DRAFT COMMON STANDARDS FOR CELLULAR THERAPIES

FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY

Fourth Edition

NOTICE

These Standards are designed to provide minimum guidelines for programs, facilities, and individuals performing cellular therapy or providing support services for such procedures. These Standards are not intended to establish best practices or include all procedures and practices that a program, facility, or individual should implement if the standard of practice in the community or applicable governmental laws establish additional requirements. Each program, facility, and individual should analyze its practices and procedures to determine whether additional standards apply. Compliance with these Standards is not an exclusive means of complying with the standard of care in the industry or community or with local, national, or international laws.

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ACKNOWLEDGEMENTS

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PART A: TERMINOLOGY, TENETS, ABBREVIATIONS, AND DEFINITIONS

A1 TERMINOLOGY

A1.1 For purposes of these Standards, the term "shall" means that the ~~s~~Standard is to be complied with at all times. The term "should" indicates an activity that is recommended or advised, but for which there may be effective alternatives. The term "may" is permissive and is used primarily for clarity.

A1.2 The phrase, "policies and Standard Operating Procedures," is used for ease of reading. When referring to a single document, either a policy or Standard Operating Procedure is sufficient.

A2 TENETS

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

A2.1 Where Applicable Law includes more stringent requirements than these Standards, Applicable Law supersedes the Standards. Conversely, when these Standards are more stringent than Applicable Law, these Standards shall be followed.

A2.2 Any activity can be delegated to an appropriate designee as that term is defined. The person appointing a designee retains ultimate responsibility.

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

~~A2.4 For the purposes of this document, the term "cellular therapy product" shall be understood to include therapeutic products composed of living cells intended for the treatment, prevention, or diagnosis of disease in humans.~~

A2.4 Good Documentation Practices are a set of systematic procedures to ensure reliable, traceable transfer of information.

A3 ABBREVIATIONS

The following abbreviations cover terms used in these Standards:

ABO	Major human blood group including erythrocyte antigens, A, B, O
AC	Accompany
AF	Affix
Anti	Antibody to the designated antigen
APP	Advanced Practice Provider/Professional
ASHI	American Society for Histocompatibility and Immunogenetics
ASTCT	American Society for Transplantation and Cellular Therapy
AT	Attached
CAP	College of American Pathologists
CFR	Code of Federal Regulations
~~*CIDR*~~	~~Cellular Immunotherapy Data Resource~~
DNA	Deoxyribonucleic acid
EBMT	European Society for Blood and Marrow Transplantation
EFI	European Federation for Immunogenetics
EU	European Union
FACT	Foundation for the Accreditation of Cellular Therapy
FDA	U.S. Food and Drug Administration
GMP	Good Manufacturing Practice
GxP	Good practice
HCT/P	Human cells, tissues, and cellular and tissue-based products
HLA	Human leukocyte antigen
~~*HPC*~~	~~Hematopoietic progenitor cell~~
IBC	Institutional Biosafety Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ISCT	International Society for Cell and Gene Therapy
JACIE	Joint Accreditation Committee – ISCT and EBMT
MNC	Mononuclear cell
QM	Quality management
RBC	Red blood cell
Rh	Rhesus systems of human red blood cell antigens; used in this document to refer to the Rh (D) antigen only, unless otherwise specified
SOP	Standard Operating Procedure
U.S.	United States

A4 DEFINITIONS

Accompany: To go, be together with, or be available to the appropriate individual(s) electronically, but not affixed or attached. Written or printed information that must accompany a cellular therapy product must be in a sealed package with, or alternatively, be attached or affixed to, the cellular therapy product container.

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

Acuity: The severity of a patient's illness or condition, indicating the level of care and resources required.

Advanced Degree: A degree beyond a bachelor's degree in a biological or related science.

Advanced practice provider/professional (APP): Physician Assistant, Nurse Practitioner, or other licensed Advanced Practitioner authorized by the applicable legal authority to provide primary patient care with physician oversight ~~as defined by Applicable Law~~. Physician Assistants are formally trained and licensed or certified by the applicable authority to provide diagnostic, therapeutic, and preventive health care services with physician supervision. Advanced Nurse Practitioner includes certified nurse anesthetists, nurse practitioners, certified nurse midwives, and clinical nurse specialists.

