

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

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**Eighth Edition**  
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## 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 establish additional requirements. Each Cord Blood Bank, facility, and individual should analyze its practices and procedures to determine whether additional standards apply. Compliance with the Standards is not an exclusive means of complying with the standard of care in the industry or community or with local, national, or international laws or regulations.

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FOUNDATION FOR THE ACCREDITATION  
OF CELLULAR THERAPY (FACT)

Draft NetCord-FACT International Cord Blood Standards  
Eighth Edition

## TABLE OF CONTENTS

		Page Number
<b>PART A</b>	TERMINOLOGY, TENETS, ABBREVIATIONS, AND DEFINITIONS	<u>1</u>
A1	Terminology	<u>1</u>
A2	Tenets	<u>1</u>
A3	Abbreviations	<u>1</u>
A4	Definitions	<u>2</u>
<b>PART B</b>	CORD BLOOD BANK OPERATIONAL STANDARDS	<u>17</u>
B1	General Requirements	<u>17</u>
B2	Quality Management	<u>18</u>
B3	Policies and Standard Operating Procedures	<u>28</u>
B4	Facilities and Safety	<u>31</u>
B5	Cord Blood Bank Operations	<u>32</u>
B6	Coding and Labeling of Cord Blood Units	<u>34</u>
B7	Equipment	<u>38</u>
B8	Supplies and Reagents	<u>40</u>
B9	Inventory Management	<u>41</u>
B10	Inventory Transfer	<u>42</u>
B11	Documents and Records	<u>44</u>
B12	Interruption of Operations at Established Sites	<u>46</u>

<b>PART C</b>	CORD BLOOD DONOR MANAGEMENT AND COLLECTION STANDARDS	<u>49</u>
	C1 General Requirements	<u>49</u>
	C2 Cord Blood Collection Personnel Requirements	<u>50</u>
	C3 Policies and Standard Operating Procedures	<u>52</u>
	C4 Informed Consent	<u>53</u>
	C5 Maternal and Infant Donor Evaluation	<u>56</u>
	C6 Cord Blood Collection	<u>58</u>
	C7 Transportation and Shipping of Unmanipulated Cord Blood Units Between the Cord Blood Collection Site and the Cord Blood Processing Facility	<u>60</u>
<b>PART D</b>	CORD BLOOD PROCESSING STANDARDS	<u>63</u>
	D1 Facility Requirements	<u>63</u>
	D2 Policies and Standard Operating Procedures	<u>65</u>
	D3 Cord Blood Processing	<u>67</u>
	D4 Samples	<u>69</u>
	D5 Cryopreservation	<u>70</u>
	D6 Conditions for Storage	<u>72</u>
	D7 Monitoring and Alarm Systems	<u>5874</u>
	D8 Disposition	<u>75</u>
	D9 Cord Blood Unit Testing	<u>76</u>
	D10 Maternal Testing	<u>78</u>
<b>PART E</b>	CORD BLOOD LISTING, SEARCH, SELECTION, RESERVATION, RELEASE, AND DISTRIBUTION STANDARDS	<u>79</u>
	<u>Draft NetCord-FACT International Cord Blood Standards</u>	
	<u>Eighth Edition</u>	

E1	General Requirements	<u>79</u>	
E2	Review of Cord Blood Unit Records	<u>80</u>	
E3	Cord Blood Unit Selection and Release for Administration	<u>81</u>	
E4	Cord Blood Unit Distribution to a Clinical Program	<u>83</u>	
E5	Transportation and Shipping of Cryopreserved Cord Blood Units	<u>84</u>	
E6	Transportation and Shipping Records	<u>85</u>	
E7	Clinical Outcome Data	86	
<b>Appendix I</b>	Key Personnel Requirements	88	
<b>Appendix II</b>	Cord Blood Unit Labeling	89	
<b>Appendix III</b>	Accompanying Documents at Distribution	91	
<b>Appendix IV</b>	Testing Requirements	93	
<b>Appendix V</b>	Specification Requirements for Cord Blood Units Stored for Clinical Administration	95	

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## PART A: TERMINOLOGY, TENETS, ABBREVIATIONS, AND DEFINITIONS

### A1 TERMINOLOGY

For purposes of these Standards, the term “shall” means that the CBB 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 and is used primarily for clarity.

### A2 \_\_\_\_\_TENETS

Basic tenets for compliance with these Standards include, but are not limited to:

A2.1 Where Applicable Law includes more stringent requirements than these Standards, those laws and regulations supersedes the Standards. Conversely, when these Standards are more stringent than Applicable Law, the Standards must be followed.

A2.2 Any activity can be delegated to an appropriate designee (as defined). The person appointing the designee retains ultimate responsibility.

A2.3 Standards related to services not provided by the applicant do not apply to the applicant organization. The responsibility to demonstrate that a requirement is not applicable rests with applicant organization.

### A3 ABBREVIATIONS

The following abbreviations are used in these Cord Blood Standards:

<i>ABO</i>	Major human blood group including erythrocyte antigens, A, B, O
<i>AC</i>	Accompany
<i>AF</i>	Affix
<u><i>Anti-</i></u>	<u>Antibody to the antigen designated</u>
<i>ASHI</i>	American Society for Histocompatibility and Immunogenetics
<u><i>ASTCT</i></u>	<u>American Society for Transplantation and Cellular Therapy</u>
<i>AT</i>	Attach
°C	Degree Celsius
<i>CAP</i>	College of American Pathologists
<i>CB</i>	Cord blood
<i>CBB</i>	Cord blood bank
<i>CBC</i>	Complete blood count (Full blood count)
<i>CB unit</i>	Cord blood unit
<i>CFU</i>	Colony forming unit
<u><i>CMV</i></u>	<u>Cytomegalovirus</u>

DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
EFI	European Federation for Immunogenetics
<u>EU</u>	<u>European Union</u>
FACT	Foundation for the Accreditation of Cellular Therapy
FDA	United States Food and Drug Administration
<u>GMP</u>	<u>Good Manufacturing Practice</u>
<u>GTP</u>	<u>Good Tissue Practice</u>
<u>GxP</u>	<u>Good practice</u>
GVHD	Graft-versus-host disease
HLA	Human leukocyte antigen
HPC	Hematopoietic progenitor cell
IRB	Institutional Review Board
ISBT	International Society of Blood Transfusion
<u>ISCT</u>	<u>International Society for Cell &amp; Gene Therapy</u>
$\mu$ g	Microgram
mL	Milliliter
<u>MNC</u>	<u>Mononuclear cell</u>
<u>MSC</u>	<u>Mesenchymal stromal cell or mesenchymal stem cell</u>
<u>NC</u>	<u>Nucleated Cell</u>
QM	Quality Management
Rh	Human erythrocyte antigen, Rhesus
Rx	Prescription
<u>SOP</u>	<u>Standard Operating Procedure</u>
TNC	Total nucleated cell
<u>U.S.</u>	<u>United States</u>
WMDA	World Marrow Donor Association

#### A4 DEFINITIONS

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

*Accompany (AC):* To go, be together with, or be available to the appropriate individual(s) electronically, but not affixed or attached. Written or printed information that must accompany the cord blood unit must be in a sealed package with, or alternatively, be attached or affixed to, the cord blood unit.

*Accreditation cycle:* The period of time from the awarding of accreditation until its expiration as set, and subject to change, by FACT. At publication of these Standards, this period is three (3) years.

*Administration:* Delivery of a cord blood unit to the recipient (via routes such as infusion).

*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 temporally 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 itself caused the response.

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

*Agreement:* A formal arrangement between parties regarding a course of action to produce or supply a service, product, or equipment.

*Allogeneic:* The biologic relationship between genetically distinct individuals of the same species.

And/or: Either or both may be affected or involved.

*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, recipients, or donors.

*Attach (AT):* 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 or Standard Operating Procedures 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.

*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:* The administration of products with the intent of providing effector cells in the treatment of disease or support of other therapy.

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

*Chain of identity:* The permanent and transparent association of a cell or gene therapy's unique identifiers from procurement of tissue or cells throughout the full product(s) lifecycle including post treatment monitoring.

*Chain of custody:* Concurrent, permanent, auditable documentation illustrating the guardianship of a cell or gene therapy product from its origin through its final disposition.

*Circular of information:* An extension of container labels that includes the use of the cord blood unit, indications, contraindications, side effects and hazards, dosage, and administration recommendations.

*Clinical Program:* An integrated medical team housed in a defined location that includes a Clinical Program Director and demonstrates common staff training, protocols, Standard Operating Procedures, quality management systems, clinical outcome analysis, and regular interaction among clinical sites.

*Colony forming unit (CFU):* A clonogenic 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 cord blood unit.

*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 administration of a cord blood unit.

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

*Controlled document:* A document related to manufacturing of a product or provision of a service that may not be modified or revised without specific approval.

*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 (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 or umbilical cord vessels after the placenta has been delivered.

*In utero:* The collection of cord blood cells from the placental 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 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 an agreement to provide supplies, reagents, or storage space or to participate in the consent for cord blood collection.

*Non-fixed Cord Blood Collection Site:* A collection site with no contractual agreement with the CBB.

*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 perform these functions through contractual agreement.

*Cord blood (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. Unless otherwise specified, the term cord blood unit in this document refers to any cord blood unit regardless of method of collection, intended use, or donor source.

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

*Critical:* The quality of any element employed in cellular therapy product manufacturing which changes the identity, purity, potency, or safety of the cellular therapy product if altered or omitted. "Element" includes, but is not limited to, materials, equipment, personnel, documents, or facilities.

*Critical procedure:* A process or procedure that has the potential to directly impact the quality, safety, identity, purity, or potency of the cellular therapy product or service.

*Cryopreservation:* Cooling of viable cells or tissues to a very low temperature while maintaining viability.

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

*Deviation:* The action of departing from an established course or accepted standard.

Planned Deviation: Allowed to occur with documented prior approval as the best course of action when adherence to the established course or accepted practice was not feasible or possible.

Unplanned Deviation: The action of departing from an established course of accepted standard without intent.

*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 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 by a person with no known genetic relationship.

*Related donor:* The infant donor whose cord blood is collected and stored for autologous use by the donor or for allogeneic use by a genetically related recipient.

*Donor screening:* The process of identifying risk factors for and clinical evidence of relevant communicable disease agents and diseases through review of medical records, physical examination results, and medical history interview, including evaluation of high-risk behaviors.

*Donor suitability:* The maternal and infant donor's medical fitness to undergo the cord blood collection procedure.

*Effective date:* The date a new version of a document is implemented and the previous version is recalled or archived.

*Electronic record:* A 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 allogeneic infant donor or maternal donor for whom all the donor screening and testing have been completed in accordance with Applicable Law and who has been determined to be free of risk factor(s) for relevant communicable diseases.

*Engraftment:* The reconstitution of recipient 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.

*Eurocode:* The facility identification code (Center Code) and product coding assigned, published, and maintained by Eurocode International Blood Labeling Systems (IBLS).

*Exceptional release:* Removal of a product that fails to meet specified criteria from quarantine or in-process status for distribution through a defined approval process.

*Facility:* A location where activities covered by these Standards are performed, including but not limited to determination of donor eligibility or suitability, product collection, processing, storage, distribution, issue, or administration.

*First-degree relative:* A family member who shares approximately 50 percent of his/her genes with a particular family member. First-degree relatives include parents, siblings, and offspring.

*Fresh:* A cellular therapy product that has never been cryopreserved.

Good Manufacturing Practice (GMP): The set of current practices followed by entities producing drug and biologic products, including cellular therapy products, to ensure that the products produced meet specific requirements for identity, strength, quality, and purity. In the U.S., GMPs are enforced under Section 501(B) of the Federal Food, Drug, and Cosmetic Act (21USC351). Cellular therapy products that are more-than-minimally manipulated, are allogeneic and obtained from donors other than first- or second-degree relatives, or that are used for non-homologous purposes are examples of products controlled under GMP regulations. Similar requirements are delineated by the European Union as EU-GMP. Other countries such as the United Kingdom, Australia, Canada, and Singapore have equally well-developed systems of regulations.

Good Tissue Practice (GTP): The methods used in, and the facilities and controls used for, the manufacture of cellular therapy products to prevent the introduction or transmission of communicable diseases, including all steps in donor screening and testing, collection, processing, storage, labeling, packaging, and distribution.

GxP: Good practice following various quality standards and regulations. The "x" is variable, with further definition of good practices defined by different Applicable Law and industry standards. The type of work that is being performed will define which GxPs should be followed.

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

*Hemodilution:* A decreased concentration of cells and solids in the blood caused by infusion of blood products or fluids.

*High resolution typing:* Determination of 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  $\alpha$  polypeptides, and domain 1 of the class II  $\alpha$  and domain 1 of the class II  $\beta$  polypeptide chains.

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

*Incomplete donor eligibility:* An infant or maternal donor for whom the donor eligibility has not been completed in accordance with all donor screening and testing required by Applicable Law.

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

*Ineligible:* An infant or maternal donor for whom all the donor screening and testing has been completed in accordance with Applicable Law and who has identified risk factor(s) for relevant communicable disease.

*Institutional Review Board (IRB) 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: A global standard for the identification, labeling, and information transfer of human blood, cell, tissue, and organ products published and maintained by ICCBBA.*

*Key position:* A job category with responsibilities that significantly affect the provision of service or product safety and quality.

*Label:* Written, printed, or graphic material affixed to, attached to, or accompanying a cellular therapy product container or package.

*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 or affix the appropriate labels and include in accompanying documentation.

*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, which would allow tracing of a cord blood unit to the identification of the infant donor and 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 shall also be called low resolution.

*Manipulation:* *Ex vivo* procedure(s) that alter(s) the cord blood unit.

*Minimally manipulated:* Processing that does not alter the relevant biological characteristics of cells or tissues. For structural tissue, processing that does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement.

*More than minimally manipulated:* Processing that does alter the relevant biological characteristics of cells or tissues. For structural tissue, processing that does alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement. Products that are more than minimally manipulated are referred to as Advanced Therapy Medicinal Products in the European Union.

*Unmanipulated:* Cord blood as obtained at collection and not subjected to any form of processing.

*Manufacturing:* Activity that includes, but is not limited to, any or all steps in the collection, processing, packaging, labeling, storage, or distribution of any human cellular or tissue-based product, and/or the screening and testing of a cell or tissue donor.

*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 cord blood units 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.

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

*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.

*Surrogate mother:* The woman who carries an infant donor not genetically her own from an embryo to delivery.

*Nonconforming cord blood unit:* Any cord blood unit that does not completely meet the requirements specified by these Standards, the Cord Blood Bank, or Applicable Law.

*Occurrence:* An instance in which an action or circumstance results in an error, accident, deviation, adverse event, adverse reaction, or complaint.

*Organizational chart:* A graphic representation of the structure, function, and reporting relationships of key personnel within an organization.

*Orientation:* An introduction to guide one in adjusting to new surroundings, employment, or activity.

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



Package insert: A document prepared by the drug manufacturer, approved by the Food and Drug Administration, and included with drug packaging that provides drug prescribing information, details, and directions that health care providers need to prescribe a drug properly including approved uses for the drug, contraindications, potential adverse reactions, available formulations and dosage, and how to administer the drug. The package insert may be used to develop promotional or labeling materials.

Packaging: Placing a cellular therapy product into an appropriate secondary or outer container for shipping or transportation.

*Partial label at distribution for administration:* A label that, because of the size of the product container or other constraints, does not contain all of the required information.

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

*Post-processing sample:* Buffy coat fraction obtained after volume reduction and before adding cryoprotectant.

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

Preparative (conditioning) regimen: The treatment(s) used to prepare a patient for cellular therapy product administration (e.g., chemotherapy, monoclonal antibody therapy, radiation therapy).

Preventive action: Action taken to eliminate the cause and prevent occurrence of a potential discrepancy, deviation, or other undesirable situation.

*Pre-processing sample:* Whole cord blood with anticoagulant.

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

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

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

Product code: An eight-character ISBT 128 code that comprises the Product Description Code, a Collection Type Code, and a Division Code.

*Product name:* The ISBT 128 Cellular Therapy Class product database name and definition (format: type of cells, comma, source of cells) for products collected from marrow, peripheral blood, cord blood, and other tissue.

