
INTERNATIONAL STANDARDS FOR CORD BLOOD COLLECTION, PROCESSING, TESTING, BANKING, SELECTION, AND RELEASE



**Third Edition
December 2006**

NOTICE

These Standards are designed to provide minimum guidelines for facilities and individuals performing cord blood collection, processing, testing, banking, selection, and release, or providing support services for such procedures. These Standards are not intended to include all procedures and practices that a Cord Blood Bank or individual should implement if the standard of practice in the community or Applicable Law establishes additional requirements. Each Cord Blood Bank and its staff should analyze its practices and procedures to determine whether additional standards apply. The Foundation for the Accreditation of Cellular Therapy and NetCord disclaim any responsibility for setting maximum standards and expressly do not represent or warrant that compliance with these Standards is an exclusive means of complying with the standard of care in the industry or community.

COPYRIGHT © 2006
INTERNATIONAL NETCORD
FOUNDATION

COPYRIGHT © 2006
FOUNDATION FOR THE ACCREDITATION
OF CELLULAR THERAPY

TABLE OF CONTENTS

Page Number

INTRODUCTION	1
ACCREDITATION	2
TERMINOLOGY, ABBREVIATIONS, AND DEFINITIONS	3
Terminology	3
Abbreviations	3
Definitions	3
PART A: CORD BLOOD BANK QUALITY MANAGEMENT	14
A1 Definition of a Cord Blood Bank.....	14
A2 Quality Management Program.....	14
A3 Organizational Structure	15
A4 Personnel Requirements	16
A5 Documents and Records Requirements.....	16
A6 Monitoring, Quality Assessments, and Audits	18
A7 Errors, Accidents, Biological Product Deviations, Adverse Events, Variances, and Complaints	19
A8 Validation and Qualification Requirements.....	20
A9 Equipment, Supplies, and Reagents	20
A10 Inventory Management	21
A11 Process Control	22
A12 Identification, Labeling, and Product Tracking.....	23
A13 Outcome Analysis	23
A14 Facilities and Safety.....	23
A15 Infant Donor Eligibility Determinations.....	24
A16 Third Party Agreements	24
PART B: CORD BLOOD BANK OPERATIONAL STANDARDS	26
B1 Cord Blood Bank Personnel Requirements	26
B2 Policies and Standard Operating Procedures.....	27
B3 Cord Blood Bank Operations	29
B4 Equipment.....	31
B5 Supplies and Reagents.....	31
B6 Labeling.....	32
B7 Documents and Records Requirements.....	34
B8 Inventory Transfer.....	38
B9 Interruption of Operations at Established Sites	39

PART C: CORD BLOOD DONOR MANAGEMENT AND COLLECTION STANDARDS ..	42
C1 Cord Blood Collection Personnel Requirements	42
C2 Cord Blood Collection Facilities	42
C3 Policies and Standard Operating Procedures.....	44
C4 Maternal and Infant Donor Evaluation	44
C5 Informed Consent.....	46
C6 Cord Blood Collection Procedures.....	47
C7 Transportation of Non-Cryopreserved Cord Blood Units Between the Cord Blood Collection Facility and the Cord Blood Processing Facility	49
C8 Validation and Qualification Requirements.....	49
C9 Documents and Records Requirements.....	50
PART D: CORD BLOOD PROCESSING STANDARDS	52
D1 Cord Blood Bank Processing Facility Personnel Requirements.....	52
D2 Cord Blood Bank Processing Facility Requirements	52
D3 Policies and Standard Operating Procedures.....	53
D4 Validation and Qualification Requirements.....	53
D5 Identification and Labeling Requirements.....	54
D6 Equipment, Supplies, and Reagents Requirements	54
D7 Cord Blood Processing	54
D8 Reference Samples	55
D9 Cryopreservation.....	55
D10 Conditions for Storage	56
D11 Monitoring and Alarm Systems	57
D12 Inventory Management	58
D13 Disposal	58
D14 Quality Management Program	58
D15 CB Unit Assays	58
D16 Maternal Testing	60
D17 Documents and Records Requirements.....	61
PART E: CORD BLOOD SELECTION AND RELEASE STANDARDS	64
E1 Cord Blood Bank Facility Requirements	64
E2 General Requirements For Unrelated Allogeneic, Directed Allogeneic, and Autologous Cord Blood Units.....	64
E3 General Requirements For Unrelated Allogeneic and Directed Allogeneic Cord Blood Units.....	64
E4 Cord Blood Selection For Unrelated Allogeneic, Directed Allogeneic, and Autologous Cord Blood Transplantation	65
E5 Cord Blood Selection For Unrelated Allogeneic and Directed Allogeneic Cord Blood Transplantation	65

E6	Cord Blood Selection For Directed Allogeneic and Autologous Cord Blood Transplantation	65
E7	Cord Blood Unit Release	66
E8	Transportation of Cryopreserved Cord Blood Units.....	66
E9	Documents and Records Requirements.....	67
E10	Clinical Outcome Data	68
APPENDICES		69
	Appendix I Cord Blood Unit Labeling Table	71
	Appendix II Modified Circular of Information Biohazard and Warning Label Table.....	73
INDEX	75
CONTACT INFORMATION	79

This page left intentionally blank.

INTRODUCTION

This third edition of NetCord-FACT International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection, and Release is a collaborative effort between NetCord and Foundation for the Accreditation of Cellular Therapy. Founded in 1998, NetCord is the international cord blood banking arm of EuroCord, an international registry for the European Group for Blood and Marrow Transplantation (EBMT). The mission of NetCord is to promote high quality cord blood banking and clinical use of umbilical cord blood for allogeneic stem cell transplantation. Through its on-line virtual office, cord blood units from member banks are made available for unrelated donor transplantation. The Foundation for the Accreditation of Cellular Therapy (FACT) was founded in 1996 by its two parent organizations, the American Society for Blood and Marrow Transplant (ASBMT) and the International Society for Cellular Therapy (ISCT). FACT was formed to establish quality standards for hematopoietic progenitor cell collection, processing, and transplantation, and to implement a voluntary inspection and accreditation process for clinical transplant centers, blood and marrow collection centers and cellular therapy product processing facilities.

The first edition of NetCord-FACT International Standards for Cord Blood was published in 2000. Standards are developed by consensus, based on the best available evidence-based science to the greatest extent possible, placing emphasis on research on clinical outcomes of cord blood recipients. Cord blood banking is an emerging and evolving field. For those areas where there is little or no definitive data on clinical outcomes relating to a particular Standard, the FACT-NetCord Standards Committee has weighed the available evidence from preclinical studies and accepted scientific theory.

The major objective of these Standards is to promote quality medical and laboratory practices throughout all phases of cord blood banking to achieve consistent production of high quality placental and umbilical cord blood units for transplantation. These Standards cover 1) collection of cord blood cells, regardless of the methodology or site of collection; 2) screening, testing, and eligibility determination of the maternal and infant donor according to Applicable Law; 3) all phases of processing and storage, including quarantine, testing, and characterization of the unit; 4) making the CB unit available for transplantation, either directly or through listing with a search registry; 5) the search process for selection of specific cord blood units; and 6) all transport or shipment of cord blood units, whether fresh or cryopreserved. To be compliant with Standards, Cord Blood Banks must use validated methods, supplies, reagents, and equipment; maintain a comprehensive, properly documented Quality Management Program; and track the clinical outcomes of patients who receive cord blood units from that bank. Standards for the transplantation of cord blood cells, either allogeneic or autologous, are covered in the Clinical Section of the FACT-JACIE International Standards for Cellular Product Collection, Processing and Transplantation.

NetCord-FACT Standards apply to cord blood units intended for use in unrelated donor transplantation and to those units collected and stored for the directed use by a specific individual recipient or family member of the infant donor. Cord Blood Banks are not required to have a specific structure and may contract services for their operations; however, to be eligible for accreditation, each bank must have processes in place to meet all NetCord-FACT International Standards. These Standards place significant responsibility on the Cord Blood Bank Director and Medical Director for implementation of systems and processes that result in high quality cord blood units.

NetCord and FACT recognize the significant benefits of international standardization of coding and labeling in cellular therapy, and support the international efforts to implement *ISBT 128*, the international information standard for transfusion and transplantation. The product definitions and modifications defined in this edition of NetCord-FACT International Standards are consistent with the currently proposed definitions and product modifications in the *ISBT 128* Standard. NetCord-FACT International Standards require the use of this terminology as applicable. Cord Blood Banks utilizing bar codes should register with ICCBBA, Inc., the organization charged with the international maintenance of this database, to obtain the necessary documents and databases. If

the final approved product names in the *ISBT 128* Standard differ from those currently proposed, the NetCord-FACT definitions and product names will be revised to match those in the *ISBT 128* Standard.

These Standards are effective March 15, 2007. All accredited Cord Blood Banks are expected to be in compliance with these Standards by that date.

ACCREDITATION

The basis for FACT-NetCord accreditation is documented compliance with the current edition of NetCord-FACT Standards. FACT-NetCord will not accredit banks wishing to comply with only a subset of the Standards, nor is there a category for FACT-NetCord affiliation.

The accreditation process includes submission of written documents and an on-site inspection of collection, processing, and storage facilities. Depending on the number of collection facilities associated with the Bank, all or a percentage of the collection sites will be visited. The inspection team includes at least three inspectors and may also include translators for international cord blood banks where English is not the primary language. The FACT-NetCord inspectorate consists of highly experienced individuals with a strong and vested interest in securing the highest quality cord blood units for transplantations and includes transplant physicians, cord blood bank directors, and cord blood bank laboratory directors. All inspectors must complete an inspector training course and participate in at least one inspection as a trainee inspector. Inspectors must be affiliated with a FACT or FACT-NetCord accredited or applicant facility and must be a member of ASBMT, ISCT, EBMT, Euro-ISCT, or NetCord.

FACT-NetCord accredited Cord Blood Banks will be reinspected routinely every three years, or in response to complaints or information that a bank or facility may be non-compliant with the Standards, or as determined by the FACT and/or NetCord Board of Directors. Accreditation may be suspended or terminated if a facility fails to comply with the Standards.

TERMINOLOGY, ABBREVIATIONS, AND DEFINITIONS

TERMINOLOGY

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

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
<i>ASHI</i>	American Society for Histocompatibility and Immunogenetics
<i>AT</i>	Attach
$^{\circ}\text{C}$	Degree Celsius
<i>CB</i>	Cord blood
<i>CBB</i>	Cord Blood Bank
<i>CB unit</i>	Cord blood unit
<i>CFU</i>	Colony forming unit
<i>DNA</i>	Deoxyribonucleic acid
<i>EFI</i>	European Federation for Immunogenetics
<i>FACT</i>	Foundation for the Accreditation of Cellular Therapy
<i>FDA</i>	United States Food and Drug Administration
<i>GVHD</i>	Graft-versus-host disease
<i>HLA</i>	Human Leukocyte Antigen
<i>HPC</i>	Hematopoietic Progenitor Cells
<i>LN₂</i>	Liquid nitrogen
μg	Microgram
<i>mL</i>	Milliliter
<i>QM</i>	Quality Management
<i>Rh</i>	Human erythrocyte antigen, Rhesus
<i>USDA</i>	United States Department of Agriculture

DEFINITIONS

The following terms are used in this document with the following definitions:

Accompany (AC): To go or be together with, but not attached. Information that must accompany the cord blood unit in a sealed package may alternatively be attached or affixed.

Adventitious agent: Any extraneous microbiological, chemical, or radiobiological substance introduced into the cord blood unit during collection, processing, or transplantation.

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 cellular therapy product for which there is a reasonable possibility that the cellular therapy product caused the response.

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

Allogeneic: Cord blood unit obtained from an infant donor and intended for infusion into a genetically distinct recipient.

Unrelated allogeneic: Cord blood unit obtained from one infant donor and intended for transplantation into another individual who is not genetically related to the infant donor.

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

Applicable Law: Any statute, regulation, or other governmental standard or specification that is applicable to cord blood collection, processing, testing, banking, or release in the jurisdiction in which the Cord Blood Bank, Collection Facility, or Processing Facility is located.

Aseptic technique: Practices designed to reduce the risk of microbial contamination of products, reagents, specimens, patients, 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 procedures have been properly implemented and are being followed.

Autologous: Cord blood unit obtained from an infant donor and intended for infusion back into the same individual.

Available for distribution: The point at which the cellular therapy product has been determined to meet all release criteria.

Biohazard legend: The universal biohazard symbol.

Biological product deviation: A deviation from Applicable Law, standards, or other established specifications that relate to the prevention of communicable disease transmission or cellular therapy product contamination; or an unexpected or unforeseeable event that may relate to the transmission or potential transmission of a communicable disease or may lead to cellular therapy product contamination.

Calibrate: To set measurement equipment against a known standard.

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

CD34: The 115 kD glycoprotein antigen, expressed by 1-2% of normal bone marrow mononuclear cells, that is defined by a specific monoclonal antibody (anti-CD34) using the standardized cluster of differentiation (CD) terminology.

Colony forming unit (CFU): A clonogenic cell able to produce 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 harvesting cellular therapy products, including labeling, regardless of technique or source.

Collection Facility: The site where the infant donor is delivered and the cord blood unit is collected.

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

Non-fixed Collection Site: A collection site without an ongoing documented agreement with a Cord Blood Bank where one or more cord blood units may be collected at the initiation of the donor's mother and/or family and with documentation that a licensed medical professional has agreed to perform the collection and has training that covers each aspect of the collection process.

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 cellular therapy product or with a service related to the collection, processing, storage, distribution, or infusion of a cellular therapy product.

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

Cord blood (CB): The whole blood, including HPC, collected from placental and/or umbilical cord blood vessels after the umbilical cord has been clamped.

Cord Blood Bank (CBB): An integrated team under a single CBB Director responsible for the collection, processing, testing, banking, selection, and release of cord blood units.

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

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

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

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

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

Designee: An individual with appropriate experience or expertise who is given the authority to assume a specific responsibility.

Director: For purposes of these Standards includes individuals with the following qualifications:

CBB Director: An individual with an earned doctoral degree in medicine or in a related scientific field, with training in immunogenetics of transplantation, basic or clinical immunology, immunohematology, basic or clinical hematology, transfusion medicine, blood or tissue banking, or cryobiology. The CBB Director has final responsibility for the CBB scientific and clinical performance and its overall compliance with these Standards including all components of the CBB's policies and Standard Operating Procedures. The CBB Director shall participate regularly in educational activities related to the field of cord blood banking and/or hematopoietic progenitor cell collection, processing, and transplantation.

CBB Medical Director: A licensed physician with training in hematopoietic cell transplantation or blood, and tissue banking. This individual is responsible for donor recruitment, eligibility and selection, the medical aspects of the collection procedures and of the CBB Processing Facilities, and compliance of the Collection and Processing Facilities with these Standards. The CBB Medical Director shall participate regularly in educational activities related to the field of donor safety, cord blood banking, and/or hematopoietic progenitor cell collection, processing, and transplantation. The CBB Medical Director may also serve as the CBB Director, CBB Collection Facility Medical Director, and/or CBB Processing Facility Director, if appropriately credentialed.

CBB Collection Facility Medical Director: A licensed physician who is responsible for the medical aspects of cord blood collection procedures and compliance of the Cord Blood Collection Facility with these Standards. The CBB Collection Facility Medical Director shall participate regularly in educational activities related to the field of donor safety, cord blood banking and/or hematopoietic progenitor cell collection, processing, and transplantation. The CBB Medical Director may serve the function of the remote site Collection Facility Medical Director and need not be licensed in the jurisdiction of the collection or be on the staff of the Collection Facility.

CBB Processing Facility Director: An individual with a relevant doctoral degree, qualified by training or experience for the scope of activities carried out in the Cord Blood Bank Processing Facility. The CBB Processing Facility Director is responsible for all operational aspects of all procedures related to receipt, testing, processing, cryopreservation, storage, release for shipment of cord blood units, and administrative operations of the CBB Processing Facility, including compliance with these Standards. The CBB Processing Facility Director shall participate regularly in educational activities related to the field of cord blood banking and/or hematopoietic progenitor cell collection, processing, and transplantation.

Distribution: Any conveyance or shipment (including importation and exportation) of a cellular therapy product that has been determined to meet all release criteria.

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

Electronic record: Any record or document consisting of any combination of text, graphics, or other data that is created, stored, modified, or transmitted in digital form by a computer.

Eligible: An infant donor and/or mother who meet all donor screening and testing requirements related to transmission of communicable disease as defined in Applicable Law by the U.S. FDA or non-U.S. equivalent agency in the jurisdiction in which the Cord Blood Bank is located.

Engraftment: The reconstitution of recipient hematopoiesis with blood cells and platelets from a donor.

Errors and accidents: Any unforeseen or unexpected deviations from Applicable Law, or other established Standards or 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.

Facility: A location where activities covered by these Standards are performed. Such activities include determination of donor eligibility or suitability, product collection, processing, storage, selection and release.

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

HPC, Cord Blood: Hematopoietic progenitor cells obtained from the umbilical cord and/or placenta at the time of delivery. HPC, Cord Blood is the proper name of a cord blood unit. *ISBT 128* official product nomenclature will be adopted when finalized.