Adverse event: Any unintended or unfavorable sign, symptom, abnormality, or condition temporally associated with an intervention 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 suspected or demonstrated to be caused by the collection or administration of a cellular therapy product or by the product itself.

Affix: To adhere in physical contact with the cellular therapy product container.

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

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

Apheresis: A medical technology in which the blood of a donor is separated into its component parts, the desired component is removed, and the remaining components are returned to the donor.

Applicable Law: Any local, national, or international statute, regulation, or other governmental law that is applicable to cellular therapy product collection, processing~~,~~ and~~or~~ administration ~~and~~ that is relevant to the location or activities of the Clinical Program, Collection Facility, or Processing Facility.~~organization.~~

Aseptic technique: Practices designed to reduce the risk of microbial contamination of cellular therapy products, reagents, specimens, recipients, or~~and~~ donors.

Assent: The expression of approval or agreement by someone who is not able to give legal consent to participate in an activity.

Attach: To fasten securely to the cellular therapy product container by means of a tie tag or comparable alternative. Any information required to be attached to a cellular therapy product container may alternatively be affixed.

Attending physician: The physician who is responsible for the delivery and oversight of care provided to cellular therapy recipients and who meets all qualifications defined in these Standards. For purposes of these Standards, this does not include physicians who do not provide cellular therapy services.

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

Autologous: Derived from and intended for the same individual.

Available for distribution: The time at which the cellular therapy product may leave the control of the facility.

Calibrate: To set measurement equipment against a known standard.

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

Cellular therapy product: Somatic cell or tissue-based product (e.g., therapeutic) ~~HPC, mononuclear cells, cord blood cells, immune effector cells, genetically modified cells, and others)~~ that is processed or manufactured to produce a therapeutic effect in a patient.~~procured from a donor and intended for processing or administration.~~

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

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

Chimerism: The coexistence of cells of more than one genotype in a single individual. ~~In cellular therapy, chimerism generally refers to the presence of allogeneic donor cells in the recipient.~~

Chimerism testing: Assessment of the presence of allogeneic donor cells in a cellular therapy product recipient using any assay of informative genetic markers that distinguishes donor from recipient cells.

Circular of Information: An extension of container labels that includes the use of the cellular therapy product, indications, contraindications, side effects and hazards, dosage, and administration recommendations. An investigator's brochure or package insert may contain this information.

Clinical Program: A~~n integrated~~ medical team ~~providing cellular therapy services and~~ housed in a defined location that typically includes a Clinical Program Director and demonstrates common staff training, ~~protocols,~~ Standard Operating Procedures, quality management systems, and clinical outcome analysis~~, and regular interaction among clinical sites~~.

Clinical Site: Any physical location where a patient or donor receives care, including inpatient, outpatient, ambulatory care facilities, and other locations. A clinical program may consist of more than one clinical site. Clinical sites can be in one or more hospitals or institutions.

Collection: Any procedure for procuring and labeling a cellular therapy product regardless of technique or source.

Collection Facility: An entity providing the service of collecting the initial cells or tissues to be used in the manufacturing of cellular therapy productsular therapy product collection.

Collection kit: A defined set of supplies, materials, and/or devices assembled and provided for the purpose of performing a cellular therapy product collection. A collection kit may be provided as a single packaged unit or as coordinated components and shall include the items necessary to support the intended collection method, product type, and transport requirements.

Collection Site: The physical location at which cells or tissues are collected.

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

Complaint: Any written, oral, or electronic communication about a problem associated with a cellular therapy product; or with a service related to the collection, processing, storage, distribution, or administration of a cellular therapy product; or clinical care.

Consent process: The process in which a healthcare professional educates a patient about the risks, benefits, and alternatives of a given procedure or intervention and obtains their permissionconsent to proceed with therapy in accordance with applicable law.

Continuum of care: The delivery of health care over a period of time. In patients with a disease, this covers all phases of illness from diagnosis to the end of life.

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

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

Corrective Action Plan: A document describing the step-by-step plan of action to achieve a defined outcome or resolution of an identified occurrence or noncompliance.

Courier: An individual trained and competent in transport or shipping of cellular therapy products.

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

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

Deviation: The action of departing from an approved process or an established course of action ~~or accepted practice~~.

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

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

Distribution: Any transportation or shipment of a cellular therapy product that has been determined to meet release criteria or urgent medical need requirements.

