9.3 Disposal.

D9.3.1 There shall be documented a policy outlining personnel authorized to discard CB units.

D9.3.2 The records for discarded CB units shall indicate the unique numeric or alphanumeric identifier of the CB unit and; the reason, date, and method of disposal; the authorizing individual; and the individual who disposed of the CB unit.

D9.3.3 For directed allogeneic or autologous CB unit discard related CB unit disposal:

D9.3.3.1 Disposal shall comply with the terms of disposal in the written agreement.

D9.3.3.2 Reasons for disposal and the process of notification shall be documented identified at the time of the written agreement.

D9.3.3 Documentation shall be complete before a unit is discarded.

D10 CORD BLOOD UNIT TESTING

D10.1 The CBB shall define tests and procedures for measuring and assaying CB units to determine their safety, viability, and integrity and to document that units meet predetermined release specifications. Results of all such tests and procedures shall become part of the permanent record of the CB unit.

D10.2 Testing control procedures shall include:

D10.2.1 The use of established and validated appropriate assays, standards, and test procedures for the evaluation of the CB unit.

D10.2.2 Adequate provisions for monitoring the reliability, accuracy, precision, and performance of test procedures and instruments.
D10.2.3 Adequate identification and handling of all reference samples so that they are accurately related to the specific CB unit being tested, to its infant donor, the infant donor’s mother, and to the specific recipient, as applicable.

D10.2.4 The following tests shall be performed on a reference sample from each CB unit obtained after processing prior to cryopreservation:

D10.2.1 Total nucleated cell count.

D10.2.2 Nucleated red blood cell count.

D10.2.3 Total number of CD34 cells.

D10.2.4 Viability and/or potency as measured by viable CD34 cells and/or CFU.

D10.2.5 Verification of new reagent lots to provide comparable results to current lots or give results in agreement with suitable reference ranges before or with placement into service.

D10.2.5 Where available, use of reference or quality control material demonstrated to give results within the defined range established for that material.

D10.2.6 Functional checks performed for testing instruments, as appropriate, prior to testing reference samples, maternal samples, or recipient samples.

D10.2.7 Documentation of ongoing proficiency testing as designated by the CB Processing Facility Director. The results shall be reviewed by the CB Processing Facility Director or designee and outcomes reviewed with the staff and representatives from the QM Program, if applicable.

D10.3 CB units shall be tested as outlined in the Testing Requirements table in Appendix IV.

D10.3.1 CBC with differential. Parameters for testing shall include enumeration of neutrophils, lymphocytes, monocytes, and platelets shall be defined. Parameters for each shall be defined.

D10.3.2 Microbial cultures shall be performed using a system validated for the growth of aerobic and anaerobic bacteria and fungi.

D10.3.2.1 CB units for unrelated use shall be free from microbial contamination.
D10.3.2 For directed CB units, the results of positive microbial tests shall include identity and sensitivities of the organism(s). Antimicrobial sensitivities shall be performed prior to release of the CB unit for administration. These results shall be reported to the prospective Clinical Program.

D10.2.6.2 CB units for unrelated use shall be free from microbial contamination.

D10.3 ABO group and Rh type shall be performed on a reference sample from each CB unit prior to listing.

D10.4 Human leukocyte antigen (HLA) typing shall be performed on a reference sample from each CB unit.

D10.4.1 HLA-A, B, and DRB1 loci shall be determined.

D10.4.2 HLA-C and DQB1 should be determined.

D10.3.3 HLA Class I and Class II typing shall be performed by DNA-based methods. For unrelated allogeneic CB units, this typing shall be performed before listing the CB unit for search.

D10.4.4 At a minimum, DNA high resolution molecular typing shall be performed for Class II DRB1 typing prior to release for administration.

D10.5 The following tests shall be performed on a reference sample from each CB unit prior to release for administration:

D10.5.1 Hemoglobinopathy screening.

D10.5.2 CFU from the final CB unit for unrelated allogeneic CB units.

D10.6 The CBB shall have a written policy for the management of positive or indeterminate results found during the screening process and/or laboratory testing of reference samples.

D10.4 Test results that are positive or outside of the established range and are relevant to the donor’s health shall be communicated to the infant donor’s mother or legal guardian and/or her physician according to Applicable Law.