Identifier: A numeric or alphanumeric sequence used to designate a cord blood unit.

Ineligible: An infant donor and/or mother who does not meet all donor screening and testing requirements related to transmission of communicable disease as defined in Applicable Law by the U.S. FDA or non-U.S. equivalent agency in the jurisdiction in which the Cord Blood Bank is located.

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

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

Institutional Review Board or Ethics Committee: A Board or Committee established by an institution in accordance with the regulations of the United States Department of Health and Human Services, or other governmental agency where applicable, to review biomedical and behavioral research involving human subjects conducted at or supported by that institution.

ISBT 128: The international information technology standard for transfusion medicine and transplantation.

Labeling: Steps taken to identify the original cord blood unit collection and any products or product modifications; to complete the required reviews; and to attach the appropriate labels.

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

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

Minimally manipulated: Processing that does not alter the relevant biological characteristics of cells or tissues.

More than minimally manipulated: Processing that does alter the relevant biological characteristics of cells or tissues.

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

Mother: Any of the following:

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

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

Surrogate mother: The woman who carries an infant donor not genetically hers, from an egg (ovum) to delivery. Under circumstances of a surrogate mother carrying the infant donor to term and the cord blood unit being collected, both the surrogate and the genetic mother shall be considered for purposes of communicable disease screening and testing; the genetic mother shall be considered for purposes of genetic information.

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

Negative selection: The manipulation of cord blood such that a specific cell population(s) is depleted.

NetCord: The international organization of cord blood banks that meet defined membership requirements of the International NetCord Foundation.

Nonconforming cord blood (CB) unit: Any cord blood unit that does not completely meet the requirements specified by these Standards, the CBB, and/or the requirements for the donor eligibility as defined in Applicable Law.

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

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

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

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

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

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

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

Processing: All aspects of manipulation, cryopreservation, packaging, and labeling cellular therapy products regardless of source, including microbial testing, preparation for storage, and removal from storage. Processing does not include collection, donor screening, donor testing, storage, or distribution.

Processing Facility: The location where cord blood processing activities are performed in support of the Cord Blood Bank. A 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.

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.

Product modifications:

B-Cell-Reduced: Cells processed by negative selection for B lymphocytes.

Buffy Coat Enriched: Cells remaining after removal of a portion of the mature erythrocytes and plasma by centrifugation and/or sedimentation using devices, supplies, and techniques validated for the procedure(s).

CD34-Enriched: Cells processed by positive selection for CD34-antigen bearing cells.

Cryopreserved: Cells frozen using devices, supplies, and techniques validated to maintain viability.

Density Enriched: Cells remaining after depletion of mature erythrocytes, polymorphonuclear leukocytes, and plasma by techniques using defined density gradient medium and devices or reagents validated for the separation of cells based on density.

Ex Vivo Expanded: Cells that have been cultured *in vitro* for the purpose of producing and/or enriching for a specific functional subset.

Gene-Manipulated: Cells that have been processed to alter their own genes or introduce new genetic material.

Plasma and RBC Reduced: Cells remaining after removal of a portion of the mature erythrocytes and plasma by sedimentation and/or centrifugation using devices, supplies, and techniques validated for the process.

Plasma Reduced: Cells remaining after removal of a portion of the plasma by sedimentation or centrifugation using devices, supplies and techniques validated for the procedure(s).

RBC Reduced: Cells remaining after removal of a portion of the mature erythrocytes by sedimentation, centrifugation, or lysis using devices, supplies, and techniques validated for the procedure(s).

T-Cell-Depleted: Cells processed by negative selection for T lymphocytes.

Proficiency test: A test to ensure 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 processes, equipment, and reagents function consistently within established limits.

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

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

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

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

Quality control: 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 cellular therapy products, including testing and product release.

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

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

Quality Management Supervisor: A qualified individual approved by the Cord Blood Bank Director, to establish methods to review, modify, approve, and implement all Standard Operating Procedures related to Quality Management and to monitor compliance with these Standards.

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

Quality Management Program: An organization's comprehensive system of quality assessment, audit, 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.

Quarantine: The identification or storage of a cord blood unit in a physically separate area clearly identified for such use, or through use of other procedures such as automated designation to prevent improper release of that product. Also refers to segregated storage of products known to contain communicable disease agents to reduce the likelihood of cross-contamination.

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

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

Registry: The organization that publishes or makes available the description of cord blood units available for transplantation and may conduct searches of the cord blood units available, 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 for distribution.

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

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

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

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

Significant warming event: Any event when the cord blood unit reaches -120° C or warmer during the life of the cryopreserved cord blood unit.

Standard Operating Procedure: Written detailed instructions required to perform a procedure.

Standard Operating Procedures Manual: A compilation of the current Standard Operating Procedures.

Standards: The current edition of the *International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection, and Release* published by NetCord and FACT.

Sterility Testing: For the purposes of these Standards, the processes used to screen for the presence of microbials.

Storage: Holding cellular therapy products for future processing and/or distribution.

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

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

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

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

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 so that it will not be used for another purpose.

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 cellular therapy product.

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

Variance: A planned deviation from recommended practice or standard operating procedure.

Verification: The confirmation of the accuracy of something or that specified characteristics have been fulfilled.

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

This page left intentionally blank.

PART A: CORD BLOOD BANK QUALITY MANAGEMENT

A1	Definition of a Cord Blood Bank.....	14
A2	Quality Management Program.....	14
A3	Organizational Structure.....	15
A4	Personnel Requirements.....	16
A5	Documents and Records Requirements.....	16
A6	Monitoring, Quality Assessments, and Audits.....	18
A7	Errors, Accidents, Biological Product Deviations, Adverse Events, Variances, and Complaints.....	19
A8	Validation and Qualification Requirements.....	20
A9	Equipment, Supplies, and Reagents.....	20
A10	Inventory Management.....	21
A11	Process Control.....	22
A12	Identification, Labeling, and Product Tracking.....	23
A13	Outcome Analysis.....	23
A14	Facilities and Safety.....	23
A15	Infant Donor Eligibility Determinations.....	24
A16	Third Party Agreements.....	24

PART A: CORD BLOOD BANK QUALITY MANAGEMENT

A1 DEFINITION OF A CORD BLOOD BANK

- A1.1 The Cord Blood Bank (CBB) consists of an integrated team, under a single CBB Director, responsible for the collection, processing, testing, banking, selection, and release of cord blood units (CB units).
- A1.2 The CBB, each Collection Facility, and each Processing Facility shall operate in compliance with Applicable Law, local and national licensing and registration requirements, and these Standards.

A2 QUALITY MANAGEMENT PROGRAM

- A2.1 The CBB shall establish and maintain a Quality Management Program that shall cover all aspects of infant donor and maternal screening and testing, cord blood collection, processing, cord blood testing, banking, making CB units available for search, selection, release, and outcome analysis.
- A2.2 There shall be a Quality Management (QM) Supervisor approved by the CBB Director, to establish and maintain systems to review, modify as necessary, approve, and implement all Standard Operating Procedures related to Quality Management and to monitor compliance with these Standards.
 - A2.2.1 The QM Supervisor shall be a different individual from the CBB Director, CBB Medical Director, or the CBB Processing Facility Director.
 - A2.2.2 The QM Supervisor shall report on the performance of the QM Program, at a minimum, on an annual basis.
 - A2.2.3 The QM Supervisor shall not have oversight of his/her own work if this person also performs other tasks in the CBB.
 - A2.2.4 The QM Supervisor shall participate regularly in educational activities related to the field of quality management, CB banking, and/or hematopoietic cell transplantation.
- A2.3 The CBB shall maintain a written QM Plan that describes the QM Program, including at a minimum:
 - A2.3.1 Organizational structure.
 - A2.3.2 Personnel requirements, qualifications, training, and competency.
 - A2.3.3 Documents and records.
 - A2.3.3.1 Policy and procedure development, implementation, and review.
 - A2.3.3.2 Records creation, review, control, and maintenance.
 - A2.3.4 Monitoring, quality assessments, and audits.
 - A2.3.5 Detection, investigation, reporting, corrective action, and follow-up of errors, accidents, biological product deviations, adverse events, and complaints .
 - A2.3.6 Equipment, supplies, and reagents.

- A2.3.6.1 Validation and qualification.
- A2.3.6.2 Calibration and maintenance.
- A2.3.6.3 Vendor qualification.
- A2.3.7 Inventory control.
 - A2.3.7.1 Materials, supplies, and reagents.
 - A2.3.7.2 CB units, reference CB unit samples, maternal samples, and records.
- A2.3.8 Process control.
 - A2.3.8.1 Product specifications.
 - A2.3.8.2 Nonconforming products.
- A2.3.9 Identification, labeling, and product tracking.
 - A2.3.9.1 Labeling process.
- A2.3.10 Outcome analysis.
- A2.3.11 Facilities and safety.
- A2.3.12 Donor eligibility determinations.
- A2.3.13 Agreements with third parties.

A3 ORGANIZATIONAL STRUCTURE

- A3.1 The QM Plan shall include an organizational chart of all participating facilities and services including, at least, Collection Facilities, Processing Facilities, and testing laboratories.
 - A3.1.1 A CBB that includes multiple Collection Facilities shall employ coordinated policies and Standard Operating Procedures, protocols, staff training and competency evaluation procedures, and quality assessment systems; and shall demonstrate evidence of regular interaction between these Collection Facilities and the CBB.
- A3.2 The QM Plan shall include an organizational chart of key personnel and functions within the CBB, the Processing Facility, and the Collection Facilities.
 - A3.2.1 The key personnel shall include at least the following:
 - A3.2.1.1 CBB Director.
 - A3.2.1.2 CBB Medical Director.
 - A3.2.1.3 CBB Collection Facility Medical Director(s) and/or the designated individual at each Collection Facility, not staffed by the CBB personnel, who is responsible for the daily operation of the Collection Facility and communication with the CBB Medical Director.

A3.2.1.4 CBB Processing Facility Director.

A3.2.1.5 QM Supervisor.

A4 PERSONNEL REQUIREMENTS

A4.1 The QM Plan shall include personnel requirements for each position in the CBB. Personnel requirements shall include at least:

A4.1.1 Current position description for each staff.

A4.1.2 A system to document for each staff member:

A4.1.2.1 Initial qualifications.

A4.1.2.2 Initial training.

A4.1.2.3 Competency for each function performed.

A4.1.2.4 Continued competency at least annually.

A4.1.2.5 Continued education, training, and retraining.

A4.2 The QM Plan shall include a system to ensure consistent training programs.

A5 DOCUMENTS AND RECORDS REQUIREMENTS

A5.1 The QM Plan shall include a system to maintain confidentiality of infant donor, mother, and recipient; of all records and communications among the Collection Facilities, Processing Facilities, CBB, Registry, and/or Clinical Transplant Program; and of staff and employee records.

A5.2 The QM Plan shall contain a system to ensure uniformity of the Standard Operating Procedures and related forms.

A5.2.1 There shall be a documented process for the development, approval, implementation, review, revision, archival, storage, retention, and retrieval of policies, Standard Operating Procedures, protocols, forms, CB unit and sample labels, educational and promotional materials, and other documents.

A5.2.2 Records of archived Standard Operating Procedures, protocols, and labels, in their historical sequence including inclusive dates of use, shall be maintained indefinitely.

A5.3 The QM Plan shall include a process for regular review of records including, but not limited to, collection, processing, storage, and transportation of CB units.

A5.4 The QM Plan shall include a process for the regular assessment of record review to identify recurring problems, potential points of failure, or need for process improvement.

A5.5 The QM Plan shall include a process for the comprehensive review of product records prior to making a CB unit available for search, including at least:

A5.5.1 CB unit total nucleated cell count.

A5.5.2 CB unit nucleated red blood cell count.

- A5.5.3 CB unit total number of CD34-positive cells.
- A5.5.4 CFU total number and/or CB unit viability.
- A5.5.5 CB unit ABO group and Rh type.
- A5.5.6 Microbial cultures of the CB unit obtained after processing.
- A5.5.7 For unrelated allogeneic CB units, HLA type.
- A5.5.8 Infant donor's ethnicity.
- A5.5.9 Infant donor's gender.
- A5.5.10 Maternal risk factors for transmission of communicable disease.
- A5.5.11 Maternal communicable disease testing results.
- A5.5.12 Family medical history for transmissible genetic diseases.
- A5.5.13 Consents.
- A5.5.14 Processing and cryopreservation parameters as defined in the Standard Operating Procedures:
 - A5.5.14.1 Total nucleated cell concentration within defined range.
 - A5.5.14.2 Hematocrit within defined range.
 - A5.5.14.3 The cryoprotectant, its final concentration, and the duration of cell exposure prior to freezing.
 - A5.5.14.4 Method of freezing and end-point temperature of cooling.
 - A5.5.14.5 Cooling rate and a freezing curve within defined range.
 - A5.5.14.6 Storage temperature.
- A5.6 The QM Plan shall include a process for comprehensive product review prior to release of a CB unit from inventory for transplantation and for documentation of this review in accordance with Applicable Law.
- A5.7 The QM Plan shall include a process for retention of records as required by Section B7 of these Standards.
- A5.8 The QM Plan shall include policies and Standard Operating Procedures to support management of electronic record systems and electronic records, to maintain pertinent electronic records, and to ensure continuous operations in the event that the electronic record system ceases to function, including a plan for data backup and to ensure compliance with Applicable Law.
- A5.9 The QM Plan shall include policies and procedures to ensure that the records of each facility involved in the collection, processing, testing, storage, transportation, search, or transplantation of the CB unit shall show plainly the identity of each facility and the extent of its responsibility.

A6 MONITORING, QUALITY ASSESSMENTS, AND AUDITS

- A6.1 The QM Plan shall include a process for assessing the CBB functions at predefined intervals, at a minimum, on an annual basis.
 - A6.1.1 The results of ongoing monitoring shall be documented, reviewed, and trends shall be analyzed on a regular basis.
 - A6.1.2 Corrective action shall be implemented and documented as indicated. Corrective action shall include both short-term action to address the immediate problem and long-term action to prevent the problem from recurring. Section A7.2 also applies.
 - A6.1.3 Opportunities for quality improvement shall be identified, reviewed, implemented as appropriate, and documented.
- A6.2 The QM Plan shall include a process for conducting independent internal quality audits of significant CBB activities to verify compliance with elements of the QM Program under review.
 - A6.2.1 Quality audits shall include aspects of all CBB functions, including at least:
 - A6.2.1.1 Maternal screening and testing.
 - A6.2.1.2 Infant donor eligibility determinations.
 - A6.2.1.3 CB unit collection.
 - A6.2.1.4 CB unit transportation.
 - A6.2.1.5 CB unit processing.
 - A6.2.1.6 CB unit labeling.
 - A6.2.1.7 CB unit storage.
 - A6.2.1.8 CB unit release from quarantine to long term storage and/or listing.
 - A6.2.1.9 CB unit release for transplantation.
 - A6.2.1.10 CB unit records.
 - A6.2.1.11 CB unit disposition. Sections D13 and E10 also apply.
 - A6.2.2 Quality audits shall be conducted by an individual with sufficient expertise to identify problems, but who is not directly responsible for the process being audited.
 - A6.2.3 The results of audits shall be used to recognize problems, detect trends, and identify improvement opportunities.
 - A6.2.4 Collection and analysis of data related to the audit shall be reviewed, reported, and documented, at a minimum, on an annual basis.
- A6.3 The QM Plan shall include a written procedure for the management of external audits and inspections.

- A7 ERRORS, ACCIDENTS, BIOLOGICAL PRODUCT DEVIATIONS, ADVERSE EVENTS, VARIANCES, AND COMPLAINTS
- A7.1 The QM Plan shall include procedures for monitoring, detecting, documenting, evaluating, and reporting errors, accidents, biological product deviations, adverse events, variances, and complaints. These shall be evaluated by the appropriate Director and/or Medical Director together with staff involved in the QM Program and other appropriate staff.
- A7.1.1 The QM Program shall review all occurrences and trend the errors, accidents, adverse events, and variances related to:
- A7.1.1.1 Collection.
 - A7.1.1.2 Transportation.
 - A7.1.1.3 Processing.
 - A7.1.1.4 Cryopreservation.
 - A7.1.1.5 Storage.
 - A7.1.1.6 Thawing.
- A7.1.2 Biological product deviations and variances shall be categorized to identify system problems and initiate corrective action.
- A7.2 Corrective actions shall be implemented as appropriate. Documentation shall be maintained and shall include:
- A7.2.1 The nature of the problem requiring corrective action.
 - A7.2.2 The identity and disposition of the affected CB unit.
 - A7.2.3 The dates of corrective action, including a designated time at which the outcome of the corrective action shall be evaluated.
 - A7.2.4 The initiation of retraining and/or re-education of employees, as appropriate.
 - A7.2.5 Performing reaudits of deficiencies, as necessary.
- A7.3 The QM Plan shall include a process to maintain records of all severe or unexpected adverse events or reactions during transplantation and engraftment.
- A7.4 A thorough investigation of all reported severe or unexpected adverse events or reactions shall be made by the CBB in collaboration with the Collection Facility, Processing Facility, Registry and/or Clinical Transplant Program, as appropriate. A written report of the investigation including conclusions, follow-up, and corrective action, if applicable, shall be:
- A7.4.1 Prepared and maintained as part of the record for that final CB unit.
 - A7.4.2 Maintained in the CB adverse event aggregate file.
 - A7.4.3 Utilized in quality monitoring and analysis of trends.