*Subcategory 1: At collection the product code will describe the composition of the cell therapy products. It can be HPC, NC, or MNC. These products may be collected for direct infusion without further manipulation, or may be further processed into other cellular therapy classes. If they are HPCs they retain the class name if they are used as a source of hematopoietic progenitor cells. If these products undergo modification such as cryopreservation and thawing, the class name will not change but the modification is added into the product description as an attribute.*

*Subcategory 2: After enumeration or manufacture/processing of the collected product, the product is identified by the target cell population.*

*For the most current list of definitions, see [www.isbt128.org/standard-terminology](http://www.isbt128.org/standard-terminology).*

*HPC, Cord Blood: A cell product containing hematopoietic progenitor cells obtained from cord blood.*

*NC, Cord Blood: A cell product containing nucleated cells obtained from cord blood.*

*MNC, Cord Blood: A cell product containing mononuclear cells obtained from cord blood.*

*DC, Cord Blood: A cell product containing dendritic cells obtained from cord blood.*

*iPSC, Cord Blood: A cell product containing induced pluripotent stem (iPS) cells obtained from cord blood.*

*MSC, Cord Blood: A cell product containing mesenchymal stromal cells derived from cord blood.*

*NK Cells, Cord Blood: A cell product containing natural killer cells obtained from cord blood.*

*T Cells, Cord Blood: A cell product containing T cells obtained from cord blood.*

*Proficiency test: A test to 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.*

*Qualified person: A person who has received training, is experienced, and has documented competence in the task assigned.*

*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 quality management activities to verify, by examination and evaluation of objective evidence, the degree of compliance with those aspects of the quality program under review.

*Quality control:* 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 management (QM):* The integration of quality assessment, assurance, control, and improvement in cellular therapy activities.

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

*Quality Management (QM) 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 Unit:* Personnel with responsibility to establish, maintain, and ensure compliance with the Quality Management Program and Quality Management Plan, and authority to approve or reject in-process materials, all components, cord blood unit containers, closures, packaging material, labeling, and cord blood units.

*Quality Unit Manager:* A qualified individual with oversight of the Quality Unit.

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

*Recipient:* The individual to whom the cord blood unit was administered.

*Record:* Documented evidence in both manual or electronic form, that activities have been performed or results have been achieved. A record does not exist until the activity has been performed.

*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.

*Release criteria:* The requirements that must be met before a cellular therapy product may leave the control of the Collection Site or CBB.

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

*Responsible person:* A person who is authorized to perform designated functions for which he or she is trained and qualified.

*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.

*Sample:* Biological material used for testing. When unmodified, refers to all applicable samples.

*Associated sample:* Birthing tissue (e.g., cord tissue, Wharton's Jelly) derived from the infant donor or maternal donor.

*Maternal sample:* Aliquot of cells, plasma, serum, or cellular material from the blood of the mother.

*Reference sample:* Aliquot of cells, plasma, serum, or cellular material from the cord blood unit, the umbilical cord, or the placenta stored for future analysis of product identity, potency, quality, purity, tissue typing, or infectious disease testing, should the need arise, after banking of the cord blood unit.

*Representative sample:* Aliquot of the final cord blood product that is stored under the same conditions as the cord blood unit, and can be used to test for viability, potency, or stability.

*Retention sample:* Aliquot of the final cord blood unit saved for future use, such as investigating adverse events or retroactive quality control activities.

*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.

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

*Standard Operating 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.

*Standard Operating Procedures Manual:* A compilation of policies and Standard Operating Procedures in electronic or paper format.

*Standards:* The current edition of the *NetCord-FACT International Standards for Cord Blood Collection, Banking, and Release for Administration* , which may be referred to herein as "these Standards" or "the Standards."

*Storage:* Holding cord blood units for future processing, distribution, or release.

*Time of collection:* The time of day at the end of the cord blood collection.

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 administration 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 cord blood unit 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 cellular therapy product 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.

*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.*

*Warming event:* Any event when a cryopreserved cord blood unit reaches -150° C or warmer during the life of the cryopreserved cord blood unit.

*Written:* Documentation in human readable form.

## PART B: CORD BLOOD BANK OPERATIONAL STANDARDS

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### B1: GENERAL REQUIREMENTS

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- B1.1 The Cord Blood Bank (CBB) shall consist of an integrated team housed in defined locations that is responsible for cord blood (CB) donor management; cord blood unit collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution; and recipient follow-up.
- B1.1.1 ~~These Standards apply to CB units collected by the CBB for unrelated allogeneic, related allogeneic, and autologous use.~~
- B1.2 ~~Claims made in educational, promotional, or recruitment materials shall be supported by scientific evidence relevant to the CBB's activities.~~
- B1.3 The CBB, each CB Collection Site, and each CB Processing Facility shall ~~operate in compliance with Applicable Law and abide by~~ these Standards ~~– and Applicable Law.~~
- B1.3.1 The CBB shall be licensed, registered or accredited, and the CB unit licensed, as required by the appropriate governmental authorities for the activities performed.
- B1.4 The CBB shall have a mechanism to list and distribute unrelated CB units for clinical use.
- B1.4.1 If the CBB utilizes a registry to provide services related to the listing, search, selection, reservation, release, or distribution of a CB unit:
- B1.4.1.1 The responsibilities of the registry shall be ~~clearly~~ documented.
- B1.4.1.2 The registry shall comply with these Standards as applicable to its responsibilities.
- B1.4.1.3 The registry should be accredited by the WMDA.
- B1.5 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, or any other aspect of banking, the responsibility of each entity shall be ~~clearly~~ documented in ~~a written~~ agreement.
- B1.5.1 Each contracted entity shall comply with these Standards as applicable to its responsibilities.

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B1.6 The CBB shall have a CBB Director, a CBB Medical Director, a CB Collection Director, a CB Processing Facility Director, and a Quality Unit Manager as outlined in the Key Personnel Requirements table in Appendix I.

B1.6.1 The CBB shall have an adequate number of qualified staff for its operations.

~~B1.6 Claims made in educational, promotional, or recruitment materials shall be supported by scientific evidence.~~

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## B2: QUALITY MANAGEMENT

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B2.1 There shall be ~~an overall~~ a Quality Management Program that incorporates all ~~key~~ CBB functions and ~~key performance- data~~.

~~B2.1.1 There shall be a Quality Unit that~~ B2.1.1 The CBB Director has responsibility for ensuring the overall Quality Management Program is effectively established and maintained.

B2.1.2 The Quality Unit ~~has responsibility for establishing and maintaining the Quality Management Program~~.

~~B2.1.3 The Quality Unit~~ shall have a reporting structure independent of ~~CB-unit~~ CBB manufacturing.

B2.1.4 The ~~Quality Unit~~ Quality Unit Manager shall not have oversight of ~~his/hers~~ their own work (if this person also performs tasks in the CBB-).

B2.2 The CBB shall establish and maintain a written Quality Management Plan that describes the Quality Management Program.

B2.2.1 The ~~CBB Director~~ Quality Unit Manager ~~or designee~~ shall be responsible for the Quality Management Plan.

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- B2.3 The Quality Management Plan shall 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, information technology services, testing laboratories, storage facilities, registries, and outcomes databases.
- B2.3.1 The Quality Management Plan shall include, or summarize and reference, an organizational chart of key positions, functions, and interactions within the CBB, the CB Collection Sites, and the CB Processing Facility.
- B2.4 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for establishment and maintenance of written agreements.
- B2.4.1 Agreements shall be established with external parties providing critical services that could affect the quality and safety of the CB unit or the health and safety of the infant donor or mother.
- B2.4.2 Agreements shall include the responsibility of both the CBB and the external party performing any relevant aspect of donor screening and testing, CB collection, processing, testing, storage, or distribution for administration to maintain required accreditations and to comply with ~~Applicable Law and~~ these Standards and Applicable Law.
- B2.4.3 Agreements shall have a defined effective date.
- B2.4.4 Agreements shall be dated and reviewed on a regular basis, at a minimum every two (2) years.
- B2.5 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures addressing personnel requirements, training, competency assessment, and continuing education for each key position in the CBB. Personnel requirements shall include:
- B2.5.1 ~~Consistent training programs.~~ A current job description for each position.
- B2.5.2 Consistent training programs.
- ~~B2.5.3~~ A description of minimum trainer qualifications.
- ~~B2.5.3~~ ~~A current job description for each position.~~

B2.5.4 A process to document the following for all staff:

B2.5.4.1 Initial qualifications.

~~B2.5.4.2 New employee orientation. Personnel identifier.~~

~~B2.5.4.3 New employee orientation.~~

~~B2.5.4.4 Initial training, competency, and retraining when appropriate in all procedures performed, quality management, and when applicable, good tissue practices and good manufacturer practices. GxP appropriate to the processes performed.~~

~~B2.5.4.5 Continued competency assessed annually for each critical functions performed, assessed annually at a minimum.~~

~~B2.5.4.6 Continuing education.~~

~~B2.5.4.6 Personnel identifier.~~

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B2.6 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures addressing change control that include:

~~B2.6.1 System for change approval and effective date.~~

~~B2.6.1.1 Change in practice shall not occur before a change control plan has been approved for implementation.~~

~~B2.6.2 A description of the proposed change.~~

~~B2.6.3 Analysis of the change for compliance with these Standards and Applicable Law.~~

~~B2.6.4 Identification of risks of the change to the donor, CB unit, or recipient.~~

~~B2.6.5 Determination of impact on existing processes, policies, and Standard Operating Procedures, and other controlled documents.~~

~~B2.6.6 Assessment of the need to verify or validate the change.~~

~~B2.6.6 System for change approval and effective date.~~

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B2.6.6.1 Assessment of the need to qualify equipment, supplies or reagents.

B2.6.7 Methods for communication of the change and training.

B2.7 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures ~~addressing for a~~ document control system that includes:

B2.7.1 Identification of the types of critical documents that are required to comply with the document control system, including:

B2.7.1.1 Policies and Standard Operating Procedures.

B2.7.1.2 Worksheets.

B2.7.1.3 Forms.

B2.7.1.4 Labels.

B2.7.1.5 Educational, promotional, and recruitment materials.

B2.7.2 Document management, including creation, assembly, approval, distribution, implementation, review, revision, storage, retention, archival, and retrieval.

B2.7.3 Assignment of a unique numeric or alphanumeric identifier, title, and document version to each document within the system.

B2.7.4 Document approval, including version, the approval date, signature of approving individual(s), communication or training on the document, and the effective date.

~~B2.7.3~~B2.7.4.1 Description of change, when an existing document is amended.

B2.7.5 Document distribution to relevant personnel, including acknowledgement of receipt.

B2.7.6 Protection of controlled documents from accidental or unauthorized modification.

B2.7.7 ~~Effective date~~Review of the document and when it was archived, if applicable, controlled documents every two (2) years at a minimum.

- B2.7.8 Retraction and archival of obsolete controlled documents to prevent unintended use.
- B2.7.9 Archival of obsolete controlled documents, including the inclusive dates of use, approval, and archival approval date.
- B2.7.10 Maintenance of records of archived documents in their historical sequence to allow retrieval of obsolete documents.
- B2.8 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures related to the management and maintenance of electronic records, if applicable.
- B2.9 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for actions to take in the event the CBB's operations are interrupted, including a continuity plan for critical functions.
- B2.10 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for maintaining confidentiality requirements of these standards including:
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- 2.10.1 Infant and maternal donor information (enrollment, evaluation, and testing).
- 2.10.2 The records for the CB unit (that document how it was collected, transported, received, processed, tested, stored, requested, and distributed).
- 2.10.3 Employees or contractors involved with any of the above (availability to the records and communication between the company employees and donor).
- B2.11 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for, and a schedule of, internal and external audits and inspections of the CBB. ~~B2.11.1 Internal audits shall be scheduled annually to verify compliance with elements of the Quality Management Program, operational policies and Standard Operating Procedures, Applicable Law, and these Standards, and Applicable Law.~~
- B2.11.2 ~~1~~ Audits shall be conducted by an individual with sufficient ~~expertise~~ knowledge in the process and competence in auditing to identify problems, but who is not solely ~~responsible~~ for the process being audited.
- B2.11.3 ~~Internal audits~~ 2 An audit plan for each audit shall include:  
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B2.11.2.1 Title.

B2.11.2.2 Name of individual(s) to complete the audit.

B2.11.2.3 Audit purpose.

B2.11.2.4 Audit scope.

B2.11.2.5 Documentation of review and approval by the CBB Director and the Quality Manager.

B2.11.3 An audit report shall include:

B2.11.3.1 Approved audit plan.

B2.11.3.2 Identification of auditor.

B2.11.3.3 Date started and completed.

B2.11.3.4 Records or processes audited.

B2.11.3.5 Summary of results to include findings, assessment of the underlying cause of errors, recommendations, and conclusions.

B2.11.3.6 Plan for follow-up, if appropriate, including a timeline.

B2.11.3.7 Documentation of review and approval by the CBB Director and Quality Manager.

B2.11.4 Audits shall be performed annually at a minimum and include at least the following:

B2.11.4.1 Audit of key CBB functions, records, and assessment of record review to identify recurring problems, potential points of failure, and the need for process improvement.

B2.11.4.2 Audit of external facilities that perform critical contracted services to verify that these facilities have met the requirements of the written agreements.

B2.11.4.3 Audit of a focused area as identified by a non-conformance, if applicable.

B2.11.5 The results of audits shall be used to recognize problems, detect trends, identify improvement opportunities, implement corrective and preventive actions when necessary, and follow-up on the effectiveness of those actions.

~~B2.11.5 — Review and approval of the audit plan, audit report, results, and conclusion by the CBB Director or designee and the Quality Unit Manager or designee.~~

B2.11.6 Audit results shall be shared with the appropriate Director ~~and/or~~ Medical Director, Quality Unit Manager, manager of the area audited, and other relevant staff.

B2.11.7 Audit reports shall be maintained indefinitely.

B2.11.8 There shall be a Standard Operating Procedure for the management of inspections of the CBB by regulatory, accrediting, or other external agencies.

B2.11.8.1 Documentation of results of inspections shall be maintained indefinitely.

B2.12 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for Occurrences-occurrences (errors, accidents, deviations, adverse events, adverse reactions, and complaints). The following activities shall be included:

B2.12.1 Planned deviations shall be pre-approved by the CBB Director or Medical Director, the Quality Unit, and other staff as appropriate.

B2.12.2 Unplanned deviations and, if necessary, associated corrective action shall be reviewed by the CBB Director or Medical Director, the Quality Unit, and other staff as appropriate.

B2.12.3 —Complaints shall be evaluated to determine if the complaint is related to a deviation or adverse reaction.

B2.12.4 Detection of Occurrences.

B2.12.4.1 There shall be a defined process that includes policies or Standard Operating Procedures for the detection and documentation of occurrences.

B2.12.5 Investigation of Occurrences.

B2.12.5.1 A thorough and timely investigation shall be conducted by the CBB in collaboration with the involved parties.

B2.12.5.2 Risk analysis shall be performed to determine the severity of the occurrence, and any impact on the quality and safety of the CB unit or the health and safety of the infant donor or mother.

B2.12.5.3 Investigations shall identify the root cause.

B2.12.6 Corrective and preventive action.

B2.12.6.1 Corrective and preventive action shall be implemented, if indicated, and documented including ~~both~~ short-term action to address the immediate problem and long-term action to prevent the problem from recurring.

B2.12.6.2 Corrective and preventive actions shall be evaluated by the CBB Director or Medical Director, the Quality Unit, and other staff, as appropriate.

B2.12.7 Documentation.

B2.12.7.1 Initial documentation shall include a description of the occurrence, the date and time of the occurrence, the involved individuals, a link to the CB unit(s) record, if applicable, when and to whom the occurrence was reported, and the immediate actions taken.

B2.12.7.2 A written occurrence report that includes risk analysis, root cause analysis, the corrective and preventive actions if applicable, conclusions, plan for follow-up, and a link to the record of the CB unit.

B2.12.7.3 The CBB Director and the Quality Unit shall review all occurrences, evaluate the corrective and preventive action plan, plan for follow-up audit, determine the disposition of the affected unit, if applicable, in a timely manner. This review shall be documented.