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

Donor advocate: An individual distinct from the cellular therapy recipient's primary treating physician whose main obligation is to protect the interests, well-being, and safety of the donor. The donor advocate may help the donor understand the process, the procedures, and the potential risks and benefits of donation.

Effective date: The day the new version of a document has been implemented and the previous version has been recalled or archived.

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

Critical electronic record: Electronic record system under facility control that is used as a substitute for paper, to make decisions, to perform calculations, or to create or store information used in critical procedures.

Eligible: An allogeneic cellular therapy product donor for whom all the donor screening and testing have been completed in accordance with Applicable Law and who has been determined to be free of risk factor(s) for relevant communicable diseases~~ agents~~.

Errors and accidents: Any unforeseen or unexpected deviations from applicable regulations, standards, or established specifications that may affect the safety, purity, or potency of a cellular therapy product.

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

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

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

Genetically modified cell: A cell that has been modified by genetic transfer or edited for therapeutic intent.

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

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

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

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

Human cells, tissues, and cellular and tissue-based products (HCT/Ps): Materials containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.

Immune effector cell (IEC): A cell that has differentiated or manufactured into a form capable of modulating or effecting a specific immune response.

Ineligible: An allogeneic cellular therapy product donor for whom all ~~the~~ donor screening and testing has been completed in accordance with ~~the~~ Applicable Law and who has identified risk factor(s) for relevant communicable diseases.

Institutional Review Board (IRB) or Ethics Committee: A Board or Committee established by an institution in accordance with the regulations of the relevant governmental agency to review biomedical and behavioral research that involves human subjects and is conducted at or supported by that institution.

Investigator's Brochure: A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects. Its purpose is to provide the investigators and others involved in the trial with the information to facilitate their understanding of the rationale for, and their compliance with, many key features of the protocol, such as the dose, dose frequency interval, methods of administration, and safety monitory procedures. The Investigator's Brochure also provides insight to support the clinical management of the study subjects during the course of the clinical trial.

ISBT 128: A global standard for the identification, labeling, and information transfer of ~~human blood, cell, tissue, and organ~~medical products of human origin published and maintained by ICCBBA.

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

Label: Written, printed, or graphic material affixed to, attached to, or accompanying a cellular therapy product container or package. Labels must contain the information as defined by applicable standards, laws, and regulations.

Labeling: The process of creating and applying the cellular therapy product label, including confirmation of the presence and accuracy of the required information as defined in these Standards.

Late effect: A health problem that occurs months or years after a disease is diagnosed or after treatment has been administered. Late effects may be caused by the primary disease or its treatment, and may include physical, mental, or social problems and/or secondary cancers.

Licensed health care professional: An individual who has completed a prescribed program of health-care related study and has been certified, registered, or licensed by the applicable authority in the jurisdiction in which ~~he or she is~~ they are performing services to perform duties within the scope of practice of that certificate, registration, or license.

Manipulation: An ex vivo procedure(s) that selectively removes, enriches, expands, or functionally alters the cellular therapy product.

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

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

Unmanipulated: A cellular therapy product as obtained at collection and not subjected to any form of processing.

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

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

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

New recipient: An individual ~~receiving~~ undergoing cellular therapy treatment for the first time in the Clinical Program whether or not that individual was previously treated by that Clinical Program.

Occurrence: An instance in which an action or circumstance results in errors, accidents, deviations, adverse events, adverse reactions, or complaints.

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

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

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

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

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

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

Periodic: Occurring at time intervals specifically defined by the organization as appropriate.

Physician-in-training: A physician in one of the postgraduate years of clinical training. Can be referred to as resident, fellow, registrar, or other designation, depending on the setting. The length of training varies according to the specialty.

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

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

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

Preventive action: Action taken to eliminate or mitigate identifiable ~~the~~ causes and prevent occurrence of a potential discrepancy or other undesirable situation.

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

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

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

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

Processing Facility: A location where cellular therapy product processing activities are performed in support of the~~a~~ Clinical Program. A Processing Facility may be part of the same institution as the Clinical Program or may be part of another institution and perform these functions through contractual agreement.

Product code: An eight-character ISBT 128 code that comprises the Product Description Code, a Collection Type Code, and a Division Code. The product code, combined with the donation identification number and facility processing code, if applicable, makes each product globally unique.