- A7.4.4 When it is determined that the CB unit was responsible for the adverse reaction, results of the investigation shall be shared with the Clinical Transplant Program and/or other appropriate organization(s) involved.
- A7.5 The QM Plan shall include a process for the review, evaluation, and documentation of complaints.
 - A7.5.1 Each complaint shall be evaluated to determine if the complaint is related to a product deviation or adverse reaction. Corrective action shall be initiated when appropriate.
 - A7.5.2 A complaint file shall be maintained.
- A7.6 Errors, accidents, biological product deviations, variances, adverse events, and complaints shall be reported to other Facilities performing CBB functions on the affected CB unit and to the appropriate regulatory agencies.
- A7.7 The QM Plan shall include a process for the assessment of functions of the electronic record keeping system, if applicable, to ensure that errors and problems are reported and resolved.
- A8 VALIDATION AND QUALIFICATION REQUIREMENTS
 - A8.1 Procedures shall be developed, implemented, and documented for the validation or qualification of significant aspects of the CBB functions.
 - A8.2 Determination of which elements of collection, transportation, testing, processing, cryopreservation, storage, and thawing are to be validated or qualified shall be made by the CBB Director or CBB Medical Director in collaboration with representatives of the QM Program.
 - A8.3 Validation studies shall be reviewed and approved by the CBB Director or designee from the QM Program.
 - A8.4 Records shall be maintained to document that procedures have been validated to achieve the expected end-points, including viability of CB cells and product integrity.
- A9 EQUIPMENT, SUPPLIES, AND REAGENTS
 - A9.1 The QM Plan shall include the following procedures for equipment used in collection, processing, or storage of CB units:
 - A9.1.1 All equipment shall be identified and records maintained, including manufacturer's name, serial number or other identifier, manufacturer's instructions, equipment location, and use of each piece of equipment, including the identification of each CB unit for which the equipment was used.
 - A9.1.2 Calibration.
 - A9.1.2.1 Equipment shall be observed, tested, and calibrated on a regularly scheduled basis as recommended by the manufacturer or, at a minimum, annually.
 - A9.1.2.2 Calibration acceptance criteria shall be defined.
 - A9.1.2.3 Records of the dates and copies of calibration results shall be maintained.

A9.1.3 Maintenance and repairs.

A9.1.3.1 Equipment shall be maintained in a clean and orderly manner and located so as to facilitate cleaning and maintenance according to established schedules.

A9.1.3.2 Records shall be maintained of the maintenance schedule, maintenance performed, and damage, malfunction, modification, or repair to equipment.

A9.1.4 Cleaning and sanitation.

A9.1.4.1 Equipment shall be cleaned and sanitized according to established schedules.

A9.1.4.2 Records of equipment cleaning and sanitation shall be maintained.

A9.1.5 Inspections.

A9.1.5.1 Equipment shall be routinely inspected for cleanliness, sanitation, and calibration and to ensure adherence to applicable equipment maintenance schedules.

A9.1.6 Display Records.

A9.1.6.1 Records of recent maintenance, cleaning, sanitizing, calibration, and other activities shall be displayed on or near each piece of equipment.

A9.2 The QM Plan shall include procedures to address management of critical supplies and reagents used in the collection, processing, and/or storage of CB units:

A9.2.1 Critical reagents and supplies shall be verified to function as expected and to meet specifications designed to prevent the spread of communicable disease.

A9.2.2 Approved suppliers for all critical reagents and supplies shall be identified and utilized.

A9.2.3 Records of the receipt, inspection, verification, acceptance, and storage of supplies and reagents shall be maintained.

A9.3 Quality control procedures shall be developed to monitor the continuing adequacy of the procedures, reagents, equipment, and supplies as used under routine operating conditions by the CBB personnel.

A10 INVENTORY MANAGEMENT

A10.1 The QM Plan shall include a process for inventory management that encompasses all materials, supplies, reagents, and labels.

A10.2 The QM Plan shall include an inventory management system for CB units that ensures each CB unit, its associated reference samples, maternal samples, and records can be located in a timely way.

- A10.2.1 The inventory management system shall be designed to prevent mix-ups, contamination of the CB units during storage, and the improper release of quarantined CB units.
- A10.2.2 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.
- A10.3 The QM Plan shall include policies related to the return of CB units to the CBB inventory.
 - A10.3.1 Unrelated allogeneic CB units shall not be returned to the CBB inventory after they have left the CBB premises.
 - A10.3.2 Directed allogeneic and autologous CB units may be returned to the CBB inventory with documentation of appropriate storage and transportation.
- A10.4 The QM Plan shall include processes for ensuring CB units are properly stored. Section D10 also applies.

A11 PROCESS CONTROL

- A11.1 The QM Plan shall include a process for controlling and monitoring the collection, processing, and storage of CB units to ensure that the products conform to specifications, are not contaminated or cross-contaminated, and maintain function and integrity.
 - A11.1.1 Donor eligibility requirements that meet Applicable Law shall be defined, implemented, and documented to include maternal health history screening, maternal testing, and CB unit testing.
 - A11.1.2 CB units from two (2) or more infant donors shall not be placed in physical contact or mixed in a single container.
 - A11.1.3 There shall be documentation and/or justification for any variance from Standard Operating Procedures.
 - A11.1.4 Any change to a Standard Operating Procedure shall be verified or validated, approved by the CBB Director, CBB Medical Director or designee before implementation, and be communicated to appropriate personnel.
- A11.2 There shall be a mechanism to identify, review, segregate if indicated, and document nonconforming CB units that do not fully meet these Standards, CBB requirements, and/or requirements for donor eligibility as defined by Applicable Law.
 - A11.2.1 The CBB shall maintain a record of nonconforming CB units that are banked and/or released.
 - A11.2.1.1 The nature of the nonconformity shall be communicated to the Clinical Transplant Program, either directly or through the Registry, at the time of initial consideration of the CB unit for clinical use.

A12 IDENTIFICATION, LABELING, AND PRODUCT TRACKING

A12.1 The QM Plan shall include processes to ensure that each CB unit is assigned a unique numeric or alphanumeric identifier by which it will be possible to link that 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.

A12.1.1 There shall be processes to ensure that the CB unit identifier is unique to prevent errors in identification.

A12.2 The QM Plan shall include processes to ensure that operations are conducted in a manner adequate to prevent mislabeling of CB units, reference samples, and associated documents.

A12.2.1 There shall be processes to verify that all labels in use are accurate, legible, and maintain physical integrity.

A12.2.2 There shall be processes to ensure the content of each label is compliant with Applicable Law and the requirements of these Standards.

A12.3 The QM Plan shall include processes for product tracking that allow tracking of the CB unit from the infant donor to the recipient or final distribution.

A12.3.1 Linkage of the CB unit to the infant donor and mother shall be retained indefinitely.

A13 OUTCOME ANALYSIS

A13.1 The QM Plan shall include processes to maintain and evaluate details of clinical outcome as necessary to ensure that the procedures in use in the CBB continuously provide a safe and effective product.

A14 FACILITIES AND SAFETY

A14.1 The QM Plan shall include processes to ensure safe, sanitary, and adequate environmental workplace conditions.

A14.1.1 The CBB space shall be of adequate size, construction, and location to maintain safe operations, prevent contamination, and ensure orderly handling.

A14.1.2 Environmental conditions for temperature, humidity, ventilation, and air filtration and classification shall be defined and, if appropriate, monitored.

A14.1.3 Separate areas shall be maintained for processing and storage of products to prevent mix-ups, product contamination, and cross-contamination.

A14.1.4 The CBB shall be secure to prevent the admittance of unauthorized individuals.

A14.1.5 Dedicated CBB Facilities shall be maintained in a clean, sanitary, and orderly manner to prevent introduction, transmission, or spread of communicable disease, and to facilitate operations and cleaning.

A14.2 There shall be procedures for biological, chemical, and radiation safety as appropriate, including:

A14.2.1 Communicable disease agents.

A14.2.2 Chemical hygiene.

A14.2.3 Hand washing.

A14.2.4 Fire safety.

A14.2.5 Radiation safety.

A14.2.6 Latex allergy.

A14.2.7 Power failures.

A14.2.8 Liquid nitrogen.

A15 INFANT DONOR ELIGIBILITY DETERMINATIONS

A15.1 There shall be procedures for determining infant donor eligibility based on infant donor and maternal screening and testing in accordance with Applicable Law.

A16 THIRD PARTY AGREEMENTS

A16.1 There shall be policies and procedures for development and implementation of written agreements with third parties whose services impact the cord blood unit.

PART B: CORD BLOOD BANK OPERATIONAL STANDARDS

B1	Cord Blood Bank Personnel Requirements.....	26
B2	Policies and Standard Operating Procedures.....	27
B3	Cord Blood Bank Operations.....	29
B4	Equipment.....	31
B5	Supplies and Reagents.....	31
B6	Labeling.....	32
B7	Documents and Records Requirements.....	34
B8	Inventory Transfer.....	38
B9	Interruption of Operations at Established Sites.....	39

PART B: CORD BLOOD BANK OPERATIONAL STANDARDS

B1 CORD BLOOD BANK PERSONNEL REQUIREMENTS

- B1.1 There shall be a CBB Director with an earned doctoral degree in medicine or in a related scientific field, with training in immunogenetics of transplantation, basic or clinical immunology, immunohematology, basic or clinical hematology, transfusion medicine, blood or tissue banking, or cryobiology. The CBB Director has final responsibility for the CBB scientific and clinical performance and its overall compliance with these Standards, including all components of the CBB's policies and Standard Operating Procedures. The CBB Director shall participate regularly in educational activities related to the field of cord blood banking and/or hematopoietic progenitor cell collection, processing, and transplantation.
- B1.2 There shall be a CBB Medical Director who is a licensed physician with training in hematopoietic cell transplantation or blood or tissue banking. This individual is responsible for donor recruitment, eligibility, and selection, the medical aspects of the collection procedures and of the CBB Processing Facilities, and compliance of the Collection and CBB Processing Facilities with these Standards. The CBB Medical Director shall participate regularly in educational activities related to the field of donor safety, cord blood banking, and/or hematopoietic progenitor cell collection, processing, and transplantation.
- B1.2.1 The CBB Medical Director may also serve as the CBB Director, CBB Collection Facility Medical Director, and/or CBB Processing Facility Director, if appropriately credentialed.
- B1.3 There shall be a CBB Collection Facility Medical Director who is a licensed physician responsible for the medical aspects of cord blood collection procedures and compliance of the Collection Facility with these Standards. The CBB Collection Facility Medical Director shall participate regularly in educational activities related to the field of donor safety, cord blood banking, and/or hematopoietic progenitor cell collection, processing, and transplantation.
- B1.3.1 The CBB Medical Director may serve the function of the Collection Facility Medical Director and need not be licensed in the jurisdiction of the collection or be on the staff of the Collection Facility.
- B1.3.2 Where there are Collection Facilities that are not staffed by the CBB personnel, there shall be a designated individual who is responsible for the daily operation of the Collection Facility and communication with the CBB Medical Director.
- B1.3.2.1 At Collection Facilities where individual healthcare practitioners perform CB collections, the individual healthcare practitioner may be the contact person.
- B1.4 There shall be a CBB Processing Facility Director who is an individual with a relevant doctoral degree, qualified by training or experience for the scope of activities carried out in the Cord Blood Bank Processing Facility. The CBB Processing Facility Director is responsible for all operational aspects of all procedures related to receipt, testing, processing, cryopreservation, storage, release for shipment of cord blood units, and administrative operations of the CBB Processing Facility, including compliance with these Standards. The CBB Processing Facility Director shall participate regularly in educational activities related to the field of cord blood banking and/or hematopoietic progenitor cell collection, processing, and transplantation.

B1.4.1 The CBB Processing Facility Director may also serve as the CBB Director and/or CBB Medical Director if appropriately credentialed.

B1.5 There shall be a CBB QM Supervisor approved by the CBB Director. Section A2.2 also applies.

B1.6 The CBB shall have adequate staff.

B1.6.1 Qualifications, training, continuing education, and continued competency for the performance of all assigned operations shall be documented for all staff.

B2 POLICIES AND STANDARD OPERATING PROCEDURES

B2.1 The CBB shall have clearly written policies and Standard Operating Procedures that are precise and unambiguous and address all aspects of the operation.

B2.1.1 Each individual Standard Operating Procedure shall include:

B2.1.1.1 An appropriate title.

B2.1.1.2 A standardized format for procedures, including worksheets, reports, and forms.

B2.1.1.3 A standardized system of numbering.

B2.1.1.4 The objective addressed.

B2.1.1.5 The personnel responsible for its execution.

B2.1.1.6 The facility, equipment, and supplies required.

B2.1.1.7 The expected range of results, if applicable.

B2.1.1.8 A reference section listing appropriate literature, if applicable.

B2.1.1.9 Examples of current worksheets, forms, reports, and labels, where applicable.

B2.1.1.10 The date(s) of initial implementation and the signature of the CBB Director.

B2.1.1.11 The date of review or revision and the signature of the CBB Director or designee.

B2.1.2 There shall be policies and Standard Operating Procedures to cover at least the following CBB operations:

B2.1.2.1 Preparation, approval, implementation, and revision of Standard Operating Procedures.

B2.1.2.2 Donor recruitment, maternal and infant donor screening, collection criteria, and consent.

B2.1.2.3 Maintenance of linkage of the CB unit to the infant donor and the recipient or the final distribution of the CB unit.

- B2.1.2.4 CB unit collection, storage, and transport to the CBB Processing Facility.
 - B2.1.2.5 Cord blood processing, cryopreservation, and storage.
 - B2.1.2.6 Documentation of who performs each step from collection to final disposition of the CB unit.
 - B2.1.2.7 Labeling of the CB unit, reference samples, and associated documents.
 - B2.1.2.8 Communicable disease testing, HLA typing, testing for hemoglobinopathies, and other testing.
 - B2.1.2.9 Storage of maternal and CB unit samples for testing.
 - B2.1.2.10 Notification of mothers or their responsible physicians of positive or indeterminate communicable disease and/or genetic test results.
 - B2.1.2.11 Notification of relevant governmental agencies, when required.
 - B2.1.2.12 Criteria for qualification and listing of CB units available for search and transplantation, including nonconforming CB units.
 - B2.1.2.13 Search, selection, and release of CB units.
 - B2.1.2.14 Quality Management. Section A applies.
 - B2.1.2.15 Data management.
 - B2.1.2.16 Confirmation of HLA typing of the CB unit.
 - B2.1.2.17 Collection and analysis of transplant outcome data.
 - B2.1.2.18 Personnel training and documentation of continued competency for the procedures performed.
 - B2.1.2.19 Facility management including supplies, maintenance and monitoring of equipment, cleaning and sanitation procedures, disposal of medical and biohazardous waste, emergency and safety procedures, and a disaster plan.
 - B2.1.2.20 Verification that infant donor and recipient are different individuals in the case of complete HLA matches.
 - B2.1.2.21 A plan to ensure continuous safe storage of the CB units in the event of a disaster.
 - B2.1.2.22 Discard and disposal of CB units.
- B2.1.3 When an electronic system is used, there shall be validated procedures for:
- B2.1.3.1 Systems development.

- B2.1.3.2 Numerical designation of system versions, if applicable.
- B2.1.3.3 Prospective validation of the system(s), including hardware, software, and databases.
- B2.1.3.4 Installation of the system(s).
- B2.1.3.5 Training and continuing competency of personnel in use of the system(s).
- B2.1.3.6 Monitoring of data integrity.
- B2.1.3.7 Backup of the electronic record system(s) on a regular schedule.
- B2.1.3.8 System maintenance and operations.
- B2.1.3.9 Electronic record entry, verification, and revision including review of data before final acceptance.

B2.2 Policies and Standard Operating Procedures Management Requirements.

- B2.2.1 All policies and Standard Operating Procedures shall comply with these Standards.
- B2.2.2 The policies and Standard Operating Procedures shall be reviewed and approved by the CBB Director or designee prior to implementation, signed and dated at least annually and after each revision.
- B2.2.3 Copies of the policies and Standard Operating Procedures of the CBB relevant to the processes being performed shall be available to the CBB personnel at all times.
- B2.2.4 The CBB Director or designee shall review all deviations or variances from the CBB policies and/or Standard Operating Procedures or from these Standards. This review shall be documented.
- B2.2.5 The CBB Director or designee shall review all errors and accidents. This review and any corrective actions taken shall be documented.
- B2.2.6 The appropriate staff shall read new and revised policies and Standard Operating Procedures prior to performing the task. This review and associated training shall be documented.