B2.12.7.4 A timeframe for follow-up audits of the effectiveness of corrective and preventive actions shall be ~~performed in a timeframe as designated, if~~ indicated in the ~~investigative~~Occurrence report.

B2.12.7.5 Occurrence reports shall be approved by the CBB Director or Medical Director, the Quality Unit, and other staff as appropriate.

B2.12.7.6 Cumulative files of occurrences shall be maintained.

B2.12.7.7 Occurrences shall be categorized, tracked, and trended to identify system problems and initiate corrective and preventive actions.

B2.12.8 Reporting.

B2.12.8.1 When it is determined that the CB unit may have been responsible for an adverse event or reaction, the Occurrence Report 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.

B2.12.8.2 Occurrences shall be reported to other facilities participating in manufacturing of the affected CB unit and to the appropriate regulatory and accrediting agencies, registries, grant agencies, Institutional Review Boards (IRBs), Ethics Committees, and ~~as necessary~~, other relevant parties.

B2.13 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for qualification of critical services, manufacturers, vendors, equipment, software, supplies, reagents, and facilities.

B2.13.1 Qualification shall include verification that suppliers of critical supplies, reagents, services, and equipment comply with these Standards and Applicable Law.

B2.13.2 Qualification studies shall be reviewed and approved by the CBB Director and the Quality Unit.

B2.14 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for validation of critical procedures of the CBB.



- B2.14.1 The CBB Director ~~or designee~~ and Quality Unit shall determine which procedures are considered critical.
- B2.14.2 Each validation or verification shall include:
- B2.14.2.1 An approved validation plan, ~~including conditions to be validated, that contains an objective, scope, procedure, test parameters, and acceptance criteria.~~
  - B2.14.2.2 ~~Acceptance criteria.~~ Description of deviations, justification, and action taken.
  - B2.14.2.3 ~~Data collection.~~ Collection of data.
  - B2.14.2.4 Evaluation of data ~~and whether acceptance criteria were met.~~
  - B2.14.2.5 Summary of results.
  - B2.14.2.6 Conclusions.
  - B2.14.2.7 References, if applicable.
  - ~~B2.14.2.7~~ ~~Documentation of review and acceptance of the methodology by the CBB Director or designee and the Quality Unit Manager or designee.~~
  - B2.14.2.8 Review and approval of the validation plan, validation report, ~~results,~~ and conclusion by the CBB Director ~~or designee and~~ and the Quality Unit Manager ~~or designee.~~
- B2.14.3 Records shall be maintained to document that procedures have been validated to achieve the expected end-points.
- B2.14.4 Significant changes to critical procedures shall be validated or verified as appropriate.
- B2.15 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the CB unit:
- B2.15.1 linkage Chain of identity.
  - B2.15.2 Chain of custody.

- B2.15.3 Linkage that allows tracking from the infant donor to the recipient or final disposition.
- B2.15.4 Tracing from the recipient or final disposition to the infant donor and mother.
- B2.15.5 Linkage of the CB unit to the infant donor and mother shall be retained confidentially and indefinitely.
- B2.15.6 Documentation of all facilities involved in each stage of CB unit manufacturing shall be maintained.
- B2.16 The Quality Management Plan shall include policies and Standard Operating Procedures in use, or summarize and reference, policies and Standard Operating Procedures to evaluate details of clinical outcome data and CB unit characteristics.
- B2.16.1 The CBB shall obtain, maintain, and analyze sufficient critical outcome data to verify that the procedures in use in the CBB consistently provide a safe and effective product.
- B2.16.2 Both individual CB unit data and aggregate data shall be evaluated.
- B2.16.3 Suboptimal results and complaints shall be investigated.
- B2.16.4 Outcome data shall be trended to identify opportunities for improvement.
- B2.17 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the transfer of inventory that meet the requirements of **B10**.
- B2.18 The Quality Unit Manager shall review and report quality management activities in a meeting, at a minimum, quarterly.
- B2.18.1 Meetings shall have defined attendees, documented minutes, and assigned actions.
- B2.18.1.1 Review findings shall be reported to staff.
- B2.19 The Quality Unit Manager shall annually review the effectiveness of the overall Quality Management Program. Documentation of review findings shall be provided to the CBB Director.

- B2.19.1 The annual report and documentation of the review findings shall be made available to key personnel and staff.

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### B3: POLICIES AND STANDARD OPERATING PROCEDURES

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- B3.1 The CBB shall establish and maintain policies or Standard Operating Procedures addressing critical aspects of operations and management ~~in addition to~~ and 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 or registration and education.
- B3.1.2 Maternal and infant donor screening and testing. ~~(including interpretation and acceptable results).~~
- B3.1.3 Informed consent.
- B3.1.4 Suitability assessment of maternal and infant donor.
- B3.1.5 Donor eligibility criteria and determination.
- B3.1.6 Interaction ~~between~~ among the donor, CB Collection Site, and the CBB.
- B3.1.7 Documentation of infant donor health at birth.
- B3.1.8 Maintenance of linkage of the CB unit and associated samples to the maternal and infant donor.
- B3.1.9 Personnel training and continued competency for the procedures performed.
- B3.1.10 Collection of CB units, associated samples, and maternal samples.
- ~~B3.1.11 — Completion of records at the CB Collection Site.~~
- B3.1.11 Storage and packaging of CB units, associated samples, maternal samples, and documentation at the CB Collection Site.

B3.1.12

Completion of records at the CB Collection Site, verification, and review.

- B3.1.13 Transport and shipping of the CB unit, associated samples, maternal samples, and completed records to the CB Processing Facility.
- B3.1.14 Labeling of the CB unit and associated samples and forms at the CB Collection Site, at the CB Processing Facility, and at release for administration.
- B3.1.15 Acceptance criteria for CB unit receipt, processing, cryopreservation, and storage.
- B3.1.16 Process control, including product specifications and management of nonconforming products and processes.
- B3.1.17 Storage information including sample location and storage temperature of associated, representative, reference, retention, and maternal samples for testing.
- B3.1.18 Acceptable levels of hemodilution of maternal samples used for communicable disease testing.
- B3.1.19 Communicable disease testing, microbial cultures, HLA typing, hemoglobinopathy testing, and other testing. Acceptance criteria for test results shall be defined.
- B3.1.20 Notification of mothers or their responsible physicians and governmental agencies of positive or indeterminate communicable disease or genetic test results.
- B3.1.21 Criteria for release of CB units from quarantine, including nonconforming CB units.
- B3.1.22 Criteria for qualification and listing of CB units for search and administration.
- B3.1.23 Listing, search, selection, and reservation of CB units.
- B3.1.24 Release and exceptional release of a CB unit.
- B3.1.25 HLA typing to include requirements for level of resolution, loci, timing, and verification of the initial typing.
- B3.1.26 For allogeneic use, verification that the infant donor and recipient are different individuals in the case of complete HLA matches.

- B3.1.27 CB unit recall, including a description of actions to be taken, responsible personnel, and notification of appropriate regulatory agencies.
- B3.1.28 Collection and analysis of transplant outcome data.
- B3.1.29 Electronic record entry, verification, and revision.
- B3.1.30 Data management.
- B3.1.31 Management of CB unit records.
- B3.1.32 CB unit disposition or disposal.
- B3.1.33 Facility management including a description of environmental monitoring.
- B3.1.34 Materials management.
- B3.1.35 Equipment monitoring, qualification, ~~and~~-maintenance, and calibration.
- B3.1.36 Cleaning and sanitation procedures including identification of the ~~personnel performing~~individuals responsible for the activities.
- B3.1.37 Disposal of medical and biohazardous waste.
- B3.1.38 Hygiene and use of personal protective attire and equipment.
- B3.1.39 Emergency and safety procedures.
- B3.1.40 Biological, chemical, and, if applicable, radiation safety.
- B3.1.41 A disaster plan to provide for continuous safe storage and transport and shipping of the CB units if required.
- B3.2 The CBB shall maintain a detailed list of all controlled documents including ~~title and~~ identifier and title.
- B3.3 Standard Operating Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to successfully 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.
- B3.3.4 A stepwise description of the procedure.
- B3.3.5 Acceptable end-points and the range of expected ~~range of results, if applicable.~~
- B3.3.6 Reference to other policies or Standard Operating Procedures ~~or policies~~ required to perform the procedure.
- B3.3.7 A reference section listing appropriate literature, if applicable.
- ~~B3.3.8 Documented approval and date of approval of each procedure by the CBB Director, Quality Unit Manager, and relevant personnel prior to implementation, and every two (2) years thereafter.~~
- ~~B3.3.9 Documented approval and date of approval of each procedural modification by the CBB Director, Quality Unit Manager, and relevant personnel prior to implementation.~~
- ~~B3.3.10 Reference to the current version of worksheets, forms, reports, and labels, if applicable.~~

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

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~~B3.5 All personnel at the CBB, CB Collection Sites, and CB Processing Facilities shall comply with these Standards and applicable policies and Standard Operating Procedures established by the CBB.~~

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~~B3.6 Review by or training of a staff member shall be documented before the staff member is allowed to perform new or revised Standard Operating Procedures.~~

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~~B3.7 Current versions of policies and Standard Operating Procedures relevant to the processes being performed shall be readily available to personnel.~~

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## B4: FACILITIES AND SAFETY

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- B4.1 All facilities, including administrative space, shall be safe and secure.
- B4.1.1 The facility shall ~~provide~~be of adequate size, construction and location with adequate lighting, ventilation, sinks, and toilets, ~~and shall be of adequate size, construction, and location~~ to maintain safe operations, prevent contamination, cross-contamination, and promote orderly handling.
- B4.1.2 The facility shall be secure to prevent the admittance of unauthorized individuals.
- B4.2 There shall be policies or Standard Operating Procedures for safety as appropriate, including:
- B4.2.1 Communicable disease agents.
- B4.2.2 Hand washing and sanitation.
- B4.2.3 Chemical ~~hygiene hazards~~.
- B4.2.4 Liquid nitrogen, including monitoring of oxygen levels.
- B4.2.5 Latex allergy.
- B4.2.6 Radiation safety, if applicable.
- B4.2.7 Fire safety.
- B4.2.8 Power failures.
- B4.2.9 Personal protective equipment, including gloves and protective clothing shall be used while handling biological specimens. Such protective equipment shall not be worn outside the work area.

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## B5: CORD BLOOD BANK OPERATIONS

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- B5.1 A CBB that includes multiple CB Collection Sites or CB Processing Facilities shall employ coordinated policies and Standard Operating Procedures, protocols, staff training and competency ~~evaluation procedures~~assessment, and quality management systems.
- B5.1.1 The CBB ~~that includes multiple CB Collection Sites or CB Processing Facilities~~ shall demonstrate evidence of regular interaction between the CBB and these sites or facilities.
- B5.2 Records of each CB unit shall be made concurrently with each stage of donor management ~~and~~, CB unit collection, transport, shipping, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution or final disposition in such a way that all steps ~~may~~can be accurately traced.
- B5.2.1 Records shall identify the person ~~immediately responsible for performing~~ each step from the donor to the recipient or final disposition of the CB unit ~~and from the recipient or final disposition to the donor,~~, including appropriate dates and times to provide a complete history of the work performed ~~and to relate the records to a particular CB unit.~~
- B5.2.2 Records shall be ~~as~~ detailed ~~as necessary~~and comprehensive for ~~a clear~~an understanding by a person experienced in CBB procedures.
- B5.3 The CBB shall have an established relationship with each ~~fixed~~ CB Collection Site to facilitate implementation of and compliance with the CBB Quality Management Program and Standard Operating Procedures.
- B5.4 There shall be maternal and infant donor evaluation procedures in place to evaluate the risk of infectious ~~and~~, genetic and malignant disease transmission from CB units.
- B5.4.1 Maternal and infant donor evaluation shall be reviewed by trained CBB personnel.
- B5.4.2 Maternal and infant donor eligibility shall be determined based upon results of screening and testing in accordance with Applicable Law.
- B5.4.3 Risks of genetic or malignant disease transmission from the CB unit shall be determined based upon results of donor screening ~~and testing.~~
- B5.4.4 The CBB shall have policies regarding the acceptance of CB units if there is a risk of infectious, genetic, or malignant disease transmission.



- B5.4.4.1 The CBB Medical Director shall give specific authorization in accordance with Applicable Law to accept CB units if the genetic or medical history of a first-degree relative of the infant donor is unknown, ~~in accordance with Applicable Law~~.
- B5.4.4.2 The CBB shall have policies to assess deferral of a donor or collected CB unit ~~from~~ unrelated use if there is a family history of a genetic or malignant disease that could be transmitted to a recipient unless testing or follow-up excludes the risks.
- B5.4.5 When a ~~mother~~ maternal or infant donor does not meet the established screening criteria, the CBB Medical Director and the Quality Unit shall document and maintain in the CB unit record the nature of the nonconformance and the rationale for inclusion of that CB unit.
- B5.5 The CBB shall use HLA testing laboratories that are capable of carrying out DNA-based intermediate and high resolution HLA-typing and are appropriately accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), College of American Pathologists (CAP), or other approved accrediting organizations providing histocompatibility services appropriate for ~~cord blood~~ CB banking.
- B5.6 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.
- B5.6.1 The CBB shall maintain documentation of ~~the~~ these laboratories' accreditation, certification, or licensure ~~of these laboratories~~ to perform this testing.
- B5.6.2 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, results, and date results are received.
- B5.7 Confidentiality.
- B5.7.1 There shall be a process for ~~maintenance of~~ maintaining confidentiality of all records and communications among the CBB, the CB Collection Sites, the CB Processing Facility, testing laboratories, storage facilities, registries, and Clinical Programs according to Applicable Law.

B5.7.2 The CBB shall have written policies and Standard Operating Procedures for circumstances where the infant donor's mother or legal guardian or her physician could be contacted.

B5.8 There shall be Standard Operating Procedures to monitor the continuing adequacy of the procedures, equipment, supplies, and reagents ~~as~~ used under routine operating conditions by the CBB personnel.

B5.8.1 The results of ongoing internal monitoring shall be documented and checked, and trends shall be analyzed on a regular basis.

~~B5.9.2 If cord tissue is collected for testing, procedures for tissue collection, processing, and storage shall be fully integrated into the Quality Management Plan.~~

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B5.9 ~~Institutional Review Board (IRB)~~ or Ethics Committee Requirements.

B5.9.1 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 appropriate governmental authority.

B5.9.2 The CBB shall maintain documentation of all its research protocols, IRB or Ethics Committee approvals or equivalent, correspondence with regulatory agencies, investigational new drug or device exemptions, annual reports, and any adverse events.

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## B6: CODING AND LABELING OF CORD BLOOD UNITS

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B6.1 ISBT 128 and Eurocode Coding and Labeling.

B6.1.1 CB units shall be identified by the proper name of the product according to ISBT 128 Standard Terminology or Eurocode.

B6.1.2 Coding and labeling technologies shall be implemented using ISBT 128 or Eurocode.

B6.2 Labeling Operations.

B6.2.1 The CBB shall have policies and Standard Operating Procedures for the following at a minimum:

B6.2.1.1 Receipt and quarantine of preprinted labels.

B6.2.1.2 Verification of accuracy against the approved template.

B6.2.1.3 Label version control.

B6.2.1.4 Proper storage of labels.

B6.2.1.5 Destruction of obsolete labels.

B6.2.2 There shall be processes to verify that all labels in use are accurate, legible, and maintain physical integrity.

B6.2.3 Labeling operations shall be conducted in a manner adequate to prevent mislabeling or misidentification of CB units, samples, and associated ~~documents~~ records.

B6.2.3.1 A process of checks in labeling procedures shall be used to prevent errors in transferring information to labels.

B6.2.3.2 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.

B6.2.3.3 When the label has been affixed to the CB unit bag, a sufficient area shall remain uncovered to permit inspection of the contents.

B6.2.3.4 Information on the CB unit being labeled shall be verified, prior to allowing the CB unit to progress to the next stage of processing, storage or distribution, by one (1) qualified staff member using a validated process or by two (2) qualified staff members.

B6.2.3.5 All data fields on labels shall be completed.

B6.2.3.6 Labeling shall be clear, legible, and printed using ink that is indelible to all relevant agents.

B6.2.3.7 Labels affixed directly to a CB unit bag shall be applied using appropriate materials as defined by the applicable regulatory authority.