Product name: The ISBT 128 Cellular Therapy Class product database name and definition (format: type of cells, comma, source of cells) for products of human origin. The most up-to-date list of definitions is available on ICCBBA's website at ISBT 128 Standard Terminology for Medical Products of Human Origin.~~collected from marrow, peripheral blood, cord blood, or other tissue.~~

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

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

~~For the most current list of definitions, see www.isbt128.org/standard-terminology.~~

Product sample: A representative quantity of product removed from the cellular therapy product; an aliquot.

Proficiency test: A test to evaluate the adequacy of testing methods and equipment and the competency of personnel performing testing.

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

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

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

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

Quality: Conformance of a product or process with 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 or exceed expectations individually and collectively.

Quality improvement: The actions, planned and performed, to implement changes designed to improve the quality of a product or process.

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

Quality Management Plan (QM Plan): A written document that describes the systems in place to implement the Qq~~q~~uality ~~m~~Management ~~p~~Program.

Quality M~~m~~anagement ~~p~~Program (QM Program): An organization's comprehensive system of quality assessment, assurance, control, and improvement. A quality management program is designed to prevent, detect, and correct deficiencies that may adversely affect the quality of the cellular therapy product or increase the risk of communicable disease introduction or transmission. May also be referred to by other terms.

~~*Quality Unit*: Personnel with responsibility for and authority to approve or reject in-process materials, cellular therapy product containers, packaging material, labeling, and cellular therapy products.~~

Quarantine: The identification or storage of a cellular therapy product 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 infectious disease agents to reduce the likelihood of cross-contamination.

Record: Documented evidence that activities have been performed or results have been achieved. A record does not exist until the activity has been performed.

Registry: An organization responsible for the coordination of the search for cellular therapy product donors (including cord blood) unrelated to the potential recipient.

Release: Removal of a product from quarantine or in-process status when it meets specified criteria.

Release criteria: The requirements that must ~~have been~~be met before a cellular therapy product may leave the control of the Collection or Processing Facility.

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

~~*Risk management plan*: A document that describes the current knowledge about the safety and efficacy of a cellular therapy product and the measures to be undertaken to identify, monitor, prevent, or minimize risk associated with the use of that product.~~

~~*Risk Evaluation and Mitigation Strategy (REMS):* A drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.~~

Risk assessment: The process of identifying potential hazards, evaluating the likelihood and severity of harm, and deciding on appropriate measures to control or eliminate the risk.

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

Shipping: The physical act of transferring a cellular therapy product within or between facilities. During shipping the product leaves the control of trained personnel at the distributing or receiving facility.

Standard Operating Procedure (SOP): A document that describes in detail the process or chronological steps taken to accomplish a specific task. Also referred to as work instructions. An SOP is more specific than a policy. ~~Also referred to as work instructions.~~

Standard Operating Procedures (SOP) Manual: A compilation of policies and Standard Operating Procedures with written detailed instructions required to perform procedures. The SOP Manual may be in electronic or paper format.

Standards: The current edition of the FACT Common Standards for Cellular Therapies, which may be referred to herein as "these Standards."

Storage: Holding a cellular therapy product for future processing, distribution, or administration.

Suitable: Donor or recipient suitability refers to issues that relate to the general health or medical fitness of the donor or recipient to undergo the collection procedure or therapy.

Target cell population: A cell population that is expected to be affected by an action or that is believed to be mainly responsible for a given activity.

Third-party manufacturing: Outsourcing of part or all of the manufacturing of a cellular therapy product to a facility separate from the facilities primarily involved.

Time of collection: The time of day at the end of the cellular therapy product collection procedure.

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

Traceability: The ability to track any product through all stages of collection, processing, and administration so that tasks can be traced one step backwards and one step forward at any point in the supply chain.

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

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

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

Unique identifier: A numeric or alphanumeric sequence used to designate a given cellular therapy product with reasonable confidence 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 cellular therapy product meeting its predetermined specifications.

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

Verification typing: HLA typing performed on an independently collected sample with the purpose of verifying concordance of that typing assignment with the initial HLA typing assignment. Concordance does not require identical levels of resolution for the two sets of typing but requires the two assignments to be consistent with one another.

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

Written: Documentation in human readable form.