- B2.3 All personnel at the CBB, Collection Facilities, and Processing Facilities shall follow the applicable policies and Standard Operating Procedures established by the CBB.

B3 CORD BLOOD BANK OPERATIONS

- B3.1 The CBB shall be secure to prevent the admittance of unauthorized personnel.
- B3.2 The responsibilities of each Collection Facility, CBB Processing Facility, and Registry as they relate to the CBB shall be clearly defined and documented.

- B3.3 The CBB shall be responsible for all components of the CB unit production process, including at least donor recruitment; maternal and infant donor screening, testing, and eligibility determination; and CB unit collection, processing, testing, storage, and release from inventory. The CBB shall ensure that all CB units are collected using Standard Operating Procedures that meet these Standards.
- B3.3.1 For collection of unrelated donor CB units, there shall be an established relationship between the Collection Facility and the CBB such that the CBB ensures implementation of and compliance with its QM Program and Standard Operating Procedures for obtaining and documenting informed consent, maternal and infant donor screening and testing, completion of medical history, and the collection, labeling, and shipment of the CB unit and maternal samples.
- B3.3.2 For collection of directed allogeneic or autologous CB units, the CBB shall have a contract with the infant donor family and shall have communicated with the collecting physician, midwife, or other healthcare professional. The CBB shall provide the appropriate policies and Standard Operating Procedures for collection, labeling, and shipment of the CB unit and maternal samples, and shall monitor the quality of the CB unit collections through its QM Program.
- B3.4 The CBB shall utilize an HLA testing laboratory accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), the European Federation for Immunogenetics (EFI), or equivalent accrediting organization outside North America and Europe.
- B3.5 All laboratories utilized by the CBB for testing of mother and infant donor samples shall be accredited, certified, or licensed to perform such testing in accordance with Applicable Law. The CBB shall maintain documentation of the accreditation, certification, or licensure of these laboratories to perform this testing.
- B3.5.1 When external laboratories are used for any aspect of CB unit or sample testing, the CBB shall maintain a record of all samples sent to such laboratories, including the identifiers, results, date sent, and date results are received.
- B3.5.2 The CBB shall maintain a record of the name and version of each test used.
- B3.6 Confidentiality.
- B3.6.1 There shall be a system to maintain the confidentiality of the infant donor, recipient, and their respective families according to Applicable Laws.
- B3.6.2 There shall be a process for maintenance of confidentiality of all records and communications among CBB, the Collection Facility sites, CBB Processing Facility, and Clinical Transplant Programs.
- B3.6.2.1 Confidential information shall be secure such that demographic data are available only when needed and only to authorized personnel.
- B3.6.2.2 Informed consent shall include knowledge that linkage of infant donor and mother with the CB unit is maintained.

- B3.6.3 The CBB shall have written policies and Standard Operating Procedures for circumstances where infant donor, mother or infant donor's legal guardian, and appropriate medical personnel could be contacted.
- B3.6.4 The CBB shall request that the Clinical Transplant Program not reveal confidential information such as the time and date of collection to the recipient, the recipient's family, or representatives of the clinical personnel.
- B3.7 Clinical Outcome Data Requirements.
 - B3.7.1 The CBB shall maintain sufficient critical outcome data to assure that the procedures in use in the CBB consistently provide a safe and effective product. Section E10 also applies.
 - B3.7.2 For unrelated allogeneic, directed allogeneic, and autologous CB units, data shall include neutrophil and platelet engraftment or recovery and survival rates.
 - B3.7.3 For allogeneic CB units only, data should include chimerism and GVHD results.
- B3.8 Institutional Review Board or Ethics Committee Requirements.
 - B3.8.1 In compliance with Applicable Law, the CBB shall have formal review of investigational protocols and maternal consent for CB banking and related activities by a mechanism that is approved by the Office of Human Research Protections under the United States Department of Health and Human Services (HHS), the United States Food and Drug Administration (FDA), or non-U.S. equivalent.
 - B3.8.2 The CBB shall maintain documentation of all its research protocols, Institutional Review Board or Ethics Committee approvals or equivalent, investigational new drug or device exemptions, annual reports, and any adverse events.
- B4 EQUIPMENT
 - B4.1 Equipment used shall not adversely affect the viability of the CB units and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease.
- B5 SUPPLIES AND REAGENTS
 - B5.1 Supplies and reagents used shall not adversely affect the viability of the CB units and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease.
 - B5.2 Supplies and reagents that come into contact with the CB unit shall be sterile.
 - B5.3 Whenever possible, supplies and reagents should be used in a manner consistent with instructions provided by the manufacturer.
 - B5.4 Supplies and reagents used for CB collection, processing, or cryopreservation, whenever possible, shall be approved for human use.
 - B5.4.1 Supplies and reagents not approved for human use by the appropriate regulatory agency may be used if:

- B5.4.1.1 The supplies or reagents are specified in a procedure that has received Institutional Review Board or Ethics Committee approval at the Institution performing the investigational test or procedure and/or Investigational New Drug or Device Exemption (or non-U.S. equivalent) or
 - B5.4.1.2 The procedure that includes the specified supplies or reagents has been used in Institutional Review Board or Ethics Committee-approved trials and has been established in the medical literature to be commonly used and acceptable for the purpose(s) specified.
- B5.5 Certificates of analysis shall be obtained and maintained on file for all critical reagents.

B6 LABELING

B6.1 Labeling Operations.

- B6.1.1 Labeling operations shall be conducted in a manner adequate to prevent mislabeling of CB units and reference samples.
- B6.1.2 There shall be a bar-coding or equivalent human and machine-readable system of identification for the maternal samples, the CB unit, CB unit reference samples, and associated documents.
 - B6.1.2.1 The identification system shall be validated.
- B6.1.3 The labeling operation shall include at least the following controls:
 - B6.1.3.1 Labels shall be held upon receipt from the manufacturer pending review and proofing against an approved copy to ensure accuracy regarding identity, content, and conformity.
 - B6.1.3.2 Labels printed on demand shall be reviewed against an approved copy to ensure accuracy regarding identity, content, and conformity.
 - B6.1.3.3 Stocks of unused labels representing different products shall be stored and maintained in a manner to prevent errors.
 - B6.1.3.4 Stocks of obsolete labels shall be destroyed.
 - B6.1.3.5 A system for container label version control shall be employed.
 - B6.1.3.6 A system of checks in labeling procedures shall be used to prevent errors in transferring information to labels.
 - B6.1.3.7 All labeling shall be clear, legible, and printed using indelible ink.
 - B6.1.3.8 The labeling system shall be validated as reliable for storage under the conditions in use.

- B6.1.3.9 There shall be processes to verify that all labels in use are accurate, legible, and maintain physical integrity.
- B6.1.4 When the label has been affixed to the CB unit bag, a sufficient area of the bag shall remain uncovered to permit inspection of the contents.
- B6.1.5 All data fields on labels shall be completed.
- B6.2 Identification.
 - B6.2.1 There shall be a written policy for labeling of the CB unit, reference samples, and associated documents.
 - B6.2.2 Each CB unit shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to trace any CB unit to its maternal and infant donor data, delivery information, family history, test results, and to all records describing the handling and final disposition of that CB unit.
 - B6.2.3 Facilities may designate an additional or supplementary unique numeric or alphanumeric identifier to the CB unit or to a test aliquot.
 - B6.2.3.1 Supplementary identifiers shall not obscure the original identifier.
 - B6.2.3.2 No more than one supplementary identifier shall be visible on a CB unit bag.
- B6.3 The information provided on the label by the initial Collection Facility shall be maintained indefinitely as part of the CB unit record.
 - B6.3.1 CB units that are subsequently processed may be packaged into new bags with new labels as appropriate.
 - B6.3.1.1 The process to establish linkage between original and new labels shall be validated.
 - B6.3.1.2 This linkage shall be maintained as a permanent part of the CB unit record.
- B6.4 Label Content.
 - B6.4.1 Each label shall include at least the elements detailed in Appendix I, Cord Blood Unit Labeling Table.
 - B6.4.2 Minimally, the partial label shall be present on the CB unit during all stages of processing.
 - B6.4.3 Any CB unit bag bearing a partial label shall be accompanied by the full information in Appendix I attached securely to the CB unit on a tie tag or enclosed in a sealed package.
- B6.5 Documentation of donor eligibility shall accompany the CB unit at distribution, according to Applicable Law. Documentation shall include:
 - B6.5.1 A statement that the donor has been determined to be eligible or ineligible based on the results of donor screening and testing.

- B6.5.2 A summary of records used to make donor eligibility determination in compliance with Applicable Law, including:
 - B6.5.2.1 Identification of the laboratory performing communicable disease testing.
 - B6.5.2.2 A listing and interpretation of the results of all communicable disease screening and testing performed.
 - B6.5.2.3 The name and address of the establishment that made the donor eligibility determination.
- B6.5.3 Instructions for use to prevent the introduction, transmission, or spread of communicable diseases.
- B6.5.4 Products distributed before completion of the required donor eligibility determination shall be distributed under quarantine, accompanied by:
 - B6.5.4.1 A statement that the donor eligibility determination has not been completed.
 - B6.5.4.2 A statement that the CB unit shall not be used until completion of donor eligibility except under the terms of urgent medical need.
- B6.6 Related allogeneic and autologous CB units distributed prior to completion of donor eligibility determination under the provision of “urgent medical need” shall be accompanied by:
 - B6.6.1 A listing of any screening or testing that has not been completed.
 - B6.6.2 Notification of the physician for the recipient using the CB unit of the incomplete screening or testing of the CB unit.
 - B6.6.3 Documentation that donor eligibility determination was completed during or after the use of the CB unit.
- B6.7 If required by Applicable Law, the CB unit label shall include:
 - B6.7.1 For products under Investigational New Drug Application the statement: “Caution: New Drug—Limited by Federal (or United States) law to investigational use.”
 - B6.7.2 For licensed products, the statement “Rx Only.”

B7 DOCUMENTS AND RECORDS REQUIREMENTS

- B7.1 General Record Requirements.
 - B7.1.1 Records of each CB unit shall be made concurrently with each stage of the CB collection, processing, testing, banking, selection, release, issue, and/or disposal; identify the person immediately responsible for each step; and include appropriate dates and times to provide a complete history of the work performed and to relate the records to a particular CB unit.
 - B7.1.1.1 Records shall be as detailed as necessary for a clear understanding by a person experienced in CBB procedures.

- B7.1.2 Records pertinent to the CB unit shall be reviewed by the CBB Processing Facility Director or designee.
 - B7.1.3 Records shall be available at the CBB or Collection Facility from which to determine the lot number, expiration date, and manufacturer of supplies and reagents used for the collection and processing of each CB unit.
 - B7.1.4 A record management system shall be established and maintained to assure protection, preservation, and ready retrieval of records.
 - B7.1.5 Records shall be available for inspection by authorized individuals upon request from a regulatory or accrediting agency.
 - B7.1.6 Identity and medical records of the infant donor and parents shall be in English or, if in another language, shall be translated to English and accompanied by a statement of authenticity by the translator prior to release of the CB unit.
- B7.2 CBB records shall be maintained indefinitely including the following:
- B7.2.1 Infant donor and parental records.
 - B7.2.1.1 Mother's full name, address and neonatal delivery date and, if available, infant donor's full name and address, and father's full name and address.
 - B7.2.1.2 Medical history of the genetic mother, the birth mother, and if his history is available, the medical history of the genetic father.
 - B7.2.1.3 Copies of consent forms.
 - B7.2.1.4 Results of maternal screening, maternal testing, and results of infant donor testing, if performed.
 - B7.2.1.5 Records of pregnancy, labor, and delivery.
 - B7.2.1.6 Records of physical assessment of the mother and infant donor.
 - B7.2.1.7 Records of maternal or infant donor adverse reactions, complaints, and reports, including results of all investigations and follow-up.
 - B7.2.2 CB unit records.
 - B7.2.2.1 Identity of all facilities and personnel involved in the collection, processing, testing, banking, selection, and release of the CB unit.
 - B7.2.2.2 CB unit processing worksheets.
 - B7.2.2.3 Supplies and reagents used including name of manufacturer or supplier, lot numbers, expiration dates, date of receipt, and relevant verification, including test results or a certificate of analysis from the vendor.

- B7.2.2.4 CB unit bag and canister characteristics, including approximate dimensions.
 - B7.2.2.5 Records of the cryopreservation procedure including the record of the cooling rate.
 - B7.2.2.6 Records of storage conditions throughout the history of the CB unit.
 - B7.2.2.7 Documentation and interpretation of all test results.
 - B7.2.2.8 Results of communicable disease tests performed prior to CB unit release, if performed, including the name and address of the testing laboratories.
 - B7.2.2.9 Documented availability of all reference samples as required in Section D8 adequate to perform histocompatibility, microbiology, and viability testing.
 - B7.2.2.10 Documentation of receipt, distribution, and disposition including destruction of CB units, integrally attached segments, and all related CB unit samples.
 - B7.2.2.11 CB unit transport records.
 - B7.2.2.12 Reasons for exclusion of CB units collected but not banked.
- B7.2.3 Directed allogeneic and autologous recipient and parental records.
- B7.2.3.1 A copy of mother's consent for collection and, if available, a copy of the father's consent for collection.
 - B7.2.3.2 A contract specifying duration of storage and possible uses of the CB unit and reference samples.
 - B7.2.3.3 Documentation of the agreement for disposition at the end of the contract and the final disposition of the CB unit.
- B7.2.4 Directed allogeneic and autologous recipient and parental records for CB units collected in non-fixed Collection Sites.
- B7.2.4.1 A written agreement between the donor family and the CBB related to CB unit collection, transport, processing, testing, storage, and release.
 - B7.2.4.2 Documentation that a licensed medical professional has agreed to perform the collection and documentation of her/his training.
- B7.2.5 Directed allogeneic recipient and parental records.
- B7.2.5.1 HLA typing of infant donor, mother, father, and recipient to include at least A, B, and DRB1, when performed.
- B7.2.6 Quality assurance records.
- B7.2.6.1 Periodic performance checks of equipment and reagents.

- B7.2.6.2 Tests of capacity of shipping containers to maintain proper temperature in transit.
- B7.2.6.3 Proficiency test results.
- B7.2.6.4 Validation studies.
- B7.2.6.5 Results of inspection and accreditation visits.
- B7.2.7 General records.
 - B7.2.7.1 Personnel employed by the CBB responsible for CB unit collection or processing, including signature, initials, and inclusive dates of employment for each.
 - B7.2.7.2 Technical personnel training, continuing education, and periodic competency testing.
 - B7.2.7.3 Errors, accidents, and corrective action taken.
 - B7.2.7.4 Equipment, including maintenance, cleaning, sanitization, and calibration records.
 - B7.2.7.5 Facilities, including records of cleaning and sanitation.
 - B7.2.7.6 Disposition of rejected supplies and reagents.
 - B7.2.7.7 Sterilization of supplies and reagents prepared within the facility, including date, time interval, temperature, and method used.

B7.3 Electronic Records.

- B7.3.1 If an electronic record-keeping system is used, there shall be a system to ensure the authenticity, integrity, and confidentiality of all records throughout the period of record retention.
 - B7.3.1.1 There shall be a system to make legible records readily accessible.
- B7.3.2 There shall be the ability to generate true copies of the records in both paper and electronic format suitable for inspection and review.
- B7.3.3 There shall be a back-up or alternative system for all electronic records that ensures continuous operation in the event that primary electronic data are not available.
 - B7.3.3.1 Documentation of periodic testing of the alternative system shall be maintained.
- B7.3.4 There shall be a system that limits access to the electronic records to authorized individuals.
- B7.3.5 All system modifications shall be authorized, documented, and validated prior to implementation.
- B7.3.6 The electronic record system shall ensure that all infant donor, CB unit, and patient identifiers are unique.

- B7.4 Records in case of divided responsibility.
 - B7.4.1 If two (2) or more facilities participate in the collection, processing, testing, selection, or release of the CB unit, the records of each facility shall plainly show the extent of its responsibility.
 - B7.4.2 Each participating facility shall furnish to the facility of final disposition a copy of collection and processing records related to the safety of the CB unit.

B8 INVENTORY TRANSFER

- B8.1 Inventory transferred to another CBB shall be accompanied by at least the following:
 - B8.1.1 All collection and processing records, including medical and genetic history, identity and results of all maternal and CB unit testing, and summary records of donor eligibility determination.
 - B8.1.2 All associated reference samples.
 - B8.1.3 The complete storage history of each CB unit, including the storage temperature records and records of any transfer of any CB unit to a different storage location.
- B8.2 The transferring and accepting CB Banks shall collaborate to ensure that:
 - B8.2.1 The inventory is transferred in a manner that maintains proper storage temperature and prevents contamination.
 - B8.2.2 Transport does not adversely affect the integrity of the CB units.
 - B8.2.3 The safety of transport personnel is ensured.
- B8.3 There shall be policies to maintain confidentiality.
- B8.4 Records shall be in a language and form that can be understood by the accepting CBB personnel.
- B8.5 There shall be a mechanism to identify the transferred CB units as distinct from those collected and processed at the accepting CBB.
- B8.6 There should be a mechanism to contact the transferring CBB Director or designee for future reference, as defined in the contract or agreement.
- B8.7 Responsibilities of the accepting CBB.
 - B8.7.1 There shall be documentation of review of records and transferred inventory to ensure that:
 - B8.7.1.1 The CB units were stored in appropriate storage bags at appropriate storage temperatures.
 - B8.7.1.2 Maintenance of appropriate storage conditions throughout the period of storage can be documented.
 - B8.7.1.3 Integrally attached segments and other reference samples for each CB unit are included in the transferred inventory.