D10.8 Prior to release to the Clinical Program, each CB unit should be tested for evidence of infection by at least the following communicable disease agents using licensed donor screening tests when available according to Applicable Law:

D10.8.1 Human immunodeficiency virus, type 1.
D10.8.2 Human immunodeficiency virus, type 2.
D10.8.3 Hepatitis B virus.
D10.8.4 Hepatitis C virus.
D10.8.5 Human T cell lymphotropic virus, type I.
D10.8.6 Human T cell lymphotropic virus, type II.
D10.8.7 Treponema pallidum (syphilis).

D10.8.8 Any additional agents required by Applicable Law at the time of release of the CB unit, and CBB policies and Standard Operating Procedures.

D11 MATERNAL TESTING

D11.1 The maternal blood sample obtained within seven (7) days before or after collection of the CB unit shall be tested for evidence of infection by as outlined in the following communicable disease agents Testing Requirements table in Appendix IV utilizing assays required for volunteer blood or tissue donations and according to Applicable Law:

D11.1.1 Human immunodeficiency virus, type 1.
D11.1.2 Human immunodeficiency virus, type 2.
D11.1.3 Hepatitis B virus.
D11.1.4 Hepatitis C virus.
D11.1.5 Human T cell lymphotropic virus, type I.
D11.1.6 Human T cell lymphotropic virus, type II.
D11.1.7 Treponema pallidum (syphilis).
D11.1.8 Cytomegalovirus.

D11.1.9 If required by Applicable Law, the maternal blood sample obtained within seven (7) days before or after collection of the CB unit shall also be tested for evidence of clinically relevant infection by the following disease agents:

D11.1.9.1 West Nile Virus.
D11.1.9.2 Trypanosoma cruzi (Chagas' Disease).
D11.2 The CBB shall have a written policy to address positive or indeterminate results found during the screening process and/or laboratory testing of maternal samples.

D11.2 Positive or indeterminate test results, excluding cytomegalovirus, shall be communicated to the mother and/or her physician according to Applicable Law and CBB policies and Standard Operating Procedures.

D11.3 All maternal samples should have negative or non-reactive test results with the exception of Cytomegalovirus antibody, Hepatitis B core antibody, and non-Treponema pallidum (syphilis) testing.

D11.3.1 If allowed by Applicable Law, maternal samples that are Hepatitis B core antibody positive and are accepted shall be Hepatitis B negative by Surface Antigen (HBsAg) nonreactive/negative by DNA testing and also negative by HBV DNA testing.

D11.3.2 If allowed by Applicable Law, maternal samples that screen test positive for Treponema pallidum (syphilis) using a non-treponemal-specific screening test and are accepted shall be negative using a treponemal-specific confirmatory test.

D11.5 Any CB units reactive for other agents shall be quarantined.

D11.4 If Applicable Law and CBB policies and Standard Operating Procedures allow release of CB units from quarantine where the maternal samples are positive/reactive for Hepatitis B core antibody and/or non-treponemal syphilis, the CBB must have a written procedure that describes the documented notification of relevant results to the Clinical Program prior to release for administration.
PART E: CORD BLOOD LISTING, SEARCH, SELECTION, RESERVATION, RELEASE, AND DISTRIBUTION STANDARDS

E1 GENERAL REQUIREMENTS

E1.1 There shall be designated facilities with adequate space for design and location that prevent mix-ups, mislabeling, or other errors in the procedures and records related to CB unit listing, search, selection, reservation, release, and distribution.

E1.2 There shall be a defined process to prevent listing of directed allogeneic and autologous CB units for unrelated use.

E1.3 The CBB shall have policies and Standard Operating Procedures for the following at a minimum:

- E1.3.1 Listing, search, selection, reservation, release, and distribution of CB units to Clinical Programs.
- E1.3.2 Verification of confirmatory HLA typing of the CB unit.
- E1.3.3 Verification that the infant donor and the recipient are different individuals in the case of complete HLA matches.

E1.4 If the CBB utilizes a registry, the CBB shall use a validated process for uploading CB unit information to the registry.

E1.5 The CBB or registry shall have a validated electronic record system that enables search and match operations and reporting of results within a defined timeframe.

E1.5.1 If an outside agency is used for search and match functions, its electronic record system shall meet these Standards.