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PART B: CLINICAL PROGRAM STANDARDS

B1: General

B2: Clinical Unit

B3: Personnel

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B6: Allogeneic and Autologous Donor Selection, Evaluation, and Management

B7: Recipient Care

B8: Clinical Research

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B10: Records

PART B: CLINICAL PROGRAM STANDARDS

B1: GENERAL

B1.1 The Clinical Program shall consist of an integrated medical team with a Clinical Program Director(s) and a defined location(s).

B1.1.1 These Standards apply to all cellular therapy services provided by the Clinical Program.

B1.1.2 The Clinical Program shall demonstrate common staff training, protocols, Standard Operating Procedures, quality management systems, clinical outcome analysis, and regular interaction among all clinical sites.

B1.2 The Clinical Program shall abide by Applicable Law.

B1.2.1 The Clinical Program shall be licensed, registered, or accredited as required by the appropriate governmental authorities for the activities performed.

B1.3 The Clinical Program shall have a designated team that includes a Clinical Program Director, a Quality Manager, and a minimum of one (1) additional physician trained or experienced in cellular therapy. ~~The designated team shall have been in place and performing cellular therapy for at least twelve (12) months preceding initial accreditation.~~

B1.4 Clinical Programs directly ~~If the Clinical Program is~~ responsible for cell collection or processing ~~these~~ activities shall comply with the Standards in~~,~~ Parts C and D as applicable~~apply~~.

B1.5 The Clinical Program shall ~~verify~~ use ~~that~~ cell collection procedures and processing facilities that meet FACT Standards with respect to their interactions with the Clinical Program.

~~B1.4.1 If clinical personnelthe Clinical Program or an intermediary facility receives cellular therapy products directly from a third-party provider, the following responsibilities shall be defined by a written agreement:~~

B1.6 If the Clinical Program or an intermediary facility receives cellular therapy products directly from a third-party provider, the following responsibilities shall be defined in policies, Standard Operating Procedures, and written agreements:

B1.6.1 Traceability and C~~c~~hain of C~~c~~ustody of cellular therapy products.

B1.6.2 Cellular therapy product storage and ~~distribution~~ transportation (Sections D9 and D10 apply).

B1.6.3 Cellular therapy product distribution for administration (Section D11 applies).

B1.6.4 Verification of cellular therapy product identity.

B1.6.5 Review and verification of cellular therapy product specifications provided by the manufacturer, if applicable.

B1.6.6 Readily available access to a summary of documents used to determine allogeneic donor eligibility.

B1.6.7 Documented evidence of allogeneic donor eligibility screening and testing in accordance with Applicable Law.

B1.7 The Clinical Program shall have administered cellular therapy products to a minimum of five (5) new recipients during the twelve (12) month period immediately preceding accreditation and shall administer to a minimum average of five (5) new recipients per year within the accreditation cycle.

B2: CLINICAL UNIT

B2.1 There shall be a designated inpatient unit of appropriate location and adequate space and design that protects the patient from transmission of infectious agents and allows for appropriate patient isolation, confidential examination, and evaluation.~~A clinical unit of adequate space, design, and location shall be identified for the treatment of patients needing inpatient or outpatient care related to the cellular therapy.~~

B2.2 There shall be designated ~~inpatient and~~ outpatient care areas that protect the patient from transmission of infectious agents and allow, as necessary, for appropriate patient isolation; confidential examination and evaluation; and preparation and administration of intravenous fluids, medications, blood products, and cellular therapy products.

B2.3 When the preparative regimen, cellular therapy product administration, or initial post-transplant and cellular therapy care is provided in an ambulatory setting, there shall be a designated area in an appropriate location and adequate space and design to minimize the risk of microbial contamination.

~~B2.4 There shall be 24-hour access to care for assessment and treatment of potential cellular therapy complications.~~

B2.4~~.1~~ There shall be provisions for prompt evaluation and treatment by a physician who specializes in the therapeutic disease area and is trained in cellular therapy and available on a 24-hour basis.

B2.5 The Clinical Program shall document facility cleaning and sanitation and maintain order sufficient to achieve adequate conditions for operation.

B2.6 The Clinical Program shall be operated in a manner designed to minimize risks to the health and safety of all individuals.

B2.7 The Clinical Program shall have a written safety manual that includes instructions for action in case of exposure, as applicable, to liquid nitrogen; communicable disease; and to chemical, biological, radiological, electrical, or fire hazards.

B2.8 All waste generated by Clinical Program activities shall be disposed of in a manner that minimizes any hazard to facility personnel and to the environment in accordance with Applicable Law.