- B8.7.1.4 Records are available to link each CB unit to its infant donor, its reference samples, and all relevant history, collection, processing, and testing records.
- B8.7.1.5 Records received include at least, the maternal consent, medical and genetic history, identity and results of all maternal and CB unit communicable disease tests, CB unit cell counts and sterility testing, the processing methods, the manufacturer and approximate dimensions of the storage bag and canister, and enumeration of attached segments and other reference samples.
- B8.7.1.6 There is access to all records described in Section B7.
- B8.7.2 There shall be a process for inspecting incoming CB units for damage and contamination.
- B8.7.3 After the CB units have been transferred, but before the transferred inventory is made available for search:
 - B8.7.3.1 The integrity and viability of thawed CB unit samples shall be validated.
 - B8.7.3.2 There shall be confirmation of the accuracy and completeness of the records including donor identity and HLA typing results.
 - B8.7.3.3 The accepting CBB shall determine whether to accept, reject, or place in quarantine incoming CB units based on established criteria designed to prevent the transmission of communicable diseases.

B9 INTERRUPTION OF OPERATIONS AT ESTABLISHED SITES

- B9.1 In the event that any collection or processing function is discontinued for a period exceeding six months, there shall be documentation of the training and continued competency of all staff to perform the duties assigned upon resumption of activities.
- B9.2 If collection activity is discontinued at any Fixed Collection Site for a period exceeding six months, the CBB Director or designee shall review and renew the collection contract with that facility.
- B9.3 If any CB processing activities are discontinued:
 - B9.3.1 There shall be competent staff to oversee, maintain, distribute the inventory, and maintain communication with all relevant Registries and Clinical Transplant Facilities, if applicable.
 - B9.3.2 A process to distribute CB unit contiguous segments and samples for testing shall be maintained.
 - B9.3.3 All records of the entire inventory in storage shall be maintained.
- B9.4 Prior to the reestablishment of either CB collection or CB processing as applicable, at least the following shall be documented:
 - B9.4.1 Review of all procedures to ensure that methods are consistent with current practices.

- B9.4.2 Inspection of all reagents and supplies to ensure none will be used past its expiration date.
 - B9.4.3 Validation, calibration, and maintenance of all equipment have been completed within the time periods specified in the Standard Operating Procedures and manufacturer's instructions.
- B9.5 Cessation of operations.
- B9.5.1 It is the responsibility of the CBB to follow all contractual obligations that are made with the directed donor families.

PART C: CORD BLOOD DONOR MANAGEMENT AND COLLECTION STANDARDS

C1	Cord Blood Collection Personnel Requirements.....	42
C2	Cord Blood Collection Facilities.....	42
C3	Policies and Standard Operating Procedures.....	44
C4	Maternal and Infant Donor Evaluation.....	44
C5	Informed Consent.....	46
C6	Cord Blood Collection Procedures.....	47
C7	Transportation of Non-Cryopreserved Cord Blood Units Between the Cord Blood Collection Facility and the Cord Blood Processing Facility.....	49
C8	Validation and Qualification Requirements.....	49
C9	Documents and Records Requirements.....	50

PART C: CORD BLOOD DONOR MANAGEMENT AND COLLECTION STANDARDS

C1 CORD BLOOD COLLECTION PERSONNEL REQUIREMENTS

- C1.1 There shall be a CBB Collection Facility Medical Director who is a licensed physician responsible for the medical aspects of cord blood collection procedures and compliance of the Cord Blood Collection Facility with these Standards. The CBB Collection Facility Medical Director shall participate regularly in educational activities related to the field of donor safety, CB banking, and/or hematopoietic progenitor cell collection, processing, and transplantation.
- C1.1.1 The CBB Medical Director may serve the function of the remote site Collection Facility Medical Director and need not be licensed in the jurisdiction of the collection or be on the staff of the Collection Facility.
- C1.2 Where there are Collection Facilities that are not staffed by the CBB personnel, there shall be a designated individual who is responsible for the daily operation of the Collection Facility and communication with the CBB Medical Director.
- C1.2.1 At Collection Facilities where individual healthcare practitioners perform CB collections, the individual healthcare practitioner may be the contact person.
- C1.3 There shall be adequate staff whose training, continuing education, and continued competency for the performance of all assigned operations shall be documented.
- C1.4 *In utero* collections shall be performed by a licensed medical professional trained in the collection procedure and licensed to practice in the jurisdiction where the collection takes place.

C2 CORD BLOOD COLLECTION FACILITIES

- C2.1 The Collection Facility is the site where the infant donor is delivered and the CB unit is collected.
- C2.2 There shall be adequate space for the performance of the collection procedure.
- C2.3 There shall be adequate space for secure storage of the CB unit, associated reference samples and documents until they are transported to the CBB Processing Facility.
- C2.4 Unrelated allogeneic CB collections.
- C2.4.1 There shall be documentation describing the agreement and interaction between the Fixed Collection Facility and the CBB.
- C2.4.2 There shall be a designated area for appropriate storage and preparation of the reagents, supplies, and equipment needed for the collection procedures.
- C2.4.2.1 Reagents and supplies shall be stored according to the manufacturer's recommendations.

- C2.4.3 Records supplied to the CBB shall include at least the following:
 - C2.4.3.1 Identity of supplies and reagents including manufacturer, lot number, and expiration date. If collection supplies and reagents are supplied by the CBB, this standard is the CBB responsibility. Section D17.2 also applies.
 - C2.4.3.2 Documentation of appropriate storage of all supplies, reagents, CB units, and reference samples.
- C2.4.4 When collection activities at a Fixed Collection Facility Site are discontinued for a period exceeding six months, Section B9 applies.
- C2.5 When directed allogeneic or autologous CB units are collected in a Fixed Collection Facility Site, Section C2.4 applies.
- C2.6 When directed allogeneic or autologous CB units are collected in Non-Fixed Collection Facility Site:
 - C2.6.1 There shall be a written agreement between the donor family and the CBB related to CB unit collection, transport, processing, testing, storage, and release.
 - C2.6.2 The CBB Medical Director or designee shall be responsible for ensuring that there are policies and procedures applicable to the Non-Fixed Collection Site that meet the requirements of these Standards and address at least collector training, storage and security of the supplies and reagents, completion of documents, the collection procedure, labeling, storage, and transportation.
 - C2.6.3 The CB unit shall be collected by a licensed medical professional trained in the collection procedure and licensed to practice in the jurisdiction where the collection takes place.
 - C2.6.3.1 There shall be documentation that a licensed medical professional has agreed to perform the collection and to document her/his training.
 - C2.6.3.2 Training shall cover each aspect of the collection process, including at least the use of the collection kit provided, cleaning of the cord, use of the collection bag to avoid microbial contamination and clots, labeling, identity check, and storage.
 - C2.6.3.3 Training shall be documented.
 - C2.6.4 Reagents, supplies, and equipment needed for the collection procedures shall be stored in an area and manner appropriate to protect their integrity and functionality.
 - C2.6.4.1 When a collection kit is prepared and sent from the CBB, there shall be a mechanism to record the temperature of the kit from the time it leaves the CBB to the return of the kit to the CBB.
 - C2.6.5 Temporary storage of the CB unit, associated reference samples, and documents shall be secure until they are transported to the CBB Processing Facility.

C3 POLICIES AND STANDARD OPERATING PROCEDURES

- C3.1 The Fixed Collection Facility Site shall have clearly written policies and procedures that are precise and unambiguous and that address all aspects of the collection operation, meet the requirements of these Standards, and are consistent with the Standard Operating Procedures of the CBB. Sections B2.1.1 and B2.2 also apply.
- C3.2 All Collection Facility personnel shall follow the policies and Standard Operating Procedures established by the CBB.
- C3.3 There shall be policies and Standard Operating Procedures to cover at least the following:
 - C3.3.1 Preparation, approval, implementation, and revision of Standard Operating Procedures.
 - C3.3.2 Donor recruitment, maternal and infant donor screening, collection criteria, and consent.
 - C3.3.3 Maintenance of linkage of the CB unit to the infant donor and the recipient or the final distribution of the CB unit.
 - C3.3.4 CB collection, storage, and transport of the CB unit to the CBB Processing Facility.
 - C3.3.5 Labeling of the CB unit, reference samples, maternal samples, and associated documents.
 - C3.3.6 Storage of maternal and CB unit samples for testing.
 - C3.3.7 Personnel training and documentation of continued competency for the procedures performed.
 - C3.3.8 Facility management including supplies, maintenance and monitoring of equipment, cleaning and sanitation procedures, disposal of medical and biohazardous waste, emergency and safety procedures, and a disaster plan.

C4 MATERNAL AND INFANT DONOR EVALUATION

- C4.1 There shall be donor evaluation procedures in place that protect the recipient against transmissible disease and protect the safety and confidentiality of the infant donor and mother. Both the potential for disease transmission from the infant donor to the recipient and the risks to the infant donor and mother from the collection procedure shall be assessed.
 - C4.1.1 Maternal and infant donor eligibility shall be determined based upon results of screening and testing in accordance with Applicable Law.
 - C4.1.2 Infant donor and maternal evaluation results shall be documented.
- C4.2 Maternal Screening.
 - C4.2.1 There shall be written criteria for maternal screening.

- C4.2.1.1 When a mother does not meet the established criteria, the CBB Medical Director or CBB Collection Facility Medical Director shall document and maintain in the permanent record the nature of the variances and the rationale for inclusion of that CB unit.
- C4.2.2 A medical and genetic history of the infant donor's family (parents, grandparents, siblings, and parent's siblings including egg, sperm, or embryo donor, if applicable) shall be obtained and documented.
 - C4.2.2.1 The history shall include the infant donor's ethnicity and the potential presence of inherited disorders that are transmissible to the recipient in the mother's and father's family including infant donor's grandparents.
 - C4.2.2.2 The CB unit shall not be accepted for unrelated donor transplantation if there is a family history (genetic mother, father, or sibling) of a genetic disease that may affect the recipient for which there is no test available or inadequate follow-up to ensure the safety of the CB unit.
- C4.2.3 A history for mother's communicable disease risk behavior shall be obtained and documented.
 - C4.2.3.1 This history shall include mother's prenatal communicable disease testing, if known, and results of other general medical testing that could influence communicable disease transmission.
 - C4.2.3.2 Previously obtained history for communicable disease transmission risk shall be updated to the time of delivery. This history shall be updated no later than 14 days after delivery.
 - C4.2.3.3 In the case of a surrogate mother who carries an infant donor not genetically hers to delivery, a communicable disease risk history of the surrogate shall also be obtained and documented.
 - C4.2.3.4 The communicable disease risk history of the sperm, egg, or embryo donor shall also be obtained and documented, if applicable.
 - C4.2.3.5 Mother's travel history shall be obtained and documented. Travel-related donor eligibility shall be determined according to Applicable Law and documented.
 - C4.2.3.6 Screening for human transmissible spongiform encephalopathy, including Creutzfeldt-Jakob disease, shall be documented.
- C4.3 Maternal Testing.
 - C4.3.1 Blood sample from the birth mother shall be obtained for communicable disease testing within seven (7) days before or after collection of the CB unit.
 - C4.3.1.1 This maternal blood sample shall be tested for evidence of communicable disease as defined in Section D16.

- C4.4 Infant Donor Screening and Testing.
 - C4.4.1 History of the current pregnancy and delivery and the infant donor's birth data shall be obtained and documented, including gender, gestational age, other results of clinical examination, and any finding suggestive of disease potentially transmissible through transplantation.
 - C4.4.2 Hemoglobinopathy testing on the infant donor or the CB unit shall be performed prior to release of the CB unit.
- C4.5 The mother shall be provided with information to contact the CBB if the infant donor later develops a serious disease.

C5 INFORMED CONSENT

- C5.1 Informed consent shall be obtained from the mother prior to or within seven (7) days after delivery of the infant donor.
 - C5.1.1 In cases of a surrogate mother, informed consent shall be obtained from both the surrogate and the genetic mother.
 - C5.1.2 If complete consent has not been obtained prior to delivery, consent shall be obtained for at least the CB collection procedure prior to delivery. At least the following information shall be provided to the mother:
 - C5.1.2.1 An explanation of the CB collection procedure.
 - C5.1.2.2 The right of the mother to refuse without prejudice.
 - C5.1.2.3 The mother will be approached at a later time for complete consent, including consent to bank the CB unit and all of the elements in Section C5.3.
 - C5.1.3 Consent obtained for the CB unit collection procedure prior to delivery shall be documented.
 - C5.1.4 Informed consent shall not be obtained while the mother is in active labor.
- C5.2 All aspects of participation in the CBB shall be discussed with the mother in a language that she understands.
- C5.3 The informed consent process shall include at least the following:
 - C5.3.1 The overall purpose.
 - C5.3.2 The possible risks and benefits to the mother and/or infant donor including medical and ethical concerns.
 - C5.3.3 The possible alternatives to CB donation.
 - C5.3.4 The right of the mother to refuse without prejudice.

- C5.3.5 Donation of the CB unit for use in transplantation and specifying the intent of the donation for either unrelated use or for directed allogeneic or autologous use.
 - C5.3.5.1 If the collection is intended for unrelated allogeneic transplantation, the CB unit is a donation that will be made available to other individuals and will not necessarily be available to the infant donor or the infant donor's family at a later date.
 - C5.3.5.2 If the collection is intended for directed allogeneic or autologous transplantation, the release of the CB unit will be limited respectively to the family, intended recipient(s), or the infant donor.
- C5.3.6 Interview for personal and family medical history.
- C5.3.7 Review of the medical records of the mother and infant donor.
- C5.3.8 An explanation of the CB collection procedure.
- C5.3.9 Collection of reference samples:
 - C5.3.9.1 Blood sample from the mother for communicable disease and other testing, as applicable.
 - C5.3.9.2 CB unit samples for communicable disease, genetic disease, and other testing, as applicable.
- C5.3.10 Storage of reference samples from the mother and the CB unit for future testing.
- C5.3.11 Maintenance of linkage for the purpose of notifying infant donor/family of communicable or genetic diseases, whenever possible.
 - C5.3.11.1 The CBB retains the right to contact the mother at any time.
 - C5.3.11.2 Information related to infant donor and family shall remain confidential.
- C5.3.12 Possible use of the CB unit for research, quality control, or validation studies.
- C5.3.13 The CBB policies for disposal of CB units including, at least:
 - C5.3.13.1 Nonconforming CB units.
 - C5.3.13.2 Directed allogeneic or autologous CB units, if no longer required.

C6 CORD BLOOD COLLECTION PROCEDURES

- C6.1 There shall be emergency medical care available for the mother and infant donor.
- C6.2 CB collection procedures and practices shall protect mother and infant donor.

- C6.2.1 Delivery practices shall not be modified in an attempt to increase CB unit volume.
- C6.3 When *in utero* CB collection is performed, there shall be additional safeguards in place to ensure the safety of mother and infant donor.
 - C6.3.1 CB collections should only be performed *in utero* from documented singleton deliveries.
 - C6.3.1.1 If CB collection is performed *in utero* in a multiple gestation pregnancy, all infants shall be delivered before any CB collection begins.
 - C6.3.2 *In utero* CB collections shall only occur in deliveries considered to be uncomplicated by the medical professional responsible for the delivery.
 - C6.3.3 CB units collected *in utero* shall only be obtained from infant donors after at least 34 weeks gestation.
 - C6.3.3.1 For directed allogeneic or autologous collections, the decision to collect from infant donors who are less than 34 weeks gestation shall be based on an evaluation of infant donor safety by the medical professional responsible for the delivery.
- C6.4 CB unit collection shall be performed according to written policies and Standard Operating Procedures.
 - C6.4.1 The identity of the collector shall be documented.
 - C6.4.2 Methods for collection shall employ aseptic technique and shall use procedures validated to result in acceptable progenitor cell viability, recovery, and microbial culture negativity rates.
 - C6.4.3 The primary CB collection bag shall be approved for use with human blood and shall be used and sealed in a manner that minimizes the risk of cell loss and of microbial contamination.
 - C6.4.4 All reagents and supplies for collection that come into contact with the cord blood shall be sterile.
- C6.5 There shall be a unique numeric or alphanumeric identifier for the CB unit, reference samples, and associated documents.
- C6.6 There shall be a written policy at the Collection Facility for labeling of the CB unit, reference samples, and associated documents. Sections B6.1 and B6.2 also apply.
- C6.7 On completion of collection, the primary collection bag shall bear or be accompanied by the information required in Appendix I, Cord Blood Unit Labeling Table.
- C6.8 There shall be a written policy for storage of CB units and reference samples at the Collection Facility prior to transport to the CBB Processing Facility.
 - C6.8.1 CB units and reference samples shall be maintained in a secure environment.