E1.6 The CBB or registry shall have policies and Standard Operating Procedures for the reservation and allocation of CB units.

E1.6.1 Reservation of a CB unit shall not be in place simultaneously for more than one potential recipient.

E1.6.2 The CBB shall notify all listing organizations registries in a timely manner when a CB unit is removed from inventory.

E2 REVIEW AND LISTING OF CORD BLOOD UNITS

E2.1 The CBB shall have policies and Standard Operating Procedures for the comprehensive review of unrelated allogeneic CB unit records prior to listing a CB unit, including at a minimum:

- E2.1.1 From the CB unit after processing prior to cryopreservation:
E2.1.1 Results of tests outlined in the Testing Requirements table in Appendix IV.
   E2.1.1.1 Total nucleated cell count.
   E2.1.1.2 Nucleated red blood cell count.
   E2.1.1.3 Total number of CD34 cells.
   E2.1.1.4 Viability and/or potency as measured by viable CD34 cells and/or CFU.
   E2.1.1.5 CBC with differential.
   E2.1.1.6 Microbial cultures.
   E2.1.2 ABO group and Rh type.
   E2.1.3 HLA type at a minimum of two digits.
   E2.1.4 Hemoglobinopathy, if available.
E2.1.2 Infant donor’s ethnicity/race.
E2.1.3 Infant donor’s gender.
E2.1.4 Infant donor’s physical examination.
E2.1.5 Maternal risk factors for transmission of communicable disease.
E2.1.6 Family medical history for transmissible genetic and malignant diseases.
E2.1.7 Hemoglobinopathy, if known.
E2.1.8 Consents.
E2.1.9 Processing and cryopreservation parameters.
E2.2 Unrelated CB units shall be made available for search on a national registry and/or the CBB’s registry inventory only after testing and medical review has been completed and a representative(s) of the QM Program has reviewed the CB unit records.
E2.3 The nature of nonconforming CB units shall be disclosed to the registry.
E3 CORD BLOOD UNIT SELECTION AND RELEASE FOR ADMINISTRATION
E3.1 The CBB shall retain indefinitely documentation of requests for CB units, requests for reference samples and maternal samples, requests for and results of testing, and transportation and shipping of CB units and samples between facilities.

E3.2 The CBB shall have a system to prevent a CB unit from being reserved for a single patient by more than one transplant center at a given time.

E3.3 Before a CB unit is released, a sample obtained from a contiguous segment of that CB unit shall be tested to verify HLA type and, if possible, cell viability. Verification typing shall be performed at least once after a CB unit is cryopreserved.

E3.3.1 If a contiguous segment is no longer available, another validated method shall be used to identify the CB unit.

E3.3.2 Any histocompatibility discrepancy shall be resolved and communicated to the registry and the Clinical Program.

E3.3.3 Where proof of identity has been obtained for the CB unit, a copy of the report shall be provided to the Clinical Program upon request for the CB unit.

E3.4 At the time of selection for administration, the CBB and/or registry shall provide all technical data to the Clinical Program, including at a minimum:

- E3.4.1 Results of tests outlined in the Testing Requirements table in Appendix IV.
  - E3.4.1.1 Total nucleated cell count.
  - E3.4.1.2 Nucleated red blood cell count.
  - E3.4.1.3 Total number of CD34 cells.
  - E3.4.1.4 Viability and/or potency as measured by viable CD34 cells and/or CFU.
  - E3.4.1.5 CBC with differential.

- E3.4.2 For directed allogeneic and autologous cord blood-related CB unit administration, antimicrobial sensitivities shall be provided if positive microbial tests are documented in the CB unit record.

- E3.4.3 ABO group and Rh type.
E3.3.4 All HLA Class I and II typing results, including prior results.

E3.3.4.1 A minimum of four digits shall be provided for DRB1.

E3.3.5 Hemoglobinopathy testing results.

E3.3.6 Any testing performed from a contiguous segment.

E3.3.7 Communicable disease testing results performed on the maternal sample and, if performed, on the CB unit-infant donor.

E3.4.3 Risks of communicable and/or genetic diseases disclosed by the maternal medical and genetic screening or clinical chart review and the results of any investigation or further testing performed.