B6.2.4 If a new label is required on a CB unit bag or sample, the original label shall not be removed or obscured.

B6.2.5 CB units that are subsequently re-packaged into new containers shall be labeled with new labels before they are detached from the original container.

B6.2.5.1 The process to establish linkage between original and new labels shall be validated.

B6.2.5.2 This linkage shall be maintained as a permanent part of the CB unit record.

B6.2.6 Integrally attached segments should include an identifier linking the segments to the applicable CB unit.

B6.2.7 Detached segments shall include an identifier linking the segments to the applicable CB unit.

### B6.3 Label Controls.

B6.3.1 A process for label version control shall be employed.

B6.3.1.1 Previous versions of labels shall be archived indefinitely.

B6.3.2 A process for label reconciliation shall be employed.

B6.3.3 The label shall be validated as reliable for storage under the conditions in use.

B6.3.4 Pre-printed labels.

B6.3.4.1 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~~ approved template to confirm accuracy regarding identity, content, and conformity.

B6.3.4.2 Stocks of unused labels representing different products shall be stored and maintained in a controlled manner to prevent errors.

B6.3.4.3 Unused obsolete labels shall be destroyed.

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- B6.3.5 Print-on-demand label systems shall be validated to confirm accuracy regarding identity, content, and conformity of labels to ~~templates approved by the CBB Director or designee~~approved templates.
- B6.4 Identification.
- B6.4.1 There shall be a human-readable system and a machine-readable system in operation for identification of the CB unit, samples, and associated ~~documents~~records.
- B6.4.2 Each CB unit shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to trace the 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 more than one fraction, there shall be a process to identify each fraction.
- B6.4.2.3 For multiple gestation deliveries, there shall be a process to link each infant donor to the correct CB unit.
- B6.4.3 If the CBB designates an additional or supplementary numeric or alphanumeric identifier to the CB unit or samples, supplementary identifiers shall not obscure the original identifier.
- B6.4.3.1 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 The content of each label shall be compliant with ~~Applicable Law and~~ these Standards and Applicable Law.
- B6.6.2 At all stages of collection, distribution, processing, cryopreservation, or storage, the CB unit shall be labeled with the proper name of the product and the unique numeric or alphanumeric identifier, at a minimum.

- B6.6.3 Each label shall ~~be accompanied by~~bear the appropriate biohazard and warning labels as found in the Circular of Information for the Use of Cellular Therapy Products, "Table 2. Biohazard and Warning Labels on Cellular Therapy Products Collected, Processed, and/or Administered in the United States" or other appropriate labels required by Applicable Law.
- B6.6.4 Each label shall include at least the required information detailed in the *Cord Blood Unit Labeling* table in Appendix II at completion of collection, post processing prior to cryopreservation, and at distribution from the CBB to the Clinical Program.
- B6.6.5 Any CB unit bearing a partial label at the time of distribution for administration from the CBB to the Clinical Program shall be accompanied by the information required in the *Cord Blood Unit Labeling* table in Appendix II. Such information shall be enclosed in a sealed package to accompany the unit.

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## B7: EQUIPMENT

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- B7.1 The CBB shall establish policies and Standard Operating Procedures for the management of critical equipment including identification, qualification, calibration, and maintenance.
- B7.1.1 All critical equipment shall be defined and qualified for the intended use.
- B7.1.2 Equipment should be used in accordance with the manufacturer's instructions.
- B7.2 Equipment shall be used in a manner that prevents CB unit mix-ups, contamination, and cross-contamination, and that does not compromise unit function and integrity.
- B7.2.1 Critical equipment shall be used only by trained personnel.**
- B7.3 Equipment records shall include the manufacturer's name, serial number or other unique 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.
- B7.3.1 There shall be a mechanism to identify which piece of equipment was used for each CB unit.

~~B7.4 — Calibration.~~

B7.4.4 Equipment shall be inspected, tested, and calibrated on a regularly scheduled basis as recommended by the manufacturer, after a critical repair or move, and, at a minimum, annually.

B7.4.1 All equipment with a critical measuring function shall be calibrated against a traceable standard, if available. Where no traceable standard is available, the basis and acceptance criteria for calibration shall be described and documented.

B7.4.2 When equipment is found to be out of calibration or specification, there shall be a defined process for action required for CB units manufactured since the last calibration.

B7.4.3 Records of the dates and copies of calibration results shall be maintained.

B7.5 Maintenance ~~and~~, repairs, and cleaning.

B7.5.1 Equipment shall be maintained in a clean and orderly manner and located ~~so~~ as to facilitate cleaning, sanitation, calibration, and maintenance according to established schedules.

B7.5.2 Records of the maintenance schedule, ~~the~~ maintenance performed, ~~and~~ damage, malfunction, modification, or repair to equipment shall be maintained.

B7.5.3 There shall be a Standard Operating Procedure that addresses the actions to take in the event of equipment malfunction or failure.

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~~B7.6 — Cleaning and sanitation.~~

~~B7.6.1 — Equipment shall be cleaned and sanitized according to established schedules.~~

~~B7.6.2 — Records of equipment cleaning and sanitation shall be maintained.~~

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B7.6 Equipment shall be routinely inspected for cleanliness, sanitation, and calibration and to confirm adherence to applicable equipment maintenance schedules.

B7.7 Records of recent maintenance, cleaning, sanitizing, calibration, and other activities shall be displayed on or near each piece of equipment.

B7.8 Equipment decommissioning or disposition shall be described and documented.

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## B8: SUPPLIES AND REAGENTS

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

B8.2 Critical supplies and 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 unit 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 during collection, processing, or storage shall be sterile and of the appropriate grade for the intended use.

B8.4.1 If suitable clinical or pharmaceutical grade reagents are not used, reagents shall undergo lot-to-lot functional verification and ~~shall~~ include acceptance criteria to confirm that new lots perform as expected compared to the previous lots.

B8.4.2 Sterilization of supplies and reagents prepared within the facility shall be documented.

B8.5 Supplies and reagents used for CB collection, processing, or cryopreservation, ~~whenever possible,~~ shall be approved for human use whenever possible.

B8.6 Certificates of analysis shall be obtained and maintained indefinitely on file for all critical reagents.

B8.7 Supplies and reagents should be used in a manner consistent with instructions provided by the manufacturer.

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

B8.8.1 Supplies and reagents shall be quarantined until they have been determined to meet criteria for release from quarantine.

B8.8.2 The disposition of rejected supplies and reagents shall be documented.

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- B8.9 The lot number, expiration date, and manufacturer of supplies and reagents used for collection, processing, testing, cryopreservation, or storage of each CB unit shall be documented and linked to each CB unit.
- B8.10 There shall be a process to prevent the use of expired reagents and supplies.
- B8.10.1 An expiration date shall be assigned to in-house prepared solutions or components.
- B8.10.2 An expiration date shall be assigned to the collection kit, and shall be consistent with the first item in the collection kit set to expire.

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## B9: INVENTORY MANAGEMENT

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- B9.1 The inventory management system for CB units shall allow each CB unit and its samples ~~and records~~ to be located in a timely manner. ~~The inventory records shall include:~~
- B9.2 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.
- B9.2.5 Date the CB unit and associated samples were stored and removed from storage.
- B9.3 The inventory management system shall clearly distinguish related CB units from unrelated CB units.
- B9.4 The inventory management system shall be designed to prevent mix-ups, contamination of the CB units during storage, and the improper release of CB units and associated samples.

B9.5 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, and its associated samples~~

B9.6 The CBB shall have policies related to the return of CB units to the CBB inventory.

B9.6.1 Unrelated CB units shall not be returned to the CBB inventory after they have left the CBB premises.

B9.6.2 —If related CB units are returned to the CBB inventory, there shall be documentation of appropriate storage and transportation.

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## B10: INVENTORY TRANSFER

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B10.1 The CBB shall have a policy or Standard Operating Procedure for the potential transfer of all or part of the CB unit inventory.

B10.1.1 The policy or Standard Operating Procedure shall require a written agreement between the transferring and ~~accepting CBBs~~receiving CBB that describes the responsibilities of each CBB, including the elements in B10, at a minimum.

B10.1.1.1 The written agreement shall specify that FACT-~~NetCord accreditation~~ accreditation does not transfer with the inventory.

~~B10.2.2 The written agreement shall specify each party's responsibilities.~~

B10.1.1.2 The transferring CBB shall provide the receiving CBB with all records in B10.4.3.

B10.2 For related CB units, the family should be made aware of the intent to transfer the units.

B10.3 The policy or Standard Operating Procedure shall require the following responsibilities of the receiving CBB:

B10.3.1 Records shall be in a language and form that can be understood by the accepting CBB personnel.

- B10.3.2 There shall be documentation of review of records and of transferred inventory to verify that the CB units meet the requirements of the written agreement for transfer of inventory.
- B10.3.3 Transferred records shall include:
- B10.3.3.1 Maternal consent.
  - B10.3.3.2 Medical and genetic history.
  - B10.3.3.3 A summary of records used to make the donor eligibility determination.
  - B10.3.3.4 Identity and results of all maternal donor communicable disease tests.
  - B10.3.3.5 All results from testing performed on the CB unit.
  - B10.3.3.6 Processing records.
  - B10.3.3.7 Cryopreservation records, including program parameters and freezing curve detailing each step of the freezing process.
  - B10.3.3.8 The manufacturer and approximate dimensions of the storage bag and canister.
  - B10.3.3.9 Number of attached segments and other samples.
  - B10.3.3.10 Other records as required to allow the receiving CBB to meet these Standards.
- B10.3.4 There shall be a validated method with continuous temperature monitoring for transfer of inventory.
- B10.3.5 ~~Standard Operating Procedure~~ There shall be a process for inspecting incoming CB units for damage ~~or~~ and risk of contamination.
- B10.3.6 After the CB units have been transferred, but before the transferred inventory is made available for search:
- B10.3.6.1 The integrity and viability of CB units shall be verified to confirm the transport or shipping method did not compromise CB unit viability.

B10.3.6.2 There shall be confirmation of the completeness of all records described in B10.43.3.

B10.3.6.3 The acceptingreceiving 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.

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## B11: DOCUMENTS AND RECORDS

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B11.1 Employee records shall be maintained in a confidential manner as required by Applicable Law.

B11.2 A record management system shall be established and maintained to allow for protection, preservation, integrity, disposal, prompt identification, location, and ready retrieval of records.

B11.2.1 Records shall be available for inspection by authorized individuals upon request from a regulatory or accrediting agency.

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

B11.3.1 Records of exported CB units shall be in a language understood by the importing organization or 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 Quality Management records.

B11.4.4 Personnel records.

B11.5 Equipment maintenance, inspection, calibration, and cleaning records shall be maintained indefinitely.

B11.6 Facility cleaning and sanitation records shall be maintained for three (3) years at a minimum.

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~~document 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 systems~~ under the control of the CBB that are used as a substitute for paper, to make decisions, to perform calculations, or to create or store information used in critical procedures.
- B11.8.2 ~~For all critical electronic record systems, there~~ There shall be policies, ~~and Standard Operating Procedures, and system elements for all critical electronic record systems~~ to ~~maintain~~describe the ~~accuracy, integrity, identity, development, validation, testing, system use, modification, backup, maintenance, and confidentiality of all records.~~personnel training.
- 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 ~~There shall be policies and Standard Operating Procedures for~~ all critical electronic operating systems to maintain the accuracy integrity, identity, and confidentiality of all records.
- B11.8.4 Critical electronic record systems, ~~there shall be an~~ have a validated alternative system to allow for continuous operation of the CBB in the event that electronic systems are not available. ~~The alternative system shall be validated, and CBB staff shall be trained in its use.~~
- B11.8.5 For all critical electronic record systems, there shall be ~~written~~ Standard Operating Procedures for record entry, verification, and revision.
- B11.8.5.1 A method shall be established for review of data before final acceptance.
- B11.8.5.2 A method shall be established for the unambiguous identification of the individual responsible for each record entry.
- B11.8.6 For all critical electronic record systems, there shall be the ability to generate true copies of the records in both human readable and electronic format suitable for inspection and review.
- B11.8.7 For all critical electronic record systems, there shall be validated procedures for and documentation of:
- B11.8.7.1 ~~Systems development~~ System development including the verification of calculations and algorithms.
- B11.8.7.2 Numerical designation of system versions.
- B11.8.7.3 Prospective validation of system, including hardware, software, and databases.
- B11.8.7.4 Installation of the system.
- B11.8.7.5 Training and continued competency of personnel in systems use.
- B11.8.7.6 Monitoring of data integrity.
- B11.8.7.7 Back-up of the electronic records system on a regular schedule.
- B11.8.7.8 System maintenance and operations.

B11.8.8 All system modifications shall be authorized, documented, and validated prior to implementation.

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## B12: INTERRUPTION OF OPERATIONS AT ESTABLISHED SITES

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B12.1 The CBB shall have a policy or Standard Operating Procedures for actions to take in the event the CBB's operations are interrupted, including a continuity plan for critical functions.

B12.2 The CBB shall have a policy or Standard Operating Procedure for the potential discontinuation of any CB collection or processing function for a period exceeding six (6) months that includes documentation of training and continued competency of all staff to perform the duties assigned upon resumption of activities.

B12.3 If CB collection activity is discontinued at any fixed CB Collection Site for a period exceeding six (6) months, the CBB Director ~~or designee~~ shall review and, if required, renew the CB collection contract with that site.

B12.3 ~~There shall be policies to address the following in the event that~~ a CBB discontinues banking of new CB units; ~~there shall be policies to address the following:~~

B12.3.1 Maintenance of competent staff to oversee, maintain, and distribute the inventory, and collect and analyze transplant outcome data.

B12.3.1.1 Continuation of staff training and competency program.

B12.3.2 Continued participation in quality assurance activities.

B12.3.2.1 Maintenance of proficiency testing.

B12.3.2.2 Quality control and maintenance of equipment required for pre-release testing, storage of CB units and associated samples, and distribution of the inventory.

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B12.3.3 Continuation of the stability program.

B12.3.4 Distribution of CB unit contiguous segments and samples for testing, including pre-release testing.

- B12.3.5 Maintenance of all records including electronic records, of the ~~entire~~ inventory in storage.
- B12.3.6 Maintenance of communication between staff and all relevant registries and Clinical Programs.
- B12.3.7 For ~~related~~ CBBs collecting related units, maintenance of communication between staff and donor families.
- B12.4 Prior to the reestablishment of either CB collection or banking the following shall be documented:
- B12.4.1 Review of ~~all~~ staff training and competency to ensure staff are competent in required tasks.
- B12.4.2 Review of procedures to confirm that methods are consistent with current practices.
- B12.4.3 Inspection of all supplies and reagents ~~and supplies~~ to confirm ~~none will be used past its expiration date~~ suitability for use.
- B12.4.4 Completion of all equipment, qualification, calibration, and maintenance ~~of all equipment~~ within the time periods specified in the Standard Operating Procedures and manufacturer's instructions.
- B12.4.5 Review by Quality Unit to ensure that all aspects of reestablished operations have been considered.
- B12.5 Cessation of operations.
- B12.5.1 The CBB shall follow all contractual obligations that are specified in written agreements with CB Collection Sites, donor families, registries, and other entities as applicable.
- B12.5.2 The CBB shall have a mechanism to manage agreements with testing laboratories, suppliers, and other vendors.



## **PART C: CORD BLOOD DONOR MANAGEMENT AND COLLECTION STANDARDS**

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### **C1: GENERAL REQUIREMENTS**

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- C1.1 These Standards shall apply to all CB activities.
- C1.2 The CBB shall provide documentation to the CB Collection Site that outlines requirements for complying with CBB collection policies and Standard Operating Procedures.
- C1.3 The CB Collection Sites shall have processes to prevent the introduction, transmission, or spread of communicable disease.
- C1.4 There shall be adequate space for the performance of the collection procedure.
- C1.5 There shall be secure storage of the CB unit, associated samples, maternal samples, and documents until they are transported or shipped to the CB Processing Facility.
- C1.6 There shall be a designated area for appropriate and secure storage and preparation of the equipment, supplies, and reagents needed for the collection procedures.
  - C1.6.1 Equipment, supplies, and reagents shall be stored according to the manufacturer's recommendations in an area and manner appropriate to protect their integrity and functionality.
    - C1.6.1.1 There shall be documentation of appropriate storage of all supplies, reagents, and CB units.
  - C1.6.2 Critical supplies and reagents shipped to CB Collection Sites from the CBB shall be in an outer container validated to maintain the designated temperature range.
  - C1.6.3 Supplies and reagents shall be used prior to their expiration dates.