- C6.8.2 CB units shall be maintained in a temperature range validated to protect cell viability.
- C6.9 Records shall be maintained at the CBB of all reports of adverse events that occur during or immediately after collection.
- C7 TRANSPORTATION OF NON-CRYOPRESERVED CORD BLOOD UNITS BETWEEN THE CORD BLOOD COLLECTION FACILITY AND THE CORD BLOOD PROCESSING FACILITY
 - C7.1 Transportation of CB units shall be in compliance with Applicable Laws.
 - C7.2 The methods of transportation of the CB unit between the Collection Facility and the CBB Processing Facility shall be designed to protect the integrity of the CB unit being transported 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 Shipping Container (Box).
 - C7.4.1 The shipping container shall maintain a designated temperature range to protect cell viability during CB unit transport as documented by prior validation of the shipping container, or by a continuous recording of the temperature of the shipping container during transport, or another method to document maintenance of temperature within the accepted range.
 - C7.4.2 The outer shipping container shall be made of material adequate to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation.
 - C7.4.3 The shipping container shall bear the information required in Appendix I, Cord Blood Unit Labeling Table.
 - C7.5 Transport Records.
 - C7.5.1 Transport records shall permit the tracing of the CB unit from the Collection Facility to its final destination.
 - C7.5.2 A shipping list identifying each CB unit, reference sample, and associated documents that are enclosed in a package shall be included.
 - C7.5.3 Transport records shall identify:
 - C7.5.3.1 The Collection Facility responsible for shipping the CB unit.
 - C7.5.3.2 The date and time of shipping.
 - C7.5.3.3 The identity of the courier.
 - C7.5.3.4 The date and time of receipt of the package.
- C8 VALIDATION AND QUALIFICATION REQUIREMENTS
 - C8.1 Section A8 applies.

C8.2 All critical equipment shall be validated and/or qualified for its intended use.

C8.3 Quality control procedures shall be developed to monitor the continuing adequacy of the procedures, reagents, equipment, and supplies as used under routine operating conditions by the facility staff.

C9 DOCUMENTS AND RECORDS REQUIREMENTS

C9.1 Section B7 applies.

PART D: CORD BLOOD PROCESSING STANDARDS

D1	Cord Blood Bank Processing Facility Personnel Requirements.....	52
D2	Cord Blood Bank Processing Facility Requirements.....	52
D3	Policies and Standard Operating Procedures.....	53
D4	Validation and Qualification Requirements.....	53
D5	Identification and Labeling Requirements.....	54
D6	Equipment, Supplies, and Reagents Requirements.....	54
D7	Cord Blood Processing.....	54
D8	Reference Samples.....	55
D9	Cryopreservation.....	55
D10	Conditions for Storage.....	56
D11	Monitoring and Alarm Systems.....	57
D12	Inventory Management.....	58
D13	Disposal.....	58
D14	Quality Management Program.....	58
D15	CB Unit Assays.....	58
D16	Maternal Testing.....	60
D17	Documents and Records Requirements.....	61

PART D: CORD BLOOD PROCESSING STANDARDS

D1 CORD BLOOD BANK PROCESSING FACILITY PERSONNEL REQUIREMENTS

D1.1 There shall be a CBB Processing Facility Director who is an individual with a relevant doctoral degree, qualified by training or experience for the scope of activities carried out in the Cord Blood Bank Processing Facility. The CBB Processing Facility Director is responsible for all operational aspects of all procedures related to receipt, testing, processing, cryopreservation, storage, release for shipment of cord blood units, and administrative operations of the CBB Processing Facility, including compliance with these Standards. The CBB Processing Facility Director shall participate regularly in educational activities related to the field of cord blood banking and/or hematopoietic progenitor cell collection, processing, and transplantation.

D1.1.1 The CBB Processing Facility Director may also serve as the CBB Director and/or CBB Medical Director if appropriately credentialed.

D1.2 There shall be adequate staff. Section B1.6 also applies.

D2 CORD BLOOD BANK PROCESSING FACILITY REQUIREMENTS

D2.1 There shall be designated facilities with adequate space for performance of processing activities; the preparation and safe, sanitary, orderly storage of the reagents and equipment needed for CB processing, testing, banking, and release; and for records.

D2.2 Facility Safety Requirements.

D2.2.1. The CBB Processing Facility shall have programs operating in compliance with Applicable Law that are designed to minimize risks to the health and safety of employees, volunteers, and visitors.

D2.2.2 There shall be procedures for biological, chemical, and radiation safety as appropriate, including:

D2.2.2.1 Bloodborne pathogens.

D2.2.2.2 Chemical hygiene.

D2.2.2.3 Hand washing.

D2.2.2.4 Fire safety.

D2.2.2.5 Radiation safety.

D2.2.2.6 Latex allergy.

D2.2.2.7 Power failures.

D2.2.2.8 Liquid nitrogen.

D2.2.3 The CBB Processing Facility shall have written policies and procedures for action in case of exposure to communicable disease or to chemical, biological, radiological, or liquid nitrogen hazards.

D2.2.4 Decontamination and disposal techniques for medical waste shall be described. Human tissue shall be disposed in such a manner as to minimize hazard to facility personnel and the environment.

D3 POLICIES AND STANDARD OPERATING PROCEDURES

- D3.1 The CBB Processing Facility shall have clearly written policies and Standard Operating Procedures that are precise and unambiguous and address all aspects of the processing operation. Sections B2.1.1 and B2.2 also apply.
- D3.2 All personnel shall follow the policies and Standard Operating Procedures established by the CBB.
- D3.3 There shall be policies and Standard Operating Procedures to cover at least the following:
 - D3.3.1 Preparation, approval, implementation, and modification of Standard Operating Procedures.
 - D3.3.2 Maintenance of documentation of who performs steps from collection to final disposition of the CB unit.
 - D3.3.3 Cord blood processing, cryopreservation, storage.
 - D3.3.4 Labeling of the CB unit, reference samples, and associated documents.
 - D3.3.5 Communicable disease testing, HLA typing, hemoglobinopathy testing, and other testing.
 - D3.3.6 Storage of maternal and CB unit reference samples for testing.
 - D3.3.7 Criteria for release of CB units from quarantine, including nonconforming CB units.
 - D3.3.8 Criteria for qualification of CB units available for search and transplantation, including nonconforming CB units.
 - D3.3.9 Quality Management. Section A applies.
 - D3.3.10 Personnel training and documentation of continued competency for the procedures performed.
 - D3.3.11 Facility management of supplies, maintenance and monitoring of equipment, cleaning and sanitation procedures, disposal of medical and biohazardous waste, emergency and safety procedures, and a disaster plan.
 - D3.3.12 Transport and alternate place of storage of CB units in the event of a disaster.
 - D3.3.13 Discard and disposal of CB units.

D4 VALIDATION AND QUALIFICATION REQUIREMENTS

- D4.1 Section A8 applies.
- D4.2 All critical equipment shall be validated and/or qualified for its intended use.
- D4.3 Quality control procedures shall be developed to monitor the continuing adequacy of the procedures, reagents, equipment, and supplies as used under routine operating conditions by the facility personnel.

D5 IDENTIFICATION AND LABELING REQUIREMENTS

D5.1 Sections A12, B6 and D7.2 apply.

D6 EQUIPMENT, SUPPLIES, AND REAGENTS REQUIREMENTS

D6.1 Sections A9, B4 and B5 apply.

D7 CORD BLOOD PROCESSING

D7.1 General Principles.

D7.1.1 Section B3 applies.

D7.1.2 In the case of directed allogeneic or autologous infant donors, a signed agreement from the requesting family shall be obtained including the name of the intended recipient, if known.

D7.1.3 Upon receipt of a CB unit shipment into the CBB Processing Facility, there shall be a system to verify the contents of the shipment, including the CB unit(s), reference samples, and associated documents, against the enclosed shipping list.

D7.1.4 Processing and cryopreservation of CB units shall be performed according to validated Standard Operating Procedures.

D7.1.5 Failure of the processing procedure to achieve acceptable end-points shall be evaluated and documented.

D7.1.6 Equipment, supplies, and reagents used shall not adversely affect the viability of the CB units and shall not permit the introduction of adventitious agents or the transmission or spread of communicable disease.

D7.1.7 Processing and cryopreservation of CB units shall be completed within 48 hours of collection.

D7.1.8 CB unit processing shall be limited to volume reduction by depletion of erythrocytes and/or plasma unless included in an Institutional Review Board or Ethics Committee-approved protocol or an Investigational New Drug protocol, Investigational Device Exemption, or non-U.S. equivalent.

D7.1.9 Any other manipulation shall only be performed:

D7.1.9.1 With Institutional Review Board or Ethics Committee approval or non-U.S. equivalent outside North America or

D7.1.9.2 Using reagents and/or devices approved for that manipulation by the appropriate governmental agency or

D7.1.9.3 Under Investigational New Drug approval, Investigational Device Exemption, or non-U.S. equivalent.

D7.2 Label at the completion of processing.

D7.2.1 At the completion of processing, the freezing bag shall bear or be accompanied by the information required in Appendix I, Cord Blood Unit Labeling Table.

D7.3 Records pertinent to the CB unit shall be reviewed by the CBB Processing Facility Director or designee.

D8 REFERENCE SAMPLES

D8.1 At a minimum, the following reference samples shall be collected from the unrelated allogeneic, directed allogeneic, or autologous CB units prior to cryopreservation:

D8.1.1 Two (2) reference aliquots with a minimum volume of 100 μ L each sealed in the tubing that is integrally attached to the freezing bag.

D8.1.1.1 The contents of each aliquot shall be representative of the CB unit.

D8.1.1.2 One (1) segment shall be used for confirmatory typing and should be used for cell viability analysis when the CB unit is requested for confirmatory typing.

D8.1.2 Cellular aliquots of at least two (2) vials or additional contiguous segments with $1-2 \times 10^6$ mononuclear cells per vial or segment.

D8.1.2.1 All cellular aliquots that will be used for viability analysis should be stored at -196°C and shall not be stored warmer than -150°C .

D8.1.2.2 When cellular aliquots are stored in LN2 vapor phase at -150°C or colder, the freezers shall be validated to show that all cellular aliquots are maintained at appropriate temperatures.

D8.1.2.3 Cellular aliquots used for purposes other than viability analysis shall be stored at -80°C or colder.

D8.1.3 Two (2) vials of serum or plasma from non-heparinized samples with a minimum volume of two (2) mL each.

D8.1.3.1 The serum or plasma should be stored at -70°C or colder.

D8.1.4 Suitable material for preparation of at least 50 μ g genomic DNA. This may be purified DNA, frozen cellular material, or blots.

D8.2 The following reference samples for unrelated allogeneic CB units shall be collected from the infant donor's mother within seven (7) days before or after the time of CB unit collection, but prior to release of that CB unit:

D8.2.1 From the birth mother, serum or plasma from non-heparinized samples of at least two (2) vials, two (2) mL each. This serum or plasma shall be stored at -70°C or colder.

D8.2.2 From the genetic mother including egg donors, if possible, suitable material for preparation of at least 50 μ g genomic DNA. This may be purified DNA, frozen cellular material, or blots.

D9 CRYOPRESERVATION

D9.1 CB units shall be cryopreserved using a controlled rate freezing or equivalent procedure validated to maintain viability.

- D9.1.1 The time after addition of cryoprotectant prior to freezing shall be minimized.
- D9.2 Cryopreservation Standard Operating Procedures shall specify the following:
 - D9.2.1 Total nucleated cell concentration within a defined range.
 - D9.2.2 Hematocrit within a defined range.
 - D9.2.3 The cryoprotectant, its final concentration, and the duration of cell exposure prior to freezing.
 - D9.2.4 Method of freezing and end-point temperature of cooling.
 - D9.2.5 Cooling rate within a defined range.
 - D9.2.6 Freezing curve parameters within a defined range.
 - D9.2.7 Storage temperature.
- D9.3 Frozen CB units shall be stored in freezing bags designed for the cryopreservation of human cells and shall be placed into metal canisters to provide protection during freezing, storage, and transportation.
 - D9.3.1 Each CB unit freezing bag and its satellite container(s), if any, shall be examined visually for damage or possible contamination prior to its use and immediately after filling. Such examination shall include inspection for overfilling of the freezing bag and breakage of seals. The results of these inspections shall be documented.

D10 CONDITIONS FOR STORAGE

- D10.1 Facilities storing CB units shall establish policies for the duration and conditions of storage and indications for discard.
 - D10.1.1 There shall be a policy directing the validation of storage duration and the ongoing monitoring of product characteristics.
 - D10.1.2 Refrigerators and freezers used for the storage of CB units, blood components, human cells, tissues or specimens, or reagents used in CB unit collection, processing, or cryopreservation shall not be used for any other purpose.
- D10.2 Procedures to minimize the risk of microbial cross-contamination of CB units shall be defined and maintained.
- D10.3 Each CB unit shall be maintained in quarantine storage until the CBB Director or designee has approved the release of the CB unit from quarantine status based upon review of maternal communicable disease risk history, other medical history, maternal test results, and CB unit sterility test results as required under Applicable Law.
 - D10.3.1 Records shall indicate when a CB unit was released from quarantine into permanent storage.
 - D10.3.2 Unrelated allogeneic CB units shall not be released for transplantation if the unit or maternal samples have positive or indeterminate screening test results for human immunodeficiency virus, human T cell lymphotropic virus, hepatitis C virus, or hepatitis B surface antigen.

D10.3.3 If directed allogeneic and autologous CB units or associated maternal samples have positive or indeterminate communicable disease test results, such units shall be kept in a separate storage device separated from negative CB units or there shall be documented evidence of performance of risk assessment of these CB units being kept with the general inventory.

D10.4 For a CBB that stores both unrelated and directed CB units there shall be a defined process to prevent listing of directed allogeneic and autologous CB units for unrelated use.

D10.5 The CB unit storage device shall be located in a secure area. The device and/or the area shall have locking capability that is used, at least, when the area is not occupied.

D10.6 Temperature

D10.6.1 Frozen storage should be at -196°C and shall not be warmer than -150°C and shall be within a temperature range determined to be appropriate for the cryoprotectant and defined in the Standard Operating Procedures.

D10.6.1.1 When CB units are stored in LN_2 vapor phase at -150°C or colder, the storage freezers shall be validated to show that all CB units are maintained at appropriate temperatures.

D10.6.2 Significant warming events at any time in the process of cryopreservation, storage, and/or shipment shall be minimized.

D10.6.3 Each significant warming event and its duration shall be documented.

D11 MONITORING AND ALARM SYSTEMS

D11.1 Freezers for CB unit storage shall have a system to monitor the temperature continuously and to record the temperature at least every four (4) hours.

D11.1.1 For CB units fully immersed in liquid nitrogen, continuous temperature monitoring is not required.

D11.1.2 Liquid nitrogen freezers shall have a mechanism to ensure that levels of liquid nitrogen are monitored and that adequate levels are maintained.

D11.2 Alarm Systems.

D11.2.1 Storage devices for CB units and associated reference samples shall have alarm systems that are continuously active.

D11.2.2 Alarm systems shall have audible and visible signals.

D11.2.3 The alarm system shall be capable of notifying designated personnel 24 hours a day.

D11.2.3.1 A procedure for notifying designated staff shall be placed at each remote alarm location and in the immediate area of each storage device.

D11.2.4 Alarm parameters shall be set to allow staff sufficient time to salvage CB units and/or reference samples.

D11.2.5 Any alarm event and its resolution shall be documented.

D11.2.6 Alarm systems shall be checked periodically for function. The records of such checks shall be maintained.

D12 INVENTORY MANAGEMENT

D12.1 There shall be an inventory management system in operation that ensures each CB unit, its associated reference samples, maternal samples, and records can be located in a timely way. Section A10.2 also applies.

D13 DISPOSAL

D13.1 The records for discarded CB units shall indicate the unique numeric or alphanumeric identifier of the CB unit and the reason, date, and method of disposal.

D13.2 Before a directed allogeneic and autologous CB unit is discarded:

D13.2.1 The family of the infant donor shall be offered the opportunity for alternative storage at another CBB or donation for research.

D13.2.2 There shall be written documentation of no further need for the CB unit.

D13.3 Disposal of any CB unit shall be documented.

D14 QUALITY MANAGEMENT PROGRAM

D14.1 CBB Processing Facility Testing Controls.

D14.1.1 CBB Processing Facility control procedures shall include:

D14.1.1.1 The use of established and validated appropriate assays, standards, and test procedures for the evaluation of the CB unit.

D14.1.1.2 Adequate provisions for monitoring the reliability, accuracy, precision, and performance of CBB Processing Facility test procedures and instruments.

D14.1.1.3 Adequate identification and handling of all reference samples so that they are accurately related to the specific CB unit being tested, to its infant donor, the infant donor's mother, or to the specific recipient, as applicable.