B2.9 There shall be a written policy for personal hygiene and the use of personal protective equipment and attire.

B2.9.1 The policy shall define the protective clothing to be worn upon entering the work area and while working within it.

B2.9.2 The policy shall define personal protective equipment appropriate for the activities and classification of the environment to be worn while handling biological specimens.

B2.9.3 Such personal protective equipment shall not be worn outside the designated work area.

B2.10 There shall be adequate equipment and materials for the procedures performed.

B2.11 There shall be access to an intensive care unit or emergency services.

B2.11.1 There shall be written guidelines for communication, patient monitoring, and prompt triage or transfer of patients to an intensive care unit, emergency department, or equivalent when appropriate.

B2.12 There shall be a pharmacy providing 24-hour availability of medications needed for the care of cellular therapy patients.

B2.12.1 The pharmacy shall have prompt access to medications adequate to treat expected complications of cellular therapy, including cytokine release syndrome (CRS), for each recipient of a cellular therapy product.

B2.13 There shall be access to renal support, such as dialysis, under the direction of nephrologists and trained personnel.

B2.14 There shall be 24-hour availability of Cytomegalovirus (CMV)-appropriate and irradiated blood products or equivalent needed for the care of cellular therapy recipients.

B2.15 There shall be attending physician oversight if general medical physicians or APPs provide care to cellular therapy patients. The scope of responsibility of general medical physicians or APPs shall be defined.

B2.16 Clinical Programs administering cellular therapies shall use laboratories that are accredited, registered, certified, or licensed in accordance with Applicable Law.

~~B2.10 All waste generated by Clinical Program activities shall be disposed of in a manner that minimizes any hazard to facility personnel and to the environment in accordance with Applicable Law.~~

~~B2.11 Personal protective equipment, including gloves and protective clothing, shall be used while handling biological specimens. Such protective equipment shall not be worn outside the work area.~~

B2.17 Clinical Programs shall use human leukocyte antigen (HLA) testing laboratories, if applicable, that are capable of carrying out DNA-based intermediate and high resolution HLA typing and are appropriately accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), College of American Pathologists (CAP), or other accrediting organizations providing histocompatibility services appropriate for the types of cellular therapy patients.

B2.18 Testing to monitor chimerism, if applicable, shall be performed in laboratories accredited for the techniques used.

B3: PERSONNEL

B3.1 CLINICAL PROGRAM DIRECTOR

B3.1.1 The Clinical Program Director shall be a physician appropriately licensed to practice medicine in the jurisdiction in which the Clinical Program is located, shall have experience in cellular therapy or administration of the therapeutic product, and shall have achieved specialty~~ist~~ certification in at least one applicable therapeutic disease area. A physician trained prior to requirements for specialty training may serve as the Clinical Program Director if ~~he/she has~~they have documented experience in the applicable therapeutic disease areas extending over ten (10) years.

B3.1.1.1 The Clinical Program Director shall have a minimum of two (2) years of experience as an attending physician responsible for the direct clinical management of patients in the applicable therapeutic disease areas throughout the continuum of care.

B3.1.2 The Clinical Program Director shall be responsible for administrative and clinical operations, including compliance with these Standards and Applicable Law.

B3.1.3 The Clinical Program Director shall be responsible for all elements of the design of the Clinical Program including quality management, the selection and care of recipients and donors, and cell collection and processing, whether internal or contracted services.

B3.1.4 The Clinical Program Director shall have oversight of the medical care provided by all members of the Clinical Program.

~~B3.1.5.1 The Clinical Program Director shall be responsible for defining physician responsibilities and verifying adequate training and education for all members of the Clinical Program.~~

B3.1.4.1 The Clinical Program Director shall be responsible for verifying competency of members of the Clinical Program annually.

B3.1.5 The Clinical Program Director shall participate in a minimum of ten (10) hours annually of educational activities related to cellular therapy.

~~B3.1.6.1 Continuing education shall include, but is not limited to, activities related to the specific cellular therapy administered within the Clinical Program.~~

B3.2 ATTENDING PHYSICIANS

B3.2.1 Attending physicians shall be appropriately licensed to practice medicine in the jurisdiction of the Clinical Program and should be specialist certified or trained in the applicable therapeutic disease areas.

B3.2.1.1 There shall be at least one (1) attending physician who has achieved specialist certification