E3.4.3.1 For related CB units, history of malignant or genetic disease in a first degree relative of the infant donor shall be disclosed to the Clinical Program.

E3.4.4 The method of CB unit processing.

E3.4.5 Any variances in collection, processing, testing, cryopreservation, storage, and/or transport or shipping procedures that may influence the integrity and/or quality of the CB unit.

E3.4.6 Physical characteristics of the CB unit, including at a minimum the number and type of bags or compartments used for storage.

E3.4.7 Information about the type of cassette the CB bag will be shipped in.

E3.4.8 Information about storage of the CB unit.

E3.4.9 Instructions for thawing and administering the CB unit.

E4 CORD BLOOD UNIT DISTRIBUTION TO A CLINICAL PROGRAM

E4.1 The CBB shall obtain written or electronic form a request from the transplant physician, designee, or registry for distribution of the CB unit prior to release of the product.

E4.2 The CBB Medical Director or qualified designee and a representative(s) from the QM Program shall conduct a comprehensive record review prior to distribution of a CB unit to a Clinical Program and document this review in accordance with Applicable Law.

E4.3 When the maternal medical and/or genetic screening history indicates potentially transmissible disease or when there is a positive or indeterminate communicable disease test result:
E4.3.1 The CB unit shall not be released unless the CBB Director or Medical Director give and a representative from the QM Program give specific authorization for release of the nonconforming ineligible CB unit in compliance with Applicable Law and documents the rationale for such authorization.

E4.3.2 There shall be documentation of the consent to use the nonconforming ineligible CB unit from the transplant physician.

E4.3.3 CB units deemed nonconforming ineligible as a result of donor screening or testing for risk for transmission of communicable disease shall be labeled with the appropriate biohazard and warning labels detailed in Appendix II, the Modified Circular of Information Biohazard and Warning Labeling table in Appendix II.

E4.4 At the time of distribution to a Clinical Program, the CB unit bag shall be labeled as required in Appendix I, the Cord Blood Unit Labeling table in Appendix I.

E4.5 A circular of information or package insert and instructions for handling, thawing, and using the CB unit, including short-term storage and preparation for administration, shall accompany the CB unit.

E4.6 If the Clinical Program lacks experience in handling CB units, a practice CB unit should be offered.

E4.6.1 The practice CB unit shall be clearly labeled as a CB unit not intended for administration.

E4.7 The CB unit should be received by the Clinical Program prior to initiation of the recipient’s preparative regimen unless approved by the transplant physician.

E5 TRANSPORTATION AND SHIPPING OF CRYOPRESERVED CORD BLOOD UNITS

E5.1 Procedures for transportation and shipping of cryopreserved CB units shall be designed and validated to protect the integrity of the CB unit and the health and safety of personnel.

E5.2 The transit time between the CBB and other facilities shall be minimized.

E5.2.1 There shall be written plans for alternative transportation or shipping in an emergency.

E5.3 Cryopreserved CB units shall be transported or shipped in a liquid nitrogen-cooled dry shipper that contains adequate absorbed liquid nitrogen and has been validated to maintain a temperature of -150°C or colder for at least 48 hours beyond the expected time of arrival at the receiving facility.
E5.3.1 The dry shipper shall contain an electronic data logger that continuously monitors temperature throughout the transportation or shipping period.

E5.3.2 The transport or shipping methods shall conform to Applicable Law regarding the mode of transportation or shipping of such devices.

E5.3.3 The dry shipper shall be labeled in accordance with Applicable Law regarding the cryogenic material used and the transportation or shipping of biologic materials.

E5.3.4 The lid of the dry shipper and the lid of the outer container shall be secured.

E5.3.5 The outer container shall be labeled with the information required in Appendix I, the Cord Blood Unit Labeling table in Appendix I.

E5.4 The CBB shall have written policies and procedures to obtain the following data from the receiving facility about the CB unit upon receipt:

E5.4.1 Date and time of receipt.

E5.4.2 Integrity of the dry shipper.

E5.4.3 Internal verification of appropriate temperature of the dry shipper range.

E5.4.4 Integrity of the CB unit.

E5.5 Once an unrelated CB unit has left the CBB premises, it shall not be returned to the general CBB inventory.