D15 CB UNIT ASSAYS

D15.1 The following assays shall be performed on a sample from each CB unit.

D15.1.1 Total nucleated cell count and nucleated red blood cell count from the final CB unit at end of processing prior to cryopreservation.

D15.1.2 Viability from the final CB unit at end of processing prior to cryopreservation.

D15.1.3 Total number of CD34-positive cells at end of processing prior to cryopreservation.

- D15.1.4 Microbial cultures of the CB unit or product obtained after processing prior to cryopreservation using a system permissive for the growth of aerobic and anaerobic bacteria and fungi.
 - D15.1.4.1 For directed donor CB units, the results of positive microbial tests shall include identity of the organism(s). Antibiotic sensitivities for aerobic bacteria shall be performed prior to release of the CB unit for transplantation. These results shall be reported to the prospective Clinical Transplant Program.
 - D15.1.4.2 CB units for unrelated use shall be free from microbial contamination.
- D15.1.5 ABO group and Rh type.
- D15.1.6 Human leukocyte antigen (HLA) type before listing for unrelated allogeneic CB units or, for directed allogeneic CB units, before release of the CB unit to the Clinical Transplant Program.
 - D15.1.6.1 HLA-A, B, and DRB1 loci shall be determined.
 - D15.1.6.2 HLA-C and DQB should be determined.
 - D15.1.6.3 HLA Class I and Class II typing shall be performed by DNA-based methods.
- D15.1.7 Hemoglobinopathy screening for unrelated allogeneic and directed allogeneic CB units prior to release for transplantation.
- D15.1.8 CFU total number from the final CB unit for unrelated allogeneic CB units performed at any time prior to release for transplant.
- D15.2 Prior to release for transplantation, each CB unit should be tested for evidence of infection by at least the following communicable disease agents. When licensed assays are available, these tests shall be performed on each CB unit:
 - D15.2.1 Human immunodeficiency virus, type 1.
 - D15.2.2 Human immunodeficiency virus, type 2.
 - D15.2.3 Hepatitis B virus.
 - D15.2.4 Hepatitis C virus.
 - D15.2.5 Human T cell lymphotropic virus, type I.
 - D15.2.6 Human T cell lymphotropic virus, type II.
 - D15.2.7 *Treponema pallidum* (syphilis).
 - D15.2.8 Any additional agents required by Applicable Law at the time of release of the CB unit.
- D15.3 The CBB shall have a written policy for the management of positive or indeterminate results found during the screening process and/or laboratory testing of CB samples.

- D15.4 Positive or indeterminate test results shall be communicated to the mother and/or her physician and according to Applicable Law.
- D15.5 If the CB unit was collected for directed allogeneic or autologous use but was subsequently released for unrelated allogeneic use, reference samples shall meet full unrelated allogeneic banking criteria as described above. Sections B, C, and D apply.

D16 MATERNAL TESTING

- D16.1 The maternal blood sample obtained within seven (7) days before or after collection of the CB unit shall be tested for evidence of infection by the following communicable disease agents utilizing assays required for volunteer tissue donations.
 - D16.1.1 Human immunodeficiency virus, type 1.
 - D16.1.2 Human immunodeficiency virus, type 2.
 - D16.1.3 Hepatitis B virus.
 - D16.1.4 Hepatitis C virus.
 - D16.1.5 Human T cell lymphotropic virus, type I.
 - D16.1.6 Human T cell lymphotropic virus, type II.
 - D16.1.7 *Treponema pallidum* (syphilis).
 - D16.1.8 Cytomegalovirus (unless previously documented to be positive).
 - D16.1.9 Any additional agents required by Applicable Law at the time of release of the CB unit.
- D16.2 The CBB shall have a written policy directing response to positive or indeterminate results found during the screening process and/or laboratory testing of maternal samples.
- D16.3 Positive or indeterminate test results, excluding cytomegalovirus, shall be communicated to the mother and/or her physician and according to Applicable Law.
- D16.4 All maternal samples should have negative or non-reactive test results with the exception of:
 - D16.4.1 Cytomegalovirus antibody.
 - D16.4.2 Hepatitis B core antibody.
 - D16.4.2.1 Maternal samples that are hepatitis B core antibody positive may be accepted if they are hepatitis B antigen negative by DNA testing.
 - D16.4.3 *Treponema pallidum* (syphilis).
 - D16.4.3.1 Maternal samples that are *Treponema pallidum* (syphilis) screen positive but negative using a specific confirmatory test may be accepted.

D17 DOCUMENTS AND RECORDS REQUIREMENTS

D17.1 Section B7 applies.

D17.2 Identity of supplies and reagents including manufacturer, lot number, and expiration date supplied by the CBB to Collection Facilities shall be recorded. Section C2.4.3.1 also applies.

This page left intentionally blank.

PART E CORD BLOOD SELECTION AND RELEASE STANDARDS

E1	Cord Blood Bank Facility Requirements.....	64
E2	General Requirements for Unrelated Allogeneic, Directed Allogeneic, and Autologous Cord Blood Units.....	64
E3	General Requirements for Unrelated Allogeneic and Directed Allogeneic Cord Blood Units.....	64
E4	Cord Blood Selection for Unrelated Allogeneic, Directed Allogeneic, and Autologous Cord Blood Transplantation.....	65
E5	Cord Blood Selection for Unrelated Allogeneic and Directed Allogeneic Cord Blood Transplantation.....	65
E6	Cord Blood Selection for Directed Allogeneic and Autologous Cord Blood Transplantation.....	65
E7	Cord Blood Unit Release.....	66
E8	Transportation of Cryopreserved Cord Blood Units.....	66
E9	Documents and Records Requirements.....	67
E10	Clinical Outcome Data.....	68

PART E: CORD BLOOD SELECTION AND RELEASE STANDARDS

E1 CORD BLOOD BANK FACILITY REQUIREMENTS

E1.1 There shall be designated facilities with adequate space for procedures and records related to CB unit selection and release.

E2 GENERAL REQUIREMENTS FOR UNRELATED ALLOGENEIC, DIRECTED ALLOGENEIC, AND AUTOLOGOUS CORD BLOOD UNITS

E2.1 The CBB shall have policies and Standard Operating Procedures for:

E2.1.1 Selection, release, and transport of CB units to Clinical Transplant Programs.

E2.1.1.1 If the CBB utilizes a Registry for any of these functions, these Standards apply to that Registry.

E2.1.2 Verification of confirmatory HLA typing of the CB unit.

E2.1.3 Verification that the infant donor and the recipient are different individuals in the case of complete HLA matches.

E2.2 The CBB shall retain documentation of requests for CB units, requests for maternal and/or CB unit reference samples, requests for and results of testing, and transportation of CB units and samples between facilities.

E2.3 Once a CB unit is identified for potential use, a sample obtained from a contiguous segment of that CB unit shall be tested to verify HLA type and, if possible, cell viability.

E2.3.1 Any histocompatibility discrepancy shall be resolved and communicated to the Clinical Transplant Program.

E2.4 The CB unit should be received by the Clinical Transplant Program prior to initiation of the recipient's preparative regimen.

E3 GENERAL REQUIREMENTS FOR UNRELATED ALLOGENEIC AND DIRECTED ALLOGENEIC CORD BLOOD UNITS

E3.1 The CBB or Registry shall maintain records of each search request.

E3.2 The CBB or Registry shall have an electronic record system that enables search and match operations for unrelated allogeneic CB units.

E3.2.1 If an outside agency is used for search and match functions, its electronic record system shall meet these Standards.

E3.3 The CBB or Registry shall utilize validated procedures for the performance of donor-recipient matching and for reporting results within a defined time limit.

E3.4 Each CBB shall maintain a policy for the allocation and reservation of CB units.

E3.4.1 Reservation of a CB unit shall not be in place for more than one patient.

- E4 CORD BLOOD SELECTION FOR UNRELATED ALLOGENEIC, DIRECTED ALLOGENEIC, AND AUTOLOGOUS CORD BLOOD TRANSPLANTATION
- E4.1 Prior to release of a CB unit, the CBB shall provide the following processing data, assay results, and infant donor and maternal medical history to the Clinical Transplant Program and, if applicable, to the Registry:
- E4.1.1 HLA Class I and II typing results.
 - E4.1.2 Total nucleated cell count and nucleated red blood cell count from the final CB unit at end of processing prior to cryopreservation.
 - E4.1.3 Viability from the final CB product at the end of processing prior to cryopreservation.
 - E4.1.4 Total number of CD34-positive cells at the end of processing prior to cryopreservation.
 - E4.1.5 For unrelated allogeneic CB units, CFU total number from the final CB unit performed prior to release for transplant.
 - E4.1.6 Communicable disease testing results performed on the maternal sample and, when licensed assays are available, on the CB unit.
 - E4.1.7 Risks of communicable and/or genetic diseases disclosed by the maternal medical and genetic screening or clinical chart review and the results of any investigation or further testing performed.
 - E4.1.8 The method of CB unit processing.
 - E4.1.9 Any variances in collection, processing, testing, storage, and/or transport procedures that may influence the integrity and/or quality of the CB unit.
 - E4.1.10 Physical characteristics of the CB unit, including at least the number of bags or compartments used for storage.
- E4.2 The CBB should provide the physical dimensions of the bag and canister.
- E5 CORD BLOOD SELECTION FOR UNRELATED ALLOGENEIC AND DIRECTED ALLOGENEIC CORD BLOOD TRANSPLANTATION
- E5.1 Samples of DNA (or material to isolate DNA) from the requested CB unit shall be provided to the Clinical Transplant Program if available and if requested.
- E5.1.1 If confirmatory HLA typing is performed, the CBB shall obtain, review, and archive the results. These results may be used in the future to support the identity of the CB unit and sample when offering the CB unit to another Clinical Transplant Program.
- E6 CORD BLOOD SELECTION FOR DIRECTED ALLOGENEIC AND AUTOLOGOUS CORD BLOOD TRANSPLANTATION
- E6.1 Microbial testing results from the CB unit obtained at end of processing prior to cryopreservation shall be reviewed.
- E6.1.1 If aerobic bacteria are documented in the CB unit, antibiotic sensitivities shall be provided.

E7 CORD BLOOD UNIT RELEASE

- E7.1 The CBB shall obtain a written or electronic request from the transplant physician, designee, or Registry for shipment of the CB unit.
- E7.2 The CBB Director or designee shall review the record of each CB unit before its release including processing, test results, and medical history. Section A5.5 also applies.
- E7.3 When the maternal medical and/or genetic screening history indicates potentially transmissible disease or when there is a positive or indeterminate communicable disease test result:
 - E7.3.1 The CB unit shall not be released unless the CBB Director or Medical Director gives specific authorization for release of the nonconforming CB unit in compliance with Applicable Law and documents the rationale for such authorization.
 - E7.3.2 There shall be documentation of the consent to use the CB unit from the transplant physician.
 - E7.3.3 CB units deemed nonconforming as a result of the risk for transmission of communicable disease by donor screening or testing shall bear appropriate biohazard and warning labels. Appendix II, Modified Circular of Information Biohazard and Warning Labeling Table applies.
- E7.4 At the time of issue for transplantation, the CB unit bag shall bear or be accompanied by the information required in Appendix I, Cord Blood Unit Labeling Table.
 - E7.4.1 Such information shall be attached securely to the CB unit on a tie tag or enclosed in a sealed package to accompany the CB unit.
- E7.5 Accompanying documentation at time of issue from the CBB shall include indications, contraindications, cautions, and instructions for the handling and use of the CB unit including short-term storage and preparation for transplantation.
- E7.6 If the Clinical Transplant Program lacks experience in handling CB units, a practice CB unit should be offered. The practice CB unit shall be clearly labeled as a CB unit not intended for transplant.

E8 TRANSPORTATION OF CRYOPRESERVED CORD BLOOD UNITS

- E8.1 Transport within a facility.
 - E8.1.1 Procedures for transport of cryopreserved CB units within the facility shall be designed to protect the integrity of the CB unit and the health and safety of facility personnel.
- E8.2 Transport between facilities.
 - E8.2.1 Procedures for transport of cryopreserved CB units shall be designed to protect the integrity of the CB unit and the health and safety of personnel.
 - E8.2.2 The transit time between the CBB and other facilities shall be minimized. There shall be plans for alternative transportation in an emergency.

E8.2.3 Cryopreserved CB units stored at -150°C or colder shall be transported in a liquid nitrogen-cooled dry shipper that contains adequate absorbed liquid nitrogen and has been validated to maintain temperature below -150°C for at least 48 hours beyond the expected time of arrival at the receiving facility.

E8.2.3.1 The dry shipper shall contain a device that continuously monitors temperature throughout the shipment period.

E8.2.3.2 The shipping methods shall conform to Applicable Law regarding the mode of transport of such devices.

E8.2.3.3 The dry shipper shall be labeled in accordance with Applicable Law regarding the cryogenic material used and the transportation of biologic materials.

E8.3 The shipping container shall bear the information required in Appendix I, Cord Blood Unit Labeling Table.

E8.4 The CBB shall obtain the following data from the receiving Clinical Transplant Program about the CB unit upon receipt:

E8.4.1 Time of receipt.

E8.4.2 Internal temperature of the shipper.

E8.4.3 Integrity of the CB unit.

E8.4.4 Integrity of the shipper.

E8.5 Once an unrelated CB unit has left the CBB premises, it shall not be returned to general CBB inventory.

E9 DOCUMENTS AND RECORDS REQUIREMENTS

E9.1 Section B7 applies.

E9.2 Transport Records.

E9.2.1 Transport records shall permit the tracing of the CB unit from the CBB to its final destination.

E9.2.2 A shipping list identifying each CB unit and document enclosed in a package shall be included.

E9.2.3 Transport records shall document:

E9.2.3.1 The CBB responsible for shipping the CB unit.

E9.2.3.2 The date and time of packaging of the CB unit at the CBB.

E9.2.3.3 The date and time the package left the facility.

E9.2.3.4 The identity of the courier.

E9.2.3.5 The date and time of receipt of package.

E9.2.3.6 Maintenance of the temperature within the specified range throughout the period of transportation.

E10 CLINICAL OUTCOME DATA

- E10.1 For every unrelated allogeneic, directed allogeneic, or autologous CB unit released, the CBB shall maintain details of clinical outcome as necessary to ensure that the procedures in use in the CBB provide a safe and effective product.
- E10.1.1 The CBB shall obtain this information directly from the Clinical Transplant Program or through the Registry, if utilized.
- E10.2 The CBB shall have a policy or procedure to obtain the following information within the recommended time period for unrelated allogeneic, directed allogeneic, and autologous CB units:
- E10.2.1 Adverse events associated with transplantation of the CB unit should be reported to the CBB within six weeks of transplant.
- E10.2.2 Time to neutrophil and platelet engraftment should be reported to the CBB within 100 days of transplant.
- E10.2.3 Survival rates should be reported to the CBB annually at a minimum.
- E10.2.4 For allogeneic CB units only, data should include chimerism and GVHD results that should be reported to the CBB annually at a minimum.
- E10.3 In the case of more than one graft product used for transplantation, the CBB shall collect and document that information.
- E10.4 The CBB shall collect viability and cell yield results on the thawed CB unit from the Clinical Transplant Program.

APPENDICES

Appendix I Cord Blood Unit Labeling Table..... 71
Appendix II Modified Circular of Information Biohazard and Warning Label Table.....73

This page left intentionally blank.

Cord Blood Unit Labeling Table

Each label shall include at least the elements detailed in the following table:

Label Element	Partial Label	At the completion of collection	Shipping container labeling for transport from collection	At completion of processing and before release	At CB unit release	Dry Shipper Labeling
Unique numeric or alphanumeric identifier	AF	AF		AF	AF	
Proper name HPC, Cord Blood	AF	AF	AF	AF	AF	
Product modifiers				AC	AC	
Statement "Directed Donor" (Directed Allogeneic and Autologous CB units)	AF	AF		AF	AF	
Statement "Autologous Use Only." (Autologous CB units)	AF	AF		AF	AF	
Collection Center Identifier		AF				
Date of Collection		AF		AC	AC	
Time of collection and time zone, if different from the CBB Processing Facility.		AC				
Name and volume or concentration of anticoagulant and other additives.		AF		AC	AC	
Recommended storage temperature		AT		AF	AF	
Donor Name (Directed Allogeneic and Autologous CB units)		AF		AF	AF	
Recipient's name, unique identifier, or family (Directed Allogeneic and Autologous CB units)		AF			AF	
Volume or weight of the CB unit at the end of collection.				AC	AC	
Volume or weight of the CB unit at the end of processing				AC	AC	
Date of cryopreservation				AC	AC	
ABO group and Rh type				AC	AC	
HLA phenotype				AC	AC	
Number of nucleated cells post processing.				AC	AC	
Gender of CB unit infant donor				AC	AC	
Identity of the CBB				AF	AF	
Statement "Properly Identify Intended Recipient and Product"					AT	
Statement "For Use By Intended Recipient Only" (Allogeneic CB units)					AT	
A statement indicating that leukoreduction filters should not be used					AT	
Statement "Do Not Irradiate"					AT	
Statement "For Nonclinical Use Only" (if applicable)					AT	
Biohazard legend and/or warning labels (if applicable) See Appendix II, Modified Circular of Information Biohazard and Warning Labeling Table.		AF		AC	AC	
Date of distribution					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"						AF
Statement "Medical Specimen", "Handle With Care"						AF
Statement indicating Cord Blood for Transplantation						AF
Shipper handling instructions						AF

AF=Affix, AT=Attach or Affix, AC=Accompany or Attach or Affix The chart has minimum requirements only. A CBB may choose to be more inclusive.