#### **C1.7 Personnel Safety Requirements.**

- C1.7.1 The CB Collection Site shall have Standard Operating Procedures that utilize universal precautions and are designed to minimize risks to the health and safety of employees, volunteers, and visitors, including:

- C1.7.1.1 Bloodborne pathogens.
  - C1.7.1.2 Hand washing or sanitation.
  - C1.7.1.3 Chemical hazards.
  - C1.7.1.4 Latex allergy.
- C1.8 Personal protective equipment, including gloves and protective clothing shall be used while handling biological specimens. Such protective equipment shall not be worn outside the work area.
- C1.9 When a CB collection kit is prepared and sent from the CBB, adequate instructions and materials shall be provided.
- C1.9.1 The CB collection kit shall be transported or shipped under conditions validated to maintain the designated temperature range from the time it leaves the CBB until it is received by the CB Collection Site or the donor’s family.
  - C1.9.2 There shall be adequate instructions and materials to store the collection kit prior to collection.
  - C1.9.3 There shall be adequate instructions and materials to collect, label, store, pack, document, and transport or ship the CB unit, associated samples, and maternal samples to the CBB.
- C1.10 Identity of supplies and reagents including manufacturer, lot number, and expiration date shall be documented for each collection.

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## **C2: CORD BLOOD COLLECTION PERSONNEL REQUIREMENTS**

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- C2.1 All CB collection personnel shall comply with these Standards, and applicable policies and Standard Operating Procedures established for collection activities.
- C2.2 The CB Collection Site shall have adequate and qualified staff to perform collection activities.
- C2.3 All CB collection personnel shall have a defined line of communication with relevant CBB personnel for all aspects of the collection activities.

- C2.4 All collections shall be performed by ~~health care professionals~~ qualified staff trained for the collection procedure.
  - C2.4.1 Training on the collection procedure shall cover each aspect of the CB collection process, and include:
    - C2.4.1.1 The appropriate storage, preparation, and use of the collection supplies and reagents.
    - C2.4.1.2 Cleaning of the umbilical cord to minimize the risk of contamination with microbes or maternal blood.
    - C2.4.1.3 Use of the CB collection bag to avoid microbial contamination and clotting.
    - C2.4.1.4 Verification of the identity of the donor.
    - C2.4.1.5 Labeling.
    - C2.4.1.6 Safety of the maternal and infant donors.
  - C2.4.2 The collecting ~~health care professional's~~ staff initial and continuous training shall be documented.
  - C2.4.3 The minimum level of activity to maintain competency shall be specified.
- C2.5 There shall be documented training on the following procedures for all relevant personnel:
  - C2.5.1 Packaging, storage, shipping and transportation of the CB unit.
  - C2.5.2 Review of medical records and physical examination records of the maternal and infant donors for risks of communicable diseases and donation suitability assessment.

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### C3: POLICIES AND STANDARD OPERATING PROCEDURES

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- C3.1 The CBB shall establish and maintain policies or Standard Operating Procedures addressing critical aspects of collection operations and management ~~in addition to and~~ those required in B2. These documents shall include all elements required by these Standards, shall be consistent with the policies and Standard Operating Procedures of the CBB, and shall address at a minimum:
- C3.1.1 Donor recruitment or registration and education.
  - C3.1.2 Maternal and infant donor screening ~~(including interpretation and acceptable results)~~.
  - C3.1.3 Informed consent.
  - C3.1.4 Suitability assessment of maternal and infant donor.
  - C3.1.5 Interaction between the CBCBB and the Collection Site ~~and the CBB, the donor family, or the practicing physician at non-fixed sites.~~
  - C3.1.6 Documentation of infant donor health at birth.
  - C3.1.7 Maintenance of linkage of the unit and biologic samples to the CB unit to the maternal and infant donor.
  - C3.1.8 Collection of CB units, associated samples, and maternal samples.
  - C3.1.9 Completion of records at the CB Collection Site (manual or electronic), verification, and review.
  - C3.1.10 Labeling of the CB unit, associated samples, forms, and maternal samples.
  - C3.1.11 Process control, including product specifications and management of nonconforming products and processes.
  - C3.1.12 Storage and packaging of CB units, associated samples, maternal samples, and documentation at the CB Collection Site.
  - C3.1.13 Transport and shipping of the CB unit, associated samples, maternal samples, and completed ~~records~~ documentation to the CB Processing Facility.

C3.1.14 Acceptable levels of hemodilution of maternal samples used for communicable disease testing.

C3.1.15 Personnel and collector training and continued competency for the procedures performed.

~~C3.1.16—Electronic record entry, verification, and revision.~~

~~C3.1.17—CB unit records.~~

C3.1.16 CB unit disposition or disposal.

C3.1.17 Equipment monitoring, qualification, ~~and~~ maintenance, and calibration.

C3.1.18 Facility management and environmental ~~managementspecifications.~~

C3.1.19 Materials management.

C3.1.20 Cleaning and sanitation procedures including identification of the individuals responsible for the activities.

C3.1.21 Disposal of medical and biohazardous waste.

C3.1.22 Hygiene and use of personal protective attire and equipment.

C3.1.23 Emergency and safety procedures.

C3.1.24 Biological, ~~and~~ chemical, ~~and, if applicable, radiation~~ safety.

C3.1.25 Disaster plan to provide for continuous safe storage and transport and shipping of the CB units if applicable.

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#### C4: INFORMED CONSENT

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C4.1 Informed consent from the mother or an agreement between the mother and the CBB shall be obtained ~~and/or~~ verified and documented by a trained individual in accordance with Applicable Law.

- C4.1.1 Informed consent or an agreement between the mother and the CBB 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 or an agreement 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.
  - C4.2.1 If an interpreter or translator is utilized, the identity of the interpreter or translator shall be documented.
  - C4.2.2 Family members shall not serve as interpreters or translators.
- C4.3 The CBB shall only perform steps in the CB banking process for which it has informed consent or a signed agreement from the mother, including:
  - C4.3.1 Collection
  - C4.3.2 Processing.
  - C4.3.3 Testing
  - C4.3.4 Long-term storage.
  - C4.3.5 Distribution.
- C4.4 The mother shall have an opportunity to ask questions.
- C4.5 The informed consent or agreement between the mother and the CBB shall include the following information for unrelated and related donations:
  - C4.5.1 The overall purpose and participation of the maternal and infant donors.
  - C4.5.2 An explanation of the collection procedure and its associated activities in terms the mother can understand.
  - C4.5.3 The possible risks and benefits to the maternal or infant donor.
  - C4.5.4 The possible alternatives to participation.

- C4.5.5 The intent of the donation for either unrelated use or for related use.
- C4.5.6 The mother will be asked to provide personal and family medical history.
- C4.5.7 Personnel will be permitted to review the medical records of the maternal and infant donors.
- C4.5.8 Samples from the maternal and infant donors will be collected for communicable disease and genetic disease testing, HLA typing, and other testing, as applicable.
- C4.5.9 Maternal and CB unit samples will be stored for future testing.
- C4.5.10 The CBB will indefinitely maintain linkage between the maternal and infant donors and the CB unit.
  - C4.5.10.1 The CBB will notify the mother or her responsible physician, and governmental agencies when required, of positive or indeterminate communicable disease or genetic test results.
  - C4.5.10.2 The CBB retains the right to follow up with the mother or relevant healthcare provider at a future date.
  - C4.5.10.3 Personal 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 as required by Applicable Law.
- C4.5.11 The CB unit should be processed, stored, and made available for use.
- C4.5.12 If the CB unit may potentially be used for reasons other than transplantation, including use as source material for manufacture of a commercial product, this shall be fully disclosed in the informed consent or agreement between the mother and CBB.
- C4.5.13 The CBB's policies for disposal of CB units, including:
  - C4.5.13.1 Nonconforming CB units.
  - C4.5.13.2 Related CB units, if these units are no longer required.
  - C4.5.13.3 Agreed-upon duration of storage for related CB units.

C4.5.13.4 The CBB's policies for disposition of related CB units in the event of cessation of operation.

C4.6 Informed consent for unrelated donation shall also include:

C4.6.1 The right of the mother to refuse participation without prejudice.

C4.6.2 If the CB unit is listed for unrelated use, the infant donor and the infant donor's family no longer have ownership of the CB unit, the CB unit is a donation that will be made available to other individuals, and the CB unit will not necessarily be available to the infant donor or the infant donor's family at a later date.

C4.6.3 If the CB unit is listed for unrelated use, information donor eligibility will be determined. Information regarding the CB unit, including donor eligibility, will be shared with registries according to Applicable Law, and with other individuals as appropriate.

C4.7 If the CB unit is intended for related use, the mother shall also be informed that the release of the CB unit will be limited to the donor family, intended recipient(s), or the infant donor.

C4.8 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.

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## C5: MATERNAL AND INFANT DONOR EVALUATION

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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 collection.

C5.1.4 There shall be a policy for follow-up of donors for management of donation-associated adverse events.



- C5.1.5 Maternal and infant donor evaluation results shall be documented.
- C5.1.6 Any abnormal result relevant to the health of the maternal or infant donor shall be reported to the relevant healthcare provider, maternal donor, and ~~governmental authority~~ according to Applicable Law, governing authorities.
- C5.2 Maternal and infant donor screening shall include a medical history, review of medical records, and review of physical examination findings.
  - C5.2.1 History shall be obtained and documented while the mother is able to concentrate on the information and is not distracted by aspects of labor.
  - C5.2.2 The history shall be obtained in a language the mother understands.
    - C5.2.2.1 If an interpreter or translator is utilized, the identity of the interpreter or translator shall be documented.
    - C5.2.2.2 Family members shall not serve as interpreters or translators.
  - C5.2.3 The mother and surrogate mother, if applicable, shall affirm and document that all the information provided is accurate to the best of her knowledge.
  - C5.2.4 The mother shall be provided with information to contact the CBB if the infant donor later develops a serious disease.
- C5.3 A medical and genetic history of the infant donor's family shall be obtained from the genetic mother.
  - C5.3.1 The history shall request information regarding the infant donor's first-degree relatives and, when applicable, egg, sperm, or embryo donors.
  - C5.3.2 The history shall include genetic history, malignant diseases, and inherited disorders that may be transmissible to the recipient.
- C5.4 A history for the mother's communicable disease risk behavior shall be obtained.
  - C5.4.1 The history for the mother's communicable disease risk shall include the mother's prenatal communicable disease testing, if known, and results of other general medical testing that could indicate a risk of communicable disease transmission.

- C5.4.2 If history for communicable disease 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.
- C5.4.3 In the case of a surrogate mother who gives birth to an infant donor not genetically hers, a communicable disease risk history of the surrogate mother shall be obtained.
- C5.4.4 Travel history of the mother and, if applicable, surrogate mother, shall be obtained.
- C5.4.5 There shall be screening for human transmissible spongiform encephalopathy, including Creutzfeldt-Jakob ~~d~~Disease and its variant forms.
- C5.4.6 In the case of sperm, egg, or embryo donation, the communicable disease risk history shall be obtained, reviewed, and documented.
- 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 infant 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 **D10.1**.
- C5.6.2 A sufficient volume of blood from the birth mother shall be obtained to meet the requirements in **D4.3.1**.
- C5.6.3 A sufficient volume of blood should be obtained to meet **D4.4**.
- C5.6.4 Hemodilution of the birth mother prior to collection of maternal samples shall be ~~assessed~~evaluated. The maternal sample acceptance criteria shall be defined.

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## C6: CORD BLOOD COLLECTION

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- C6.1 CB collection practices shall protect the maternal and 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 protect the safety of the mother and the infant donor.
- ~~C6.2.1 In utero CB collections should only be performed 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.~~
- C6.2.1 In utero CB collections shall only occur in uncomplicated deliveries as determined by the licensed health care professional responsible for the delivery.
- C6.2.2 In utero CB collections performed in a multiple gestation pregnancy shall be based on an evaluation of infant donor safety by the licensed health care professional responsible for the delivery, and all infants shall be delivered before any CB collection begins
- C6.2.3 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 maternal donor shall be verified.
- C6.3.2 The identity of the cord blood collector shall be documented.

- C6.3.3 Methods for CB collection shall employ aseptic techniques.
- C6.3.4 CB collection procedures shall be validated to result in acceptable CB volume, progenitor cell counts and viability, cell recovery, progenitor cell viability, cell recovery, and rate of microbial contamination.
- C6.3.5 The CB collection bag shall be approved for use with human blood and sealed to prevent leakage and minimize the risk of cell loss, and of microbial contamination.
- C6.3.6 All supplies and reagents 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, associated samples, maternal samples, and associated documents.
- C6.5 There shall be written Standard Operating Procedures at the CB Collection Site for labeling of the CB unit, associated samples, maternal samples, and associated documents that permits tracking and tracing among the CB unit, infant donor, maternal donor, samples, and documentation.
- C6.6 At completion of CB collection, the primary collection bag shall have affixed or attached, or be accompanied by, the information required in the *Cord Blood Unit Labeling* table in Appendix II.
- C6.7 There shall be written Standard Operating Procedures for storage of CB units, 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, associated samples, and maternal samples shall be maintained in a secure environment in a defined temperature range.
- C6.7.2 CB units shall be maintained in a temperature range validated to protect cell viability.
- C6.8 The chain of custody of the CB unit shall be maintained from collection to receipt at the CBB.
- C6.9 Records shall be maintained at the CBB of all reports of adverse events that occur during or immediately after CB collection.

## C7: TRANSPORTATION AND SHIPPING OF UNMANIPULATED CORD BLOOD UNITS BETWEEN THE CORD BLOOD COLLECTION SITE AND THE CORD BLOOD PROCESSING FACILITY

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- C7.1      Transportation and shipping of CB units shall be in compliance with Applicable Law.
- C7.2      The methods of transporting 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 is qualified to maintain a designated temperature range around the CB unit to protect cell viability during CB unit transport and shipping.
  - C7.5.1    The immediate environment shall be made of material adequate to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling during transportation and shipping.
  - C7.5.2    The process for transportation and shipping shall be validated to maintain a designated temperature range in the immediate environment of the CB unit.
  - C7.5.3    When a CB unit is shipped, the temperature inside the immediate environment shall be continuously monitored, or the unit shall be shipped in a rigorously validated container.
    - C7.5.3.1    When a CB unit is shipped without continuous temperature monitoring, there shall be a documented evaluation of the risk of the shipping process.
- C7.6      The outer container shall be labeled with the information required in the *Cord Blood Unit Labeling* table in Appendix II.
  - C7.6.1    The outer container shall be secured.

C7.7 Transportation and Shipping Records.

- C7.7.1 A list identifying each CB unit and its associated samples, maternal samples, and documents that are enclosed in a package shall be included.
- C7.7.2 Transportation and shipping records shall permit the tracking of the CB unit from the CB Collection Site to its final destination.
- C7.7.3 Transportation and shipping records shall include:
  - C7.7.3.1 The CB Collection Site responsible for transporting or shipping the CB unit.
  - C7.7.3.2 The date and time of transport or shipment departure.
  - C7.7.3.3 The identity of each courier.
  - C7.7.3.4 The date and time of receipt of the package.
  - C7.7.3.5 The condition of the package upon receipt.



## PART D: CORD BLOOD PROCESSING STANDARDS

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### D1: FACILITY REQUIREMENTS

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- D1.1 The CB Processing Facility shall be licensed, registered, or accredited as required by the appropriate governmental authorities for the activities performed.
- D1.2 There shall be designated facilities of adequate space, design, and location for the intended procedures.
- D1.2.1 The designated facilities shall be divided into defined areas of adequate size to prevent mix-ups, mislabeling, contamination, or cross-contamination of CB units during the following activities:
- D1.2.1.1 Preparation of, and safe, sanitary, and orderly storage of, the equipment, supplies, and reagents needed for processing, testing, cryopreservation, storage, and release.
  - D1.2.1.2 Processing activities and ancillary functions.
  - D1.2.1.3 Storage of CB units prior to release or distribution.
  - D1.2.1.4 Maintenance of records. –
- D1.3 The CB Processing Facility shall be secure ~~in order~~ to prevent the entrance of unauthorized ~~personnel~~individuals.
- D1.3.1 The CB Processing Facility shall have oversight of ~~non-processing personnel visiting the CB Processing Facility~~visiting individuals who are not employed at the facility to maintain compliance with these Standards.
- D1.4 The CB Processing Facility shall provide adequate lighting, ventilation, air quality, and access to hand sanitation 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.
- D1.5.1 There shall be documentation of facility cleaning and sanitation.