E6 TRANSPORTATION AND SHIPPING RECORDS REQUIREMENTS

E6.1 Transportation and shipping records shall permit the tracking and tracing of the CB unit from the CBB to its final destination.

E6.2 A list identifying each the CB unit, intended recipient, intended destination, transportation and shipping records, and documentary warnings and other associated documents enclosed in a package shall be included.

E6.3 Transportation and shipping records shall document:

E6.3.1 The CBB responsible for transporting or shipping the CB unit.

E6.3.2 The date and time of packaging of the CB unit at the CBB.

E6.3.3 The date and time the package left the CBB.
E6.3.4  The identity of the courier and tracking information.

E6.3.5  The date and time of receipt of the package.

E6.3.6  Maintenance of the temperature within the specified range throughout the period of transportation or shipment.

E7  CLINICAL OUTCOME DATA

E7.1  For every CB unit released for administration, the CBB shall maintain details of clinical outcomes as necessary to ensure that the procedures in use in the CBB provide a safe and effective product.

E7.1.1  The CBB shall obtain this information directly from the Clinical Program or, if utilized, through a registry or outcomes database.

E7.2  The CBB shall have a policy or procedure to obtain the following information within the recommended time period for every CB unit released for administration:

- **E7.2.1** Viability and cell yield results on the thawed CB unit should be reported to the CBB.
- **E7.2.2** Adverse events associated with administration of the CB unit should be reported to the CBB promptly and within six weeks of transplant in accordance with Applicable Law.
- **E7.2.3** Serious adverse events related to the CB unit should be reported to the CBB in accordance with Applicable Law.
- **E7.2.4** Time to neutrophil and platelet engraftment should be reported to the CBB within six months of transplant.
- **E7.2.5** Survival rates should be reported to the CBB annually at a minimum.
- **E7.2.6** For allogeneic CB units only, data should include engraftment and chimerism.
- **E7.2.7** and GVHD results that should be reported to the CBB annually at a minimum.
- **E7.2.8** In the case of more than one graft product used for administration, the CBB should collect and document that information and, if possible, which donor product engrafted.
### CORD BLOOD UNIT LABELING

<table>
<thead>
<tr>
<th>Label Element</th>
<th>Partial label</th>
<th>At completion of collection</th>
<th>Outer container labeling at transport or shipping from collection</th>
<th>At completion of processing prior to cryopreservation</th>
<th>At distribution to Clinical Program</th>
<th>Outer container labeling at distribution to Clinical Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unique numeric or alphanumeric identifier</td>
<td>F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
</tr>
<tr>
<td>Proper name*</td>
<td>F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
</tr>
<tr>
<td>Product modifiers and manipulations*</td>
<td>F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
</tr>
<tr>
<td>Statement Related Donor †</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Statement “Directed Allogeneic Donor” or “Autologous Use Only” †</td>
<td>I  I  I  I</td>
<td>I  I  I  I</td>
<td>I  I  I  I</td>
<td>I  I  I  I</td>
<td>I  I  I  I</td>
<td>I  I  I  I</td>
</tr>
<tr>
<td>Statement “Caution: New Drug – Limited by Federal (or United States) law to investigational use.” ‡</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
</tr>
<tr>
<td>Statement “Rx Only.” ‡</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
</tr>
<tr>
<td>Collection site identifier</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
</tr>
<tr>
<td>Date of collection</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Time of collection and time zone, if different from the CB Processing Facility</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Name and volume or concentration of additives</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Name and volume or concentration of anticoagulants</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Recommended storage temperature</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Donor name (Directed Allogeneic and Autologous Related CB units)†</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
</tr>
<tr>
<td>Recipient family or individual name and unique identifier, if known</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Recipient’s name and unique identifier (if unknown after processing prior to cryopreservation)</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
</tr>
<tr>
<td>Volume or weight of the CB unit at the end of collection</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Volume or weight of the CB unit at the end of processing</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Date of cryopreservation</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>ABO group and Rh type</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>HLA phenotype</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Number of nucleated cells post processing</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Gender of CB unit infant donor</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Identity of the CBB*</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Statement “Properly Identify Intended Recipient and Product”</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Statement “For Use By Intended Recipient Only” (Allogeneic CB units)†</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>A statement indicating that leukoreduction filters should not be used</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
</tr>
<tr>
<td>Statement “Do Not Irradiate”</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
</tr>
<tr>
<td>Statement “For Nonclinical Use Only” †</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
<td>T  T  T  T</td>
</tr>
<tr>
<td>Biohazard legend and/or warning labels (see Appendix II, Modified Circular of Information Biohazard and Warning Labeling Table) ‡</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Donor eligibility summary. See Appendix III</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Date and time of distribution</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Shipping facility name, address, phone number</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Receiving facility name, address, phone number</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Identity of person or position responsible for receipt of the shipment</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Statement “Medical Specimen”. “Handle With Care”*</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
<td>C  C  C  C</td>
</tr>
<tr>
<td>Statement indicating Cord Blood for Transplantation</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
</tr>
<tr>
<td>Shipper handling instructions*</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
<td>F  F  F  F</td>
</tr>
</tbody>
</table>