This page left intentionally blank.

Modified Circular of Information Biohazard and Warning Labels										
Status			Product Labels							
Title 21 CFR Citation ^F	All Donor Screening and Testing Completed	Abnormal Results of Donor Screening	Abnormal Results of Donor Testing	Donor is resident in country on USDA ^E BSE list OR Testing performed in non-CLIA-certified laboratory.	Urgent Medical Need	Biohazard Legend [per 21 CFR 1271.3(h)]	For Autologous Use Only	Not Evaluated for Infectious Substances	WARNING: Advise patient of communicable disease risks	WARNING: Reactive test results for (name of disease agent or disease)
Donor Eligibility Determination Required [21 CFR 1271.45(b)]										
1	Allogeneic donors with incomplete donor eligibility determination ^{A,B}	No	No	No	Yes			X		
2	Allogeneic donors found ineligible	Yes	No/Yes	Yes	NA	X		X		X
	A. first-degree or second-degree blood relative ^C	Yes	Yes	No	NA	X		X		
	A. first-degree or second-degree blood relative ^C	Yes	No/Yes	Yes	Yes	X		X		X
	Unrelated donor	Yes	Yes	No	Yes	X		X		
	Unrelated donor (USA Regulation ^G)	Yes	No	No	Yes	X		X		
Donor Eligibility Determination Not Required [21 CFR 1271.90(a)]										
3	Autologous donors ^D	No	No	No			X			
	Autologous donor	Yes	No/Yes	Yes		X				X
	Autologous donor	Yes	Yes	No		X				

A. The donor eligibility must be finalized during or after the use of the cellular therapy product. The results must be communicated to the treating physician [21 CFR 1271.60 (b)4].
 B. Abnormal results of any screening or testing requires labeling as in item 2 in this table (21 CFR 1271.65 applies).
 C. Notification of the recipient's and donor's physicians of abnormal screening and/or testing results is required.
 D. Any abnormal donor screening or testing results (even though neither screening nor testing is mandated for this group of donors) require appropriate labeling [21 CFR 1271.90 (b)].
 E. USDA – United States Department of Agriculture.
 F. USA Federal Register, Code of Federal Regulations, Part 1271, Human Cells, Tissues, and Cellular Based Products, Revised January 1, 2004.
 G. Applies to any cord blood unit collected, processed, stored, transported or transplanted in the US.

Modified table from the *Circular of Information for the Use of Cellular Therapy Products*, AABB et al. July 2005.

This page left intentionally blank.

INDEX

A

ABO group, 3, 17, 59, 71
Accidents, 14, 19, 20, 37
Accompany (AC), 3, 71
Accreditation, 30, 37
Adverse event, ..3, 14, 19, 20, 31, 35, 49, 68
Adverse reaction, 3, 20
Affix (AF), 3, 71
Agreement....5, 8, 10, 15, 24, 36, 38, 40, 42, 43, 54
 family, 30, 36, 39
Alarm, 57, 58
Allogeneic..... 4
 family agreements, 36
 return to inventory, 22
American Society for Histocompatibility and Immunogenetics (ASHI), 3, 30
Aseptic technique, 4, 48
Assay..... 58, 59
 and CB unit requirements, . 22, 28, 34, 38, 39, 44, 53
 and infant donor requirements, . 28, 46, 59
 and maternal requirements, 17, 22, 23, 24, 28, 33, 35, 38, 39, 44, 45, 46, 53, 56, 60
 CD34-positive, 9, 17, 58, 65
 colony forming units, 17, 59, 65
 Creutzfeldt-Jakob disease, 45
 hematocrit, 17, 56
 hemoglobinopathy, 28, 46, 53, 59
 human leukocyte antigen, .. 17, 28, 30, 36, 53, 64
 microbial culture, 17, 36, 59, 65
 nucleated red blood cell count, . 16, 58, 65
 total nucleated cell, 16, 17, 56, 58, 65
 viability, 11, 17, 36, 55, 58, 64, 65
Attach (AT), 3, 4, 39, 71
Audit, 4, 10, 18
Autologous 4
 family agreements, 36, 40, 60
 return to inventory, 22
Available for distribution, 4, 23, 33, 34

B

Biohazard, 4, 28, 44, 66, 71, 73
Biological product deviation, 4, 14, 19, 20
Birth See Delivery
Birth mother See Mother, birth

C

Calibration, 4, 15, 20, 21, 37
CB unit
 autologous, ... 4, 22, 30, 31, 34, 43, 55, 57, 68

 directed allogeneic, ..4, 22, 31, 36, 47, 55, 59, 68
 nonconforming, 8, 15, 22, 28, 47, 53, 66
 search, 10, 28, 64
 unique identifier, 11, 23, 30, 33, 37, 48, 58, 71
 unrelated allogeneic, 4, 17, 22, 30, 31, 42, 45, 47, 55, 56, 57, 59, 60, 64, 65, 68
CD34, 4, 9, 17, 58, 65
CFU See Assay, colony forming units
Chimerism, 31, 68
Cleaning, 21, 23, 28, 37, 43, 44, 53
Clinical analysis See Outcome
Clinical Transplant Program, .. 16, 19, 20, 22, 30, 31, 59, 64, 65, 67, 68
CMV See Cytomegalovirus
Collection facility 42
 fixed collection, 5, 39, 42, 43, 44
 medical director, 6, 15, 26, 42, 45
 non-fixed collection, 5, 43
Collection procedures, 47, 49
Colony forming units, 17, 59, 65
Communicable disease 4, 5, 44, 45, 65
 and personnel exposure, 52
 and quality management program, . 17, 23
 positive or indeterminate results, 28
 quarantine, 10
 records, 34
 supplies, reagents, equipment, facilities, 21, 23, 31, 54
Competency, 5, 16, 27, 28, 29, 37, 42, 44, 53
Complaints, 14, 19, 20, 35
Confidentiality, 16, 30, 31, 37, 38, 47
Consent, 30, 31, 39, 46, 47, 66
Container, 22, 32, 49, 56, 67, 71
Contract See Agreement
Corrective action, ... 5, 14, 18, 19, 20, 29, 37
Creutzfeldt-Jakob disease, 45
Cryopreservation, 55, 56
Cytomegalovirus, 60

D

Delivery 4, 8, 23, 33, 35, 42, 45, 46, 48
 ex utero birth, 5
 in utero birth, 5, 42, 48
Designee 5, 20, 22, 29, 35, 38, 39, 43, 55, 56, 66
 and CB unit requests, 66
 and records, 35, 55
 and standard operating procedures, 27, 29
Deviation, 6, 11
Director
 CBB Collection Facility Medical Director, 6, 15, 19, 26, 42, 45

CBB Director, .5, 6, 14, 15, 19, 20, 22, 26, 27, 29, 39, 52, 56, 66
 CBB Medical Director, 6, 14, 15, 19, 20, 22, 26, 27, 42, 45, 52
 CBB Processing Facility Director, 6, 14, 16, 19, 26, 27, 35, 52, 55
 Discard, 28, 34, 44, 47, 53, 56, 58
 Disposal, 28, 34, 44, 47, 53, 58
 Disposition, 18, 19, 23, 33
 Distribution, 6, 10, 23, 27, 33, 36, 44, 71
 Documents and records, .. 16, 17, 34, 35, 37, 38, 43, 50, 61, 67
 Donor eligibility, 15, 18, 22, 30, 33, 34, 38, 44, 45
 Donor, 4, 5, 6, 7, 8, 14, 16, 22, 23, 24, 27, 28, 30, 31, 35, 36, 37, 39, 42, 44, 45, 46, 47, 48, 54, 55, 58, 64, 65, 71

E

Educational materials, 16
 Egg donor See Mother, genetic
 Eligible, 6
 Engraftment, 31, 68
 Equipment
 and quality, 9, 10, 14, 15, 20, 21, 31, 36
 maintenance, 21, 28, 44, 53
 records, 20, 21
 Equipment, 20, 21, 31, 42
 Errors, 6, 14, 19, 20, 29, 32, 37
 Ethics Committee, 7, 31, 32, 54
 European Federation for Immunogenetics (EFI), 3, 30
 Expiration
 product, 22
 supplies and reagents, .. 22, 35, 40, 43, 61

F

Facilities and safety, 23, 24
 Father, 35, 36, 45
 FDA See Food and Drug Administration (FDA)
 Food and Drug Administration (FDA), 3, 6, 7, 31

G

Genetic disease, .. 17, 28, 38, 39, 45, 47, 65, 66
 Genetic mother See Mother, genetic
 Graft-versus-host disease (GVHD), 3, 31, 68

H

HBc See Hepatitis B virus
 HBsAg See Hepatitis B virus
 HCV See Hepatitis C virus
 Hematocrit 17, 56
 Hematopoietic progenitor cells, 7
 Hemoglobinopathy, 28, 46, 53, 59
 Hepatitis B virus, 57, 59, 60

Hepatitis C virus, 56, 59, 60
 HIV See Human immunodeficiency virus
 HPC See Hematopoietic progenitor cells
 HPC, Cord Blood, 5, 7, 71
 HTLV .. See Human T cell lymphotropic virus
 Human immunodeficiency virus, ... 56, 59, 60
 Human leukocyte antigen, 17, 28, 30, 36, 53, 64
 Human T cell lymphotropic virus, .. 56, 59, 60

I

Identification, 23
 Identifier, 7, 11, 20, 23, 30, 33, 48, 58, 71
 Ineligible donor, 7, 33, 73
 Ineligible, 7, 33, 73
 Infant donor 7, 28, 31, 35, 36, 39, 44, 45, 46, 47, 48, 54, 58, 64
 definition, 7
 eligibility, .. 6, 15, 22, 24, 30, 33, 38, 44, 45
 Infectious disease See Communicable disease
 Informed consent, 46, 47
 Institutional Review Board, 7, 31, 32, 54
 Interruption of operations, 39, 40
 Inventory 17, 21, 22, 30, 38, 39, 57, 58, 67
 materials, supplies and reagents, ... 15, 21
 transfer, 38, 39
 Inventory management, 21, 22
 ISBT 128, 7

L

Labeling, 7, 15, 23, 28, 30, 32, 33, 34, 43, 44, 48, 49, 53, 54, 66, 67, 69, 71, 73
 Labels
 accompany (AC), 3, 71
 affix (AF), 3, 71
 attach (AT), 3, 4, 39, 71
 bar-coding, 32
 biohazard and warning, 66, 69, 71, 73
 label content, 18, 33, 34, 54
 not for transplant, 66
 partial, 8, 71
 Linkage, 7, 23
 Liquid nitrogen, 3, 24, 52, 57, 67

M

Manipulation, 7, 8, 9, 54
 Maternal
 donor evaluation, 17, 22, 23, 24, 27, 28, 30, 38, 44, 45, 46, 66
 testing, .. 17, 18, 22, 23, 24, 28, 33, 35, 38, 39, 44, 45, 46, 53, 56, 60
 Microbial contamination, 4, 43, 48, 56, 59
 Microbial culture, 17, 59, 65
 Monitoring and alarm systems, 58
 Monitoring, 18
 Mother 8, 31, 35, 44, 45, 46, 47, 55, 60
 birth, 8, 35, 55

egg, 8, 35, 45, 46, 55
 genetic, 8, 35, 45, 46, 55
 surrogate, 8, 35, 45, 46, 55

N

Nucleated red blood cell count, 16, 58, 65

O

Operations, 29, 31
 Organization, 15
 Outcome, 8, 14, 15, 23, 28, 31, 68

P

Personnel, 16, 26, 27, 42
 Policies, 27, 28, 29, 44, 53
 Process control, 22
 Processing facility 52
 director 6, 16, 19, 22, 26, 27, 35, 52, 55
 Processing, 8, 54, 55
 Product tracking, 23
 Promotional materials, 16
 Proper name of a cord blood unit.. See HPC,
 Cord Blood

Q

Qualification 11, 20
 collection procedure, 20, 49, 50, 53
 cryopreservation, 20, 53
 equipment, supplies, and reagents, 49, 53
 labeling, 32, 54
 length of CB unit storage, 56
 processing procedure, 20, 49, 53
 Quality assessment, 18
 Quality assurance, 10, 37
 Quality audit, 10, 18
 Quality control, 10, 21, 47, 50, 53
 Quality Management Supervisor, . 10, 14, 16,
 27
 Quality management,
 documents and records, 16, 17
 equipment, supplies, and reagents, 20, 21
 errors, accidents, biological product
 deviations, adverse events, variances,
 complaints, 19, 20
 facilities and safety, 23, 24
 identification, labeling, product tracking, 23
 infant donor eligibility, 24
 inventory management, 21, 22
 monitoring, quality assessments, audits,
 18
 organization, 15, 16
 outcome analysis, 23
 personnel, 16
 plan, 14
 process control, 22
 validation and qualification, 20
 Quarantine, 10, 18, 22, 34, 53, 56, 57

R

Reagents, .14, 15, 20, 21, 31, 32, 35, 36, 37,
 40, 42, 43, 48, 50, 52, 53, 54, 56, 61
 Recipient, .10, 23, 27, 28, 30, 31, 47, 54, 58,
 64, 71
 Records
 CB unit, 15, 18, 19, 31, 33, 35, 56
 consent, 35, 36, 39, 66
 creation, 14, 43
 display, 21
 divided responsibility, 38
 electronic, 6, 17, 20, 29, 37, 64
 retention, 14, 17, 18, 19, 20, 21, 22, 30,
 33, 34, 35, 36, 37, 38, 43, 45, 49, 52,
 58, 61, 64
 review, 16, 35, 47, 55, 66
 transfer, 38
 transport, 49, 67
 Reference samples, 10, 55
 Registry, 10, 16, 19, 22, 29, 64, 65, 66, 68
 Release, .4, 6, 10, 18, 22, 28, 30, 43, 46, 47,
 53, 56, 57, 59, 65, 66

S

Safety 10
 biological, 24, 52
 chemical, 24, 52
 cord blood unit, 38, 45
 donor, 44, 48
 mother, 44, 48
 personnel, 38, 52, 66
 procedures, 28, 44, 53
 radiologic, 24, 52
 requirements, 52
 volunteers and visitors, 52
 Samples 10, 36, 38, 39, 55, 64
 CB unit, .15, 21, 22, 28, 32, 36, 38, 39, 44,
 47, 48, 53, 54, 55, 56, 58, 59, 64, 65
 maternal, 15, 21, 28, 30, 32, 38, 44, 45,
 46, 47, 48, 53, 54, 56, 57, 58, 60
 Search, 10, 28, 53, 64
 Segment, 5, 55, 64
 Selection and release, 64, 65, 66
 Shipping container, 37, 49, 67
 Standard operating procedure, 11, 15, 22,
 26, 27, 28, 29, 31, 44, 48, 53, 54, 56, 64
 Sterility, 11, 56, 57
 Storage, 56, 57
 Supplies, ... 14, 15, 20, 21, 27, 28, 31, 32, 35,
 37, 40, 42, 43, 44, 48, 50, 53, 54, 61
 Surrogate mother See Mother, surrogate
 Survival rates See Outcome
 Syphilis See Treponema pallidum

T

Temperature
 and storage, 38, 57
 and transportation, 49

significant warming event,..... 11, 57
 Tests..... See Assay
 Thawing,..... 19
 Total nucleated cell, 16, 17, 56, 58, 65
 Trace, 11, 23, 33
 Track, 11, 15, 23
 Transportation
 between facilities,..... 28, 49, 66, 67
 cryopreserved, 53, 64, 66, 67
 non-cryopreserved, 28, 49
 records, 49, 67
 shipping container (box),..... 37, 49, 67
 within a facility, 66
 Treponema pallidum, 59, 60

U

Unique identifier, 11, 23, 33, 48, 58

Unique, 11, 23, 33, 48, 58, 71

V

Validation..... 11, 20
 collection procedure, 20, 49, 50, 53
 cryopreservation protocol, 20, 53
 equipment, supplies, and reagents, 49, 53
 labeling, 32, 54
 length of CB unit storage, 56
 processing procedure, 20, 49, 53
 viability, 39
 Variance, 11, 19, 20, 22, 29, 45
 Verification, 11, 21, 28, 64
 Viability, 11, 17, 36, 55, 58, 64, 65, 68

W

Warming, 11, 57

FACT Accreditation Office

University of Nebraska Medical Center
986065 Nebraska Medical Center
Omaha, NE 68198-6065
U.S.A.

Phone: (402) 559-1950

Fax: (402) 559-1951

E-mail: fact@unmc.edu

Website : www.factwebsite.org