- D1.6 CB Processing Facility environmental conditions that affect the safety and potency of the CB unit, including temperature; humidity; ventilation; and air pressure, filtration, and classification, shall be defined and qualified, and as appropriate for the degree of classification, controlled, monitored, and recordeddocumented to demonstrate ongoing compliance.
- D1.7 The CB Processing Facility shall have an adequate number of qualified staff for its operations.
- D1.8 Personnel Safety Requirements.
- D1.8.1 The CB Processing Facility shall have Standard Operating Procedures that utilize universal precautions and are also designed to minimize risks to the health and safety of employees, volunteers, and visitors, including at least:
- D1.8.1.1 Bloodborne pathogens.
  - D1.8.1.2 Hand washing and/or sanitation.
  - D1.8.1.3 Chemical hazards.
  - D1.8.1.4 Latex allergy.
- D1.8.2 Personal protective equipment, including gloves and protective clothing shall be used while handling biological specimens. Such protective equipment shall not be worn outside the work area.
- ~~D1.8.3 The Processing Facility shall have a written for action in case of exposure, communicable disease, to chemical, biological, radiological, hazards.~~
- D1.8.3 The CB Processing Facility shall have written policies and Standard Operating Procedures for action in case of exposure to communicable disease agents or to chemical, biological, liquid nitrogen, or, if applicable, radiological hazards.
- D1.8.3.1 Communicable disease agents.
  - D1.8.3.2 Hand washing and sanitation.
  - D1.8.3.3 Chemical hazards.
  - D1.8.3.4 Liquid nitrogen, including monitoring of oxygen levels.

D1.8.3.5 Latex allergy.

D1.8.3.6 Radiation safety, if applicable.

D1.8.3.7 Fire safety.

D1.8.3.8 Power failures.

D1.8.4 ~~Medical~~ All waste shall be disposed of in a manner to minimize hazard to facility personnel and the environment in accordance with Applicable Law.

D1.8.5 Oxygen ~~levels~~ sensors shall be ~~monitored~~ appropriately placed and utilized in areas where ~~wherever~~ liquid nitrogen is stored or in use.

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## D2: POLICIES AND STANDARD OPERATING PROCEDURES

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D2.1 The CB Processing Facility shall establish and maintain policies or Standard Operating Procedures addressing critical aspects of operations and management ~~in addition to~~ and those required in B2. These documents shall include all elements required by these Standards, shall be consistent with the policies and Standard Operating Procedures of the CBB, and shall address at a minimum:

D2.1.1 Donor and recipient confidentiality.

D2.1.2 Acceptance criteria for CB unit receipt, processing, cryopreservation, and storage.

D2.1.3 Maternal and infant donor screening and testing.

D2.1.4 Process control, including product specifications and management of nonconforming products and processes.

D2.1.5 Prevention of mix-ups and cross- contamination.

D2.1.6 Labeling of the CB unit and associated documents and samples.

D2.1.7 Storage of CB unit and all samples to include alternative storage if the primary storage device fails.

- D2.1.8 Acceptable levels of hemodilution of maternal samples used for communicable disease testing.
- D2.1.9 Communicable disease testing, microbial cultures, HLA typing, hemoglobinopathy testing, and other testing. \_Acceptance criteria for test results shall be defined.
- D2.1.10 Criteria for release of CB units from quarantine, including nonconforming CB units.
- D2.1.11 Transportation and shipping, including methods and conditions within the processing facility and to and from external facilities.
- D2.1.12 HLA typing to include requirements for level of resolution, loci, timing, and verification of the initial typing.
- D2.1.13 Electronic record entry, verification, and revision.
- D2.1.14 CB unit records.
- D2.1.15 CB unit disposition or disposal.
- D2.1.16 Personnel training and continued competency for the procedures performed.
- D2.1.17 Facility management including a description of environmental monitoring.
- D2.1.18 Materials management.
- D2.1.19 Equipment monitoring, qualification, ~~and~~ maintenance, and calibration.
- D2.1.20 Cleaning and sanitation procedures including identification of the individuals responsible for the activities.
- D2.1.21 Disposal of medical and biohazardous waste.
- D2.1.22 Hygiene and use of personal protective attire and equipment.
- D2.1.23 Emergency and safety procedures.
- D2.1.24 Biological, chemical, and, if applicable, radiation safety.

D2.1.25 A disaster plan to provide for continuous safe storage and transport and shipping, if applicable, of the CB units.

D2.2 All CB Processing Facility personnel shall comply with these Standards, and applicable policies and Standard Operating Procedures established by the Processing Facility.

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### D3: CORD BLOOD PROCESSING

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D3.1 Acceptance Criteria.

D3.1.1 Upon receipt of a CB unit package into the CB Processing Facility, the shipping container and contents shall be inspected and the records reviewed for the following:

D3.1.1.1 Receipt within an acceptable amount of time as defined by the CBB.

D3.1.1.2 The integrity of the outer container, ~~and the temperature during shipping is within a specified range.~~

D3.1.1.3 Verification of the contents against the list of enclosed items.

D3.1.1.4 The CB unit for appropriate appearance, integrity, labeling, and identification.

D3.1.1.5 The associated samples, maternal samples, and documents for appropriate labeling and identification.

D3.1.1.6 Temperature during shipping or transport is within a specified range.

D3.1.2 Occurrences outside of acceptance criteria shall be evaluated.

D3.1.3 For unrelated CB units, an appropriately signed consent authorizing processing, testing, and storage of the CB unit and samples for the intended purpose shall be confirmed before processing is completed.

D3.1.4 ~~The CBB shall be a only perform steps in the CB banking process for which it has informed consent or a signed agreement with the donor family for collection, processing, testing, storage, disposal, and the name and contact information of the donor family from the mother, including:~~

D3.1.4.1 Collection.

D3.1.4.2 Processing.

D3.1.4.3 Testing.

D3.1.4.4 Long-term storage.

D3.1.4.5 Distribution.

D3.1.5 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.

D3.2 Processing.

D3.2.1 CB units shall be properly labeled and clearly identified prior to acceptance for processing.

D3.2.2 At all stages of processing, the CB unit shall be labeled with the proper name of the product and the unique numeric or alphanumeric identifier, at a minimum.

D3.2.3 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.

D3.2.4 Processing and cryopreservation of CB units shall be performed according to Standard Operating Procedures validated to result in acceptable cell viability, recovery, ~~and~~ potency, and free from microbial contamination introduced during processing.

D3.2.4.1 Critical control points shall be identified and their specifications defined.

D3.2.4.2 TNC recovery should be  $\geq 60\%$  after processing prior to cryopreservation.

D3.2.4.3 Failure of the processing procedure to achieve specifications for critical control points shall be evaluated with appropriate action documented.

- D3.2.5 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.
    - D3.2.5.1 Where processing of CB units is not in a closed system, processing shall take place in an environment with specified air quality and cleanliness.
    - D3.2.5.2 The effectiveness of measures to avoid contamination and cross-contamination shall be verified and monitored.
  - D3.2.6 Cryopreservation of unrelated CB units shall be initiated within 48 hours of CB collection.
  - D3.2.7 Cryopreservation of related CB units shall be initiated within 72 hours of CB collection.
  - D3.2.8 More than minimal manipulation of a CB unit shall be performed in accordance with Applicable Law and:
    - D3.2.8.1 Using reagents and/or devices approved for that manipulation by the appropriate governmental agency or
    - D3.2.8.2 With an ~~IRB Institutional Review Board~~ or Ethics Committee-approved protocol or
    - D3.2.8.3 With an active approved Investigational New Drug Application, Investigational Device Exemption, or non-U.S. equivalent.
  - D3.2.9 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.
  - D3.3 At the completion of processing prior to cryopreservation, the freezing bag shall be labeled with the information as required by the *Cord Blood Unit Labeling* table in Appendix II.
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## D4: SAMPLES

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- D4.1 At a minimum, the following samples shall be collected from the CB unit post-processing prior to cryopreservation:
- D4.1.1 A minimum total volume of at least 200  $\mu\text{L}$  divided into at least two (2) segments with each sealed and integrally attached to each freezing bag.
    - D4.1.1.1 The contents of each contiguous segment shall be representative of the CB unit.
    - D4.1.1.2 When a CB unit is initially requested, a minimum of one (1) contiguous segment shall be used to verify the results of HLA typing.
    - D4.1.1.3 When a CB unit is initially requested for clinical use, potency shall be tested in accordance with the *Testing Requirements* table in Appendix IV and shall meet the specifications outlined in the *Specification Requirements* table in Appendix V.
    - D4.1.1.4 At the time of removal for testing, one (1) qualified person using a validated process or two (2) qualified people shall verify the identity of the segment.
  - D4.1.2 Additional samples of a minimum total of  $2 \times 10^6$  nucleated cells divided into at least two (2) vials or additional contiguous segments.
    - D4.1.2.1 Representative and retention samples intended for viability or potency analysis shall be stored under the same conditions as the CB unit.
    - ~~D4.1.2.2. Reference samples used for purposes other than viability or potency analysis shall be stored at  $-70^\circ\text{C}$  or colder.~~
  - D4.1.3 At least one retention sample from the CB unit should be stored indefinitely.
  - D4.1.4 Suitable material for preparation of at least 20  $\mu\text{g}$  genomic DNA.
  - D4.1.5 A minimum total volume of 3.6 mL of plasma from the CB unit divided into at least two (2) vials.
    - D4.1.5.1 The plasma shall be stored at  $-70^\circ\text{C}$  or colder.

D4.2 Maternal samples to be maintained from the birth mother, shall include a minimum total volume of 3.6 mL of serum or plasma divided into at least two (2) vials— and stored at -70°C or colder.

D4.3 For unrelated donors excepting egg or embryo donors, suitable material should be collected from the genetic mother for preparation of at least 20 µg a sufficient sample of genomic DNA with the exception of egg or embryo donors.

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## D5: CRYOPRESERVATION

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D5.1 CB units shall be cryopreserved using controlled rate freezing or an equivalent procedure validated to achieve adequate~~optimal~~ cell recovery, viability, potency, and stability.

D5.1.1 TNC concentration ~~should~~ be within a defined range.

D5.1.2 The duration from addition of cryoprotectant to initiation of freezing shall be minimized and validated by the CBB.

D5.1.3 The duration from completion of freezing to storage at -150°C or colder shall be minimized and validated by the CBB.

D5.2 Cryopreservation Standard Operating Procedures shall specify that the following information is recorded for each CB unit:

D5.2.1 TNC concentration.

D5.2.2 The cryoprotectant, and its final concentration, ~~and the duration of cell exposure prior to freezing.~~

D5.2.3 The duration of cell exposure prior to initiation of freezing.

D5.2.4 Method of freezing and end-point temperature of cooling.

D5.2.5 Continuous monitoring of the temperature within a defined range.

D5.2.6 Freezing curve parameters, including cooling rate within a defined range.



- D5.3 CB units shall be stored in freezing bags or other validated containers designed and approved for the cryopreservation of human cells ~~and~~.
- D5.3.1 Approved containers shall be placed into individual metal canisters to provide protection during freezing, storage, transportation, and shipping.
- D5.3.2 Each ~~freezing bag~~cryopreservation container and ~~tubing~~components shall be examined visually for damage or possible contamination prior to use.
- D5.3.3 Representative samples to be used for viability or potency assays shall be cryopreserved and stored under the same conditions as the CB unit.
- D5.4 Processes must minimize the risk of overfilling and underfilling freezing ~~bags~~containers.
- D5.4.1 After filling, each freezing bag~~container~~ and segment shall be visually examined for possible leaking, overfilling or underfilling, or breakage of seals. The results of these inspections shall be documented.

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## D6: CONDITIONS FOR STORAGE

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- D6.1 Storage devices containing CB units and samples shall be located in a ~~secure area. The device or the area shall have locking capability that is used when the area is not occupied by the CBB staff at a minimum.~~ secure area with controlled access.
- D6.2 Refrigerators and freezers used for the storage of CB units, samples, blood components, human cells, tissues, specimens, or reagents used in CB unit or other birthing tissue collection, processing, or cryopreservation shall not be used for any other purpose.
- D6.3 Procedures to minimize the risk of microbial or cross-contamination ~~of~~between CB units during storage shall be defined and maintained.
- D6.4 Processes for storing CB units in quarantine shall be defined in Standard Operating Procedures.

- D6.4.1 Quarantined CB units shall be easily distinguishable and stored in a manner that minimizes the risks of microbial contamination and cross-contamination and inappropriate distribution.
- D6.4.2 Each CB unit shall be maintained in quarantine storage until the CBB Medical Director, or designee, and Quality Unit have approved the release from quarantine status.
- D6.4.2.1 This reviewapproval shall be based upon review of maternal communicable disease risk history, other medical history, maternal test results, and CB unit microbial culture results as required by Applicable Law.
- D6.4.3 Records shall indicate when a CB unit was released from quarantine into permanent storage.
- D6.4.4 CB units shall remain quarantined if the maternal donor samples or CB unit has ~~ve~~ reactive or positive screening test results for communicable disease or increased infectious disease risk based on ~~obtained through~~ the donor screening process.
- D6.5 Temperature.
- D6.5.1 CB units shall be stored at -150°C or colder in the liquid or vapor phase of nitrogen.
- D6.5.1.1\_ If CB units are not fully immersed in liquid nitrogen, the storage ~~freezersdevice~~ shall be qualified to showprevent unit storage above -150°C and include a continuous temperature monitoring system that ~~all CB units are maintained at appropriate records~~ temperatures at least every four hours.
- D6.5.1.2 ~~Transfer~~Temperature conditions during transfer of cryopreserved CB units shall be validated and monitored.
- D6.5.2 Warming events at any time after cryopreservation shall be minimized.
- D6.5.2.1 The duration of warming events shall be documented, and the impact on the CB unit and representative samples shall be assessed.
- D6.5.2.2 If a warming event may have decreased the potency of an unrelated CB unit and representative samples, the unit shall not be made available for distribution for administration.

- D6.5.2.3 If a warming event may have decreased the potency of a related CB unit, the unit shall only be made available for administration as a nonconforming unit after approval of the CBB Medical Director and the transplant physician.
- D6.6 There shall be a written stability program to assess cryopreserved CB units for post-thaw viability, potency, and container integrity.
  - D6.6.1 A minimum of three (3) CB units per manufacturing method and storage conditions shall be assessed annually.
    - D6.6.1.1 CB units with the longest storage duration for each manufacturing method shall be included in each annual assessment.
  - D6.6.2 Specifications for acceptance of stability results shall be defined.
    - D6.6.2.1 The stability program shall include requirements to assess additional CB units if a CB unit fails to meet specifications.

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## D7: MONITORING AND ALARM SYSTEMS

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- D7.1 Refrigerators used for storage of CB units before cryopreservation shall have a validated system to monitor and record the temperature continuously or at a minimum every four (4) hours.
- D7.2 Where CB units are not fully immersed in liquid nitrogen, freezers used for CB unit storage shall have a validated system to monitor the temperature continuously.
  - D7.2.1 The temperature shall be recorded every four (4) hours, at a minimum.
- D7.3 Where CB units are fully immersed in liquid nitrogen, there shall be a validated mechanism to consistently maintain levels of liquid nitrogen in liquid nitrogen freezers.
- D7.4 Alarm Systems.
  - D7.4.1 Storage devices for CB units and samples shall have validated alarm systems that are continuously active.

D7.4.2 Alarm systems shall have both audible and visible signals.

D7.4.3 Alarm systems shall be checked periodically for technical function. The records of such checks shall be maintained.