*If applicable.
⁹If there are CBUs of the same name in multiple countries, the identifier must distinguish between the CBUs on the label.
⁸If CBU is shipped.
⁷If required by Applicable Law.
⁶If known.

F=Affix, T=Attach or Affix, C=Accompany or Attach or Affix; the chart has minimum requirements only. A CBU may choose to be more inclusive.

Facilities who have fully implemented ISBT 128 labeling shall follow the ISBT 128 Standard for the location of information.
## Appendix II Modified Circular of Information Biohazard and Warning Labels

<table>
<thead>
<tr>
<th>Status</th>
<th>Product Labels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Biohazard Legend [per 21 CFR 1271.3(h)]</td>
</tr>
<tr>
<td>All Donor Screening and Testing Completed</td>
<td>Yes</td>
</tr>
<tr>
<td>Abnormal Results of Donor Screening</td>
<td>No</td>
</tr>
<tr>
<td>Abnormal Results of Donor Testing</td>
<td>No</td>
</tr>
<tr>
<td>Abnormal Results of Donor Testing performed in non-CLIA-certified laboratory</td>
<td>No</td>
</tr>
<tr>
<td>Urgent Medical Need</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Donor Eligibility Determination Required [21 CFR 1271.45(b)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title 21 CFR Citation</td>
</tr>
<tr>
<td>1. Allogeneic donors with incomplete donor eligibility determination</td>
</tr>
<tr>
<td>2. Allogeneic donors found ineligible</td>
</tr>
<tr>
<td>A first-degree or second-degree blood relative</td>
</tr>
<tr>
<td>A second-degree blood relative</td>
</tr>
<tr>
<td>Unrelated donor</td>
</tr>
<tr>
<td>Unrelated donor (USA Regulation)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Donor Eligibility Determination Not Required [21 CFR 1271.90(a)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title 21 CFR Citation</td>
</tr>
<tr>
<td>3. Autologous donors</td>
</tr>
<tr>
<td>Autologous donor</td>
</tr>
<tr>
<td>Autologous donor</td>
</tr>
<tr>
<td>Autologous donor</td>
</tr>
</tbody>
</table>

A. The donor eligibility must be finalized during or after the use of the cellular therapy product. The results must be communicated to the treating physician [21 CFR 1271.60(d)(4)].
B. Abnormal results of any screening or testing requires labeling as in item 2 in this table (21 CFR 1271.65 applies).
C. Notification of the recipient’s and donor’s physicians of abnormal screening and/or testing results is required.
D. Any abnormal donor screening or testing results (even though neither screening nor testing is mandated for this group of donors) require appropriate labeling [21 CFR 1271.90(b)].
E. USDA – United States Department of Agriculture.
G. Applies to any cord blood unit collected, processed, stored, transported or transplanted in the US.

Modified table from the Circular of Information for the Use of Cellular Therapy Products, AABB et al. 2009. This table was modified to account for issues unique to CB banking. For the current version, visit www.factwebsite.org.
ACCOMPANYING DOCUMENTS AT DISTRIBUTION

CB units shall be accompanied upon leaving the CBB with the elements detailed in the following table at a minimum as required by Applicable Law¹:

| Statement that the donor has been determined to be either eligible or ineligible, based upon results of donor screening and testing | X | X |
| Summary of records used to make the donor-eligibility determination² | X | X |
| Name and address of the establishment that made the donor-eligibility determination | X | X |
| Listing and interpretation of the results of all communicable disease screening and testing performed | X | X | X | X |
| Identification of the laboratory performing communicable disease testing meeting regulatory requirements.³ | X | If applicable | If applicable | If applicable |
| Documentation of notification of the physician using the product of the results of all testing and screening | X | X | X | X (testing only) |
| Statement that the donor-eligibility determination has not been completed | X |
| Listing of any required screening or testing that has not yet been completed | X |
| Documentation that donor eligibility was completed during or after use of the CB unit and that the physician using the CB unit was informed of the results of that determination. | X |
| Instructions for use to prevent the introduction, transmission, or spread of communicable diseases | X | X | X | X |

¹ All elements are required for CB units manufactured in or designated for use in the U.S.
² Access (electronic or otherwise) to the source documents by the distributing facility and/or receiving facility is sufficient.
³ Includes laboratories certified under CLIA of 1988, as amended from time to time, or those that have met equivalent requirements as determined by the Centers for Medicare and Medicaid Services.
# TESTING REQUIREMENTS

<table>
<thead>
<tr>
<th>Specifications and Tests</th>
<th>Sample to be Tested</th>
<th>Fresh sample of CB obtained and tested after processing prior to cryopreservation</th>
<th>Fresh or frozen sample of CB tested any time before listing*</th>
<th>Cryopreserved post-processing sample of CB tested before release to the Clinical Program</th>
<th>Maternal sample obtained within seven (7) days before or after CB collection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cell Count</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total nucleated cell count</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBC with differential</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nucleated red blood cell count</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Viability</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total viability</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viable CD34</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CFU or other validated potency assay</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td><strong>Microbial culture</strong></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABO/Rh</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HLA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low resolution: HLA-A, B, DRB1</td>
<td>X (unrelated)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High resolution: HLA-A, B, C, DRB1</td>
<td>X (continuous segment – related and unrelated)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hemoglobinopathy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infectious Disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV 1</td>
<td>X, X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>HIV 2</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>HTLV I</td>
<td>X, X, X</td>
<td></td>
<td></td>
<td>X, X, X, X</td>
<td></td>
</tr>
<tr>
<td>HTLV II</td>
<td>X, X, X</td>
<td></td>
<td></td>
<td>X, X, X, X</td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Chagas</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>West Nile Virus</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>CMV</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Additional tests*</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

*Recommended. For potency testing, testing is recommended prior to release; however, if post-processing testing was not performed historically, a potency assay must be performed prior to release for administration by the CBB or Clinical Program.

*In the U.S., the CBB may need to conduct more than one test to adequately and appropriately test for a single communicable disease agent or disease. Refer to the CBER website (fda.gov/BiologicsBloodVaccines) for a list of approved tests. Testing is performed following manufacturer’s instructions using FDA-licensed, approved, or cleared donor screening tests for relevant communicable disease agents and diseases (RCDADs) as defined by U.S. FDA. FDA-licensed, approved, or cleared donor screening tests are available for WNV and HBV NAT and T. Cruzi testing may be implemented per facility-specific guidance prior to an FDA testing requirement.

*In Europe, member countries of the European Union may amend and/or introduce additional requirements. In some settings, testing by more than one method may be required for some infectious agents. This table is not intended to reflect all national variations but rather present general requirements within the EU. The tests must be carried out by a qualified laboratory, authorized as a testing center by the competent authority in the Member State, using CE-marked testing kits where appropriate. The type of test used must be validated for the purpose in accordance with current scientific knowledge.

*Additional tests for infectious transmissible agents may be required in accordance with Applicable Law or institutional policy. In certain circumstances, additional testing may be required depending on the donor’s history and the characteristics of the tissue or cells donated (e.g., toxoplasma, CMV, EBV, Trypanosoma cruzi, etc.) and may include emergent disease testing.

*In Europe, HTLV I is performed only on a selected donor population with increased risk of infection and HTLV II is not required per EU Directive.

*Each CB unit should be tested for evidence of infection for communicable disease agents using licensed donor screening tests when available according to Applicable Law. Per the EU Directive, required maternal testing is repeated on the CB unit if stored for a long period of time, or alternatively NAT technology is used. This testing must be performed prior to release for administration when testing is required by Applicable Law or institutional policy.