~~D7.4.4 The alarm system shall be capable of notifying designated personnel 24 hours a day.~~

D7.4.4 If trained personnel are not always present in the immediate area of the storage device, a system shall be in place that alerts responsible personnel of alarm conditions on a 24-hour basis.

D7.4.5 Alarms shall be set to activate at a temperature or level of liquid nitrogen that will allow ~~staff sufficient~~ time to salvageprotect CB units and samples.

D7.4.6 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.

D7.4.6.1 Instructions shall include a procedure for notifying processing personnel.

D7.4.8 Any alarm event and its resolution shall be documented.

D7.5 Contingency plans or qualified storage devices of appropriate temperature shall be available for maintaining CB units and samples at the storage temperature within the acceptable range in the event the primary storage device fails.

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## D8: DISPOSITION

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D8.1 The CBB shall have defined criteria for the disposition and location of discard of a CB unit including:

D8.1.1 CB units released for listing on a registry.

D8.1.2 CB units released for clinical use.

D8.1.3 CB units released for research.

D8.1.4 CB units released for quality assurance activities.

D8.1.5 CB units that are discarded and persons authorized to approve discard.

- D8.1.6 CB units released for commercial use.
- D8.2 CB units shall meet the requirements outlined in the *Specification Requirements* table in Appendix V.
- D8.3 Nonconforming CB units.
- D8.3.1 The CBB shall have a policy for the management of CB units that are not accepted into inventory.
- D8.3.2 The CBB shall have a written policy for the management of CB units that do not meet in-process or final endpoints or specifications.
- D8.3.3 The CBB shall have a written policy to address positive or indeterminate results found during the screening process or laboratory testing of samples.
- D8.4 Disposal.
- D8.4.1 The records for discarded CB units shall indicate the unique numeric or alphanumeric identifier of the CB unit; the reason, date, location and method of disposal; and the individual who disposed of the CB unit.
- D8.4.2 If processing is initiated before obtaining a signed consent, the CB unit shall be clearly identified and distinguished from consented CB units during all processing stages.
- D8.4.2.1 Unrelated CB units lacking signed consent shall not be cryopreserved and shall be discarded.
- D8.4.2.2 Cryopreserved related CB units lacking a signed consent or agreement shall be maintained in quarantine status until consent or agreement has been obtained.
- D8.4.2.3 The CBB must develop a plan for disposition of units where full consent or agreement is not obtained.
- D8.4.3 For related CB unit disposal:
- D8.4.3.1 Disposal shall comply with the terms of disposal in the written agreement.

D8.4.3.2 Reasons for disposal and notification of the donor's family shall be documented.

D8.4.3.3 The maternal donor must clearly give her consent if the unit is to be used for clinical, research, or other purposes.

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## D9: CORD BLOOD UNIT TESTING

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- D9.1 The CBB shall define tests and procedures to determine CB unit safety, viability, potency, and integrity and to document that CB units meet predetermined release specifications as outlined in the *Specification Requirements* table in Appendix V.
- D9.1.1 Records of all such test results and procedures shall become part of the permanent record of the CB unit.
- D9.1.2 The CBB shall maintain records for each test methodology used for CB units that have been banked. These methodologies must be traceable to individual CB units.
- D9.2 Testing procedures shall include:
- D9.2.1 The use of established and validated assays, equipment, and test procedures for the evaluation of the CB unit.
- D9.2.2 Adequate provisions for monitoring the reliability, accuracy, precision, and performance of test procedures and instruments.
- D9.2.3 Adequate identification and handling of all samples so that they are accurately related to the specific CB unit being tested, to its infant donor, to the maternal donor, and to the specific recipient, as applicable.
- D9.2.4 Verification of new reagent lots to provide comparable results between lots or give results in agreement with suitable reference ranges before or with placement into service.
- D9.2.5 Where available, use of reference or quality control material demonstrated to give results within the defined range established for that material.

- D9.2.6 Functional checks performed for testing instruments, as appropriate, prior to testing of CB units.
- D9.2.7 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 Quality Unit.
- D9.3 CB units shall be tested as outlined in the *Testing Requirements* table in Appendix IV.
- D9.3.1 CBC with differential testing shall include enumeration of neutrophils, lymphocytes, monocytes, and platelets. Parameters for neutrophils, lymphocytes, and platelets shall be defined.
- D9.3.2 Microbial cultures shall be performed using a system validated for the growth of aerobic and anaerobic bacteria and fungi.
- D9.3.2.1 CB units for unrelated use shall be free from microbial contamination.
- D9.3.2.2 For related CB units, the results of positive microbial tests shall include identity and sensitivities of the organism(s). These results shall be reported to the infant donor's mother and her physician, in accordance with ~~Applicable Law and~~ the CBB's policies and Standard Operating Procedures and Applicable Law.
- D9.3.3 HLA Class I and Class II typing shall be performed by DNA-based methods.
- D9.4 Test results that are positive or outside of the established range and are relevant to the infant donor's health shall be communicated to the infant donor's mother or legal guardian and her physician according to ~~Applicable Law and~~ CBB policies and Standard Operating Procedures and Applicable Law.

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## D10: MATERNAL TESTING

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- D10.1 The maternal blood sample obtained within seven (7) days before or after collection of the CB unit shall be tested for evidence of infection as outlined in the *Testing Requirements* table in Appendix IV, utilizing assays required for volunteer tissue donations and according to Applicable Law.

- D10.1.1 The CBB shall ensure that samples are collected and stored for infectious disease testing.
- D10.2 Positive or indeterminate test results, excluding cytomegalovirus, shall be communicated to the maternal donor and/or her physician according to Applicable Law and CBB policies and Standard Operating Procedures.
- D10.3 All maternal samples should have negative or non-reactive test results with the exception of Cytomegalovirus antibody, Hepatitis B core antibody, and non-Treponemal-specific syphilis testing.
- D10.3.1 If allowed by Applicable Law, maternal samples that are Hepatitis B core antibody positive and are accepted shall be HBV negative by DNA testing and Hepatitis B Surface Antigen (HBsAg) non-reactive/negative.
- D10.3.2 If allowed by Applicable Law, maternal samples that test positive for syphilis using a non-Treponemal-specific screening test and are accepted shall be negative using a Treponemal-specific confirmatory test.
- D10.4 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 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

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### E1: GENERAL REQUIREMENTS

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- E1.1 There shall be a designated ~~facilities with defined areas~~area for CB unit listing, search, selection, reservation, release, and distribution to prevent mix-ups, mislabeling, or other errors.
- E1.2 The CBB shall have policies and Standard Operating Procedures for the following at a minimum:
- E1.2.1 Selection, reservation, release, and distribution of CB units to Clinical Programs.
  - E1.2.2 For unrelated use:
    - E1.2.2.1 Review of records.
    - E1.2.2.2 Qualification for listing and search of the CB units.
    - E1.2.2.3 Verification of HLA typing of the CB unit.
  - E1.2.3 For related use:
    - E1.2.3.1 Review of records.
    - E1.2.3.2 Continued storage and release.
    - E1.2.3.3 A process to prevent listing of related units for unrelated use.
    - E1.2.3.4 Verification of HLA typing of the CB unit.
  - E1.2.4 A mechanism to ensure that CB units are released in accordance with Applicable Law and the agreement at the time of informed consent.
- E1.3 If the CBB utilizes a registry, the CBB shall use a validated process for uploading CB unit data and HLA information to the registry.
- E1.4 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.

- E1.4.1 If ~~an outside agency~~ a third party is used for search and match functions, its electronic record system shall meet these Standards.
- E1.5 The CBB or registry shall have policies and Standard Operating Procedures for the reservation and allocation of CB units that include:
- E1.5.1 Prevention of simultaneous reservation of a CB unit for more than one potential recipient ~~or for more than one potential Clinical Program.~~
- E1.5.2 Notification of all registries on which the CB unit is listed that it is no longer available at the time a CB unit is removed from inventory.

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## E2: REVIEW OF CORD BLOOD UNIT RECORDS

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- E2.1 The CBB shall have policies and Standard Operating Procedures for the comprehensive review of CB unit records~~z~~ including at a minimum:
- E2.1.1 Consents or agreements.
- E2.1.2 Infant ~~donor's~~ donor's ethnicity/race.
- E2.1.3 Infant ~~donor's~~ donor's gender.
- E2.1.4 Eligibility determination, if required by Applicable Law.
- E2.1.5 Infant ~~donor's~~ donor's physical examination.
- E2.1.6 Maternal risk factors for transmission of communicable disease~~z~~.
- E2.1.7 Family medical history for transmissible genetic and malignant diseases.
- E2.1.8 Processing and cryopreservation parameters.
- E2.1.9— Results of tests outlined in the *Testing Requirements* table in Appendix IV.
- E2.1.10 Hemoglobinopathy~~z~~ if known.
- E2.2 Unrelated CB units shall be made available for search on a registry or the CBB's inventory only after processing~~z~~ medical, and quality review has been completed.

E3.3 The nature of ineligible or nonconforming CB units shall be disclosed to the registry and the requesting party.

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### E3: CORD BLOOD UNIT SELECTION AND RELEASE FOR ADMINISTRATION

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E3.1 The CBB shall maintain documentation of requests for CB units, requests for samples, requests for and results of testing, and records of transportation and shipping of CB units and samples between facilities according to Applicable Law, institutional policy, or for a minimum of ten (10) years after the date of distribution or disposition, whichever is longer.

E3.2 Before a CB unit is released, a sample obtained from a contiguous segment of that CB unit shall be tested to verify HLA typing ~~and, if possible, cell viability.~~

E3.2.1 The CB unit shall be tested to verify HLA typing at least once after a CB unit is cryopreserved.

E3.2.2 If a contiguous segment was never available, another validated method shall be used to identify the CB unit.

E3.2.3 Any histocompatibility discrepancy shall be resolved and communicated to the registry and the Clinical Program.

E3.2.3.1 For allogeneic use, in the case of a complete HLA match, verification that the infant donor and the recipient are different individuals ~~in the case of a complete HLA match~~ shall be documented.

E3.2.3.2 For autologous use, verification that the CB unit, the infant donor, and the recipient are the same individual shall be documented.

E3.2.4 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.

E3.3 Before a CB unit is released, it shall be tested for potency (see Appendix IV).

E3.3.1 Potency testing should be performed on a contiguous segment if available or a representative sample.

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

- E3.4.1 Results of tests outlined in the *Testing Requirements* table in Appendix IV.
- E3.4.1.1 There shall be ~~documentation of notification of evidence that~~ the physician using the CB unit ~~of the results has been notified~~ of all testing and screening results as required by Applicable Law.
- E3.4.1.2 In the case of incomplete donor eligibility, at the time of distribution, there shall be documentation that the 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 as required by Applicable Law.
- E3.4.2 For related CB units with positive microbial tests documented in the CB unit record, antimicrobial sensitivities shall be provided.
- E3.4.3. ~~Gender~~ Sex of the infant donor.
- E3.4.4 Risks of communicable and genetic diseases disclosed by the maternal medical and genetic screening or clinical chart review and the results of any investigation or further testing performed.
- E3.4.4.1 The CBB shall disclose to the Clinical Program if the genetic or medical history of a first-degree relative is unknown.
- E3.4.4.2 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.
- E3.4.5 The method of CB unit processing.
- E3.4.6 Any variances in the collection, labelling, processing, testing, cryopreservation, storage, transport, or shipping procedures that may influence the integrity or quality of the CB unit.
- E3.4.7 Physical characteristics of the CB unit, including the number and type of bags or compartments used for storage.
- E3.4.8 Information about the type of cassette in which the CB unit will be shipped.
- E3.4.9 Instructions for storage of the CB unit.

- E3.4.10 Instructions for thawing and administering the CB unit, including expected range of results based upon CBB internal validation results or published documentation.

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#### E4: CORD BLOOD UNIT DISTRIBUTION TO A CLINICAL PROGRAM

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- E4.1 The CBB shall obtain, in written or electronic form, a request from the ~~cellular therapy~~treating physician, designee, or registry for distribution of the CB unit prior to release of the CB unit.
- E4.2 The CBB Medical Director ~~or designee~~ and the Quality Unit shall conduct and document a comprehensive record review, ~~in accordance with Applicable Law,~~ prior to distribution of a CB unit to a Clinical Program.
- E4.3 ~~When~~The CBB shall have a plan to reconcile donor eligibility when the maternal medical or genetic screening history indicates potentially transmissible disease ~~or when there is,~~ a positive or indeterminate communicable disease test result, ~~or incomplete donor eligibility.~~
- E4.3.1 A CB unit intended for allogeneic use with incomplete donor eligibility or determined to be ineligible shall be distributed only if there is documented urgent medical need for the CB unit. Documentation shall include the approval of the ~~recipient's~~recipient's physician, the CBB Medical Director, and the Quality Unit.
- E4.3.2 If donor eligibility is incomplete, and completion of screening and testing is possible, the eligibility determination shall be completed, and the results provided to the ~~recipient's~~recipient's physician.
- E4.4 A CB unit with a positive microbial test result shall be released according to Applicable Law.
- E4.5 At the time of distribution to a Clinical Program, the CB unit ~~bag~~ shall be labeled as required in the *Cord Blood Unit Labeling* table in Appendix II.
- E4.6 A circular of information or package insert ~~and~~including instructions for handling, thawing, ~~and,~~ using the CB unit, ~~including,~~ short-term storage, and preparation for administration, shall accompany the CB unit.

- E4.7 Elements detailed in the *Accompanying Documents at Distribution* table in Appendix III shall accompany the CB unit at distribution to a Clinical Program according to Applicable Law.
- E4.8 A practice CB unit should be available if requested by the Clinical Program.
- E4.8.1 The practice CB unit shall be clearly labeled with the statement, "For Nonclinical Use Only."
- E4.9 The CB unit should be received by the Clinical Program prior to initiation of the ~~recipient's~~recipient's preparative regimen unless approved by the ~~cellular therapy~~treating physician.

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## E5: TRANSPORTATION AND SHIPPING OF CRYOPRESERVED CORD BLOOD UNITS

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- E5.1 Procedures for transportation and shipping of cryopreserved CB units shall be validated.
- E5.2 The transit time between the CBB and other facilities shall be minimized.
- E5.2.1 There shall be a written ~~plans~~process 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~~qualified 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 Dry shippers shall be requalified annually, at a minimum.
- E5.3.2 Function of the dry shipper shall be verified before each use to ensure that it continues to maintain temperature as expected.
- E5.3.3 The dry shipper shall contain an electronic data logger that continuously monitors temperature throughout the transportation or shipping period.
- E5.3.4 The transport or shipping methods shall conform to Applicable Law regarding the mode of transportation or shipping of such devices.
- E5.3.5 The dry shipper shall be labeled in accordance with Applicable Law regarding the cryogenic material used and the transportation or shipping of biologic materials.

- E5.3.6 The dry shipper shall be ~~configured~~prepared and labeled in a way to maintain an upright position as recommended by the manufacturer.
- E5.3.7 All container lids shall be secured.
- E5.3.8 The outer container shall be labeled with the information required in the *Cord Blood Unit Labeling* table in Appendix II.

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## E6: TRANSPORTATION AND SHIPPING RECORDS

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- 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 The package shall include a list identifying the CB unit, intended recipient, intended destination, transportation and shipping records, and any warnings and other associated documents.
- 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 dry shipper left the CBB.
  - E6.3.4 The identity of the courier and tracking information.
  - E6.3.5 The date and time of delivery of the dry shipper.
  - E6.3.6 Maintenance of the temperature within the specified range throughout the period of transportation or shipment.
- E6.4 Transportation or shipping to or from third-party manufacturers must ensure that the original CB unit identifier is retained and is traceable in accompanying documentation.
- E6.4.1 Shipping records must comply with standards required for direct shipments.

E6.5 The CBB shall have policies and Standard Operating Procedures to obtain the following data from the receiving facility about the CB unit upon receipt:

- E6.5.1 Date and time of receipt.
- E6.5.2 Identity of the personnel receiving the CB unit.
- E6.5.3 Integrity of the dry shipper.
- E6.5.4 Verification of appropriate temperature range.
- E6.5.5 Integrity of the CB unit.
- E6.5.6 Verification that required documentation is available.

~~E6.5.6~~ If6 Once an unrelated ~~CB unit~~ CB unit has left the custody of the CBB ~~premises~~, the CB unit shall not be returned to the general CBB inventory.

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## E7: CLINICAL OUTCOME DATA

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E7.1 The CBB shall have a policy or Standard Operating Procedure to request the following information within the recommended time period for every CB unit released ~~for administration~~ for hematopoietic reconstitution: clinical application:

E7.1.1 Further processing or manipulation prior to administration.

E7.1.2 Method of thawing.

E7.1.3 Viable nucleated cell yield results on the thawed CB unit.

~~E7.1.2 Method for thawing and any further processing prior to administration.~~

E7.1.4 Microbial screening performed on the thawed CB unit.

E7.1.5 Administered cell dose.

E7.1.6 Complaints associated with the CB unit.

E7.1.7 Adverse events associated with administration of the CB unit.



~~Time~~E7.1.8 For hematopoietic reconstitution, time to neutrophil and platelet engraftment<sub>7z</sub>

E7.1.8.1 For allogeneic CB units<sub>7z</sub> data should include chimerism<sub>7z</sub>

E7.1.8.2 In the case of more than one graft product used for administration<sub>7z</sub> the CBB should collect and document that information and, if possible, which product engrafted<sub>7z</sub>

~~E7.1.8.3~~ If the CB unit was modified by ex vivo expansion prior to administration, the CBB should collect this information.

E7.1.9 For hematopoietic reconstitution survival rates annually at a minimum.

E7.1.10 For hematopoietic reconstitution GVHD results annually at a minimum.

E7.2 The CBB shall have a policy to request outcome data that is relevant to other uses for which a CB unit was released<sub>7z</sub>

E7.3 The CBB shall have a Standard Operating Procedure that describes the process and methods for analyzing the aggregate data obtained from the clinical use of released CB units.

KEY PERSONNEL REQUIREMENTS

	Education and Experience	Job Responsibilities	Continuing Education (A minimum of 10 hours annually in any combination of these disciplines)
<b>CBB Director</b>	<ul style="list-style-type: none"> <li>• Doctoral degree in medicine or in a related scientific field</li> <li>• Training and a minimum of two (2) years of experience in immunogenetics of transplantation<sup>1</sup>, basic or clinical immunology, immunohematology, basic or clinical hematology, transfusion medicine, blood or tissue banking, or cryobiology</li> </ul>	<ul style="list-style-type: none"> <li>• Final responsibility for CBB operations</li> <li>• <u>Overall responsibility for the Quality Management Program and Quality Plan.</u></li> <li>• Overall CBB compliance with these Standards, including all components of the CBB's policies and Standard Operating Procedures</li> </ul>	CB banking; cellular therapy product collection, processing, and administration
<b>CBB Medical Director</b>	<ul style="list-style-type: none"> <li>• Licensed physician</li> <li>• Training in hematopoietic cell transplantation or blood or tissue banking</li> </ul>	<ul style="list-style-type: none"> <li>• Donor recruitment</li> <li>• Donor eligibility</li> <li>• Medical aspects of CB collection procedures, CB processing procedures, and review of the release and outcome data of the CB unit, including compliance with these Standards</li> </ul>	Donor safety; CB banking; cellular therapy product collection, processing, and administration
<b>CB Collection Director</b>	<ul style="list-style-type: none"> <li>• Health care professional</li> <li>• Bachelor's degree</li> <li>• Training and experience in hematopoietic cell transplantation, blood and tissue banking, or CB collection</li> </ul>	<ul style="list-style-type: none"> <li>• Collection activities</li> <li>• Communication with individual CB Collection Sites</li> </ul>	Donor safety; CB banking; cellular therapy product collection, processing, and administration
<b>CB Processing Facility Director</b>	<ul style="list-style-type: none"> <li>• Relevant doctoral degree</li> <li>• Qualified by training or experience for the scope of activities carried out in the CB Processing Facility</li> </ul>	<ul style="list-style-type: none"> <li>• 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</li> </ul>	CB banking; cellular therapy product collection, processing, and administration
<b>Quality Unit Manager<sup>2</sup></b>	<ul style="list-style-type: none"> <li>• Relevant training in quality management</li> </ul>	<ul style="list-style-type: none"> <li>• <u>Establish, maintain and ensure compliance with the Quality Management Program and Quality Management Plan.</u></li> <li>• Establish and maintain systems to review, modify as necessary, approve, and implement all policies and Standard Operating Procedures</li> <li>• Monitor performance of the Quality Management Program, the quality of the CB units, and compliance with these Standards</li> <li>• Release of CB units, as required by Applicable Law.<sup>3</sup></li> </ul>	Quality management; CB banking; cellular therapy product collection, processing, and administration

<sup>1</sup>If the CBB Director does not have specific training and expertise in HLA, the CBB shall confirm HLA expertise is available and utilized by the CBB.

~~2. The Quality Unit Manager shall be a different individual from the CBB Director, CBB Medical Director, CB Collection Director, and the CB Processing Facility Director.~~

~~3. The Quality Unit can override the release of a CB unit.~~



## APPENDIX II

### CORD BLOOD UNIT LABELING<sup>1</sup>

Applicable standard	B6.6.4	C7.6	B6.6.4 & D3.3	B6.6.4	B6.6.5	E5.3.6
Label Element	At completion of collection	Outer container labeling at transport or shipping from	Post processing prior to cryopreservation	At distribution from the CBB to Clinical Program	Partial label at distribution for administration <sup>7</sup>	Outer container labeling at distribution from the CBB to Clinical Program <sup>8</sup>
Unique numeric or alphanumeric identifier	AF		AF	AF	AF	
Proper name of product <sup>2</sup>	AF		AF	AF	AF	
Product Code <sup>2</sup>			AF	AF	AF	
Product attributes (manipulations) <sup>2</sup>			AC	AC	AC	
Statement Related Donor <sup>3</sup>	AF		AF	AF	AF	
Statement "Autologous Use Only" <sup>3</sup>				AF	AC	
Statement "Caution: New Drug – Limited by Federal (or United States) law to investigational use." <sup>6</sup>				AC	AC	
Statement "Rx Only" <sup>6</sup> ( <i>Rx = Prescription</i> )				AC	AC	
Collection site identifier	AC				AC	
Date of collection	AC		AC	AC	AC	
Time of collection and time zone, if different from the CB Processing Facility	AC				AC	
Name and volume or concentration of additives			AC	AC	AC	
Name and volume or concentration of anticoagulants	AF		AC	AC	AC	
Recommended storage temperature	AC		AF	AF	AC	
Donor name (Related CB units) <sup>3</sup>	AC		AT	AC	AC	
Recipient family or individual name and unique identifier, if known <sup>3</sup>	AC		AT	AC	AC	
Recipient's name and unique identifier				AC	AC	
Volume or weight of the CB unit at the end of collection			AC	AC	AC	
Volume or weight of the CB unit at the end of processing			AC	AC	AC	
Date of cryopreservation			AC	AC	AC	
ABO group and Rh type				AC	AC	
HLA phenotype				AC	AC	
Number of nucleated cells post processing			AC	AC	AC	
Gender of CB unit infant donor			AC	AC	AC	
Identity of the CBB <sup>4</sup>			AF	AF	AC	
Statement "Properly Identify Intended Recipient and Product"				AC	AC	
Statement "For Use By Intended Recipient Only" (Allogeneic CB units) <sup>3</sup>				AC	AC	
A statement indicating that leukoreduction filters should not be used				AC	AC	
Statement "Do Not Irradiate"				AC	AC	
Statement "For Nonclinical Use Only" <sup>3</sup>				AC	AC	
Biohazard legend and/or warning labels (see B6.6.3) <sup>3</sup>	AC		AC	AC	AC	
Donor eligibility summary. See Appendix III.				AC	AC	
Date and time of distribution				AC	AC	AF
Shipping facility name, address, phone number		AF				AF
Receiving facility name, address, phone number		AF				AF
Identity of person or position responsible for receipt of the shipment		AF				AF
Statement "Do Not X-Ray" <sup>5</sup>		AF				AF
Statements "Medical Specimen", "Handle With Care" <sup>5</sup> or equivalent as defined by Applicable Law		AF				AF
Statement indicating Cord Blood for Transplantation						AF
Conditions for exceptional release				AC		

Shipper handling instructions <sup>5</sup>		AF				AF
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<sup>1</sup>Additional requirements may apply for licensed products and in accordance with Applicable Law.

<sup>2</sup>Product proper names, attributes, and manipulations are listed in Chapter Three of the *ISBT 128 Standard Terminology for Blood, Cellular Therapy, and Tissue Product Descriptions*. Available: <http://www.iccbba.org/standardterminology.pdf>. This includes all potential attributes, in addition to the core attributes referenced in this table (Anticoagulant, Volume, Storage Temperature): Intended Use, Manipulation, Cryoprotectant, Blood Component from Third Party Donor, Preparation, Genetically Modified, Irradiation, Modification, Mobilization, Pooled Single, Cultured, Enrichment, and Reduction.

<sup>3</sup>If applicable.

<sup>4</sup>If there are CBBs of the same name in multiple countries, the identifier must distinguish between the CBBs on the label.

<sup>5</sup>If CB unit is shipped.

<sup>6</sup>If required by Applicable Law. (“Rx Only” means “Prescription Only”.)

<sup>7</sup>A partial label at distribution is a label that, because of the size of the CB unit or other constraints, does not contain all of the required information.

<sup>8</sup>See Standard E4.5 and E5.3.6.

AF=Affix, AT=Attach or Affix, AC=Accompany or Attach or Affix; a CBB 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.

ACCOMPANYING DOCUMENTS AT DISTRIBUTION

CB units collected in or designated for use in the U.S. shall be accompanied upon leaving the CBB with at least the elements detailed in the following table at a minimum as required by Applicable Law<sup>1</sup>:

Documentation	Allogeneic Donors-Eligible	Allogeneic Donor-Ineligible <sup>2</sup>	Allogeneic Donor-Incomplete <sup>2</sup>
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 determination <sup>3</sup>	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 testing performed	X	X	X
Statement that the communicable disease testing was performed by a laboratory meeting regulatory requirements <sup>4</sup>	X	If applicable	If applicable
Statement noting the reason(s) for the determination of ineligibility		X	
Statement that the donor-eligibility determination has not been completed			X
Statement that the CB unit must not be transplanted or infused until completion of the donor-eligibility determination, except under condition of urgent medical need			X
Listing of any required screening or testing that has not yet been completed			X
Results of donor screening that has been performed			X
Documentation that the physician using the CB unit was notified of incomplete testing or screening			X
Instructions for CB unit use to prevent the introduction, transmission, or spread of communicable diseases <sup>1</sup>	X	X	X
Instructions for reporting serious adverse reactions or events to the distributing facility <sup>1</sup>	X	X	X

<sup>1</sup>For autologous CB units, instructions for unit use to prevent the introduction, transmission, or spread of communicable diseases and for reporting serious adverse reactions or events to the distributing facility are always required for autologous products. Furthermore, a donor eligibility determination is not required by FDA. However, if any donor screening or testing is performed and risk factors or reactive test results are identified, accompanying documentation shall be provided.

<sup>2</sup>May only be distributed after release by the CBB Medical Director due to urgent medical need. For ineligible CB units or incomplete donor eligibility determination, the CB unit shall be shipped in quarantine. For units distributed prior to completion of donor eligibility, determination shall be completed if possible and the physician shall be informed of the results.

<sup>3</sup> Access (electronic or otherwise) to the source documents by the distributing facility or receiving facility is sufficient.

<sup>4</sup>This includes laboratories certified to perform such testing on human specimens under the Clinical Laboratory Improvement Amendments of 1988 or those laboratories that have met equivalent requirements as determined by the Centers for Medicare and Medicaid Services, or those that have met equivalent non-U.S. requirements.



APPENDIX IV

TESTING REQUIREMENTS

Test	CB Samples Obtained						Maternal Samples
	Pre-processing (end of collection)	Post-processing prior to cryo-preservation	Any time prior to cryo-preservation	On an appropriate sample type at any time prior to listing	Thawed contiguous segment or representative sample prior to release to the Clinical Program	On an appropriate sample type at any time prior to release	Obtained within seven (7) days before or after CB collection
<b>Cell Count</b>							
CBC with differential	X						
Total nucleated cell count		X			Should be performed		
Nucleated red blood cell count		X					
Total CD34		X					
Total Viable CD34		X			Should be performed		
<b>Viability</b>							
% Viability of Total nucleated cell count		X			X		
% Viability of CD34					X		
<b>HLA Tissue Typing</b>							
CFU or other validated potency assay		Should be performed_x			X		
<b>HLA Tissue Typing</b>							
Low Resolution: HLA-A, HLA-B, HLA-DRB1, HLA-C				X			
Low Resolution, HLA-C				Should be performed			
High Resolution: HLA-A, HLA-B, HLA-DRB1, HLA-C						X	
High Resolution, HLA-C						x	
Verification Typing					X <sup>2</sup>		
<b>Infectious Disease<sup>3</sup></b>							
HIV 1				X <sup>4</sup>			X
HIV 2				X <sup>4</sup>			X
Hepatitis B				X <sup>4</sup>			X
Hepatitis C				X <sup>4</sup>			X
HTLV I				X <sup>4,5</sup>			X <sup>5</sup>
HTLV II				X <sup>4,5</sup>			X <sup>5</sup>
Syphilis				X <sup>4</sup>			X
CMV				X <sup>4</sup>			X
Additional tests <sup>3</sup>				X <sup>4</sup>			X
<b>Other</b>							
Microbial culture		X					
ABO/Rh blood group			X				
Hemoglobinopathy						◆	



X – All CB units regardless of intended use.

◆ - CB units for unrelated use only.

<sup>1</sup>If post-processing testing was not performed historically, a potency assay must be performed prior to release for administration by the CBB.

<sup>2</sup>Verification of the HLA typing results can be performed at any resolution. A CBB may choose to perform this verification using the results of the high resolution HLA typing if that typing is performed on contiguous segments at the time of release to the Clinical Program. Verification typing shall be performed on a thawed segment or thawed representative sample.

<sup>3</sup>Appendix IV defines the minimum testing criteria for both cord blood and maternal blood samples. It is not possible to capture all regional variations in testing requirements. As such, additional tests for infectious transmissible agents may be required to be performed 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. West Nile Virus, Zika Virus, toxoplasma, CMV, EBV, *Trypanosoma cruzi* [Chagas disease]) and may include emergent disease testing.

<sup>4</sup>Each CB unit should be tested for evidence of infection for communicable disease agents using licensed, approved, or cleared 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 to test the original maternal sample. Testing specifications vary from country to country. This testing must be performed prior to release for administration when testing is required by Applicable Law or institutional policy.

<sup>5</sup>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.

## APPENDIX V

### SPECIFICATION REQUIREMENTS FOR CORD BLOOD UNITS STORED FOR CLINICAL ADMINISTRATION<sup>1</sup>

Test	Unrelated Specification		Related Specification	
	Post-Processing prior to cryopreservation Sample	Thawed contiguous segment or representative sample prior to release to the Clinical Program	Post-Processing prior to cryopreservation Sample	Thawed contiguous segment or representative sample prior to release to the Clinical Program
Total nucleated cell count	≥ 5.0 x 10 <sup>8</sup>		Enumerated	
Total nucleated cell recovery	Should be ≥60%		Should be ≥60%	
Viability of total nucleated cell count	≥ 85%		≥ 70%	
Viable CD34 count	≥ 1.25 x 10 <sup>6</sup>		<u>≥ 0.25% of acceptable value of TNC count</u>	
Viability of CD34 cells		≥ 70%		
CFU (or other validated potency assay) <sup>2</sup>		Growth (or positive result for potency)		Growth (or positive result for potency)
Microbial Screen	Negative for aerobes, anaerobes, fungus		Negative for aerobic and anaerobic bacteria and fungi – OR – identify and provide results of antibiotic sensitivities	
Donor screening and testing	Acceptable as defined by Applicable Law and NetCord-FACT Standards		Acceptable as defined by Applicable Law and NetCord-FACT Standards	
Identity		Verified		Verified

<sup>1</sup>Endpoints for hematopoietic reconstitution.

<sup>2</sup>There should be evidence of potency by CFU or other validated potency assay on a fresh post-processing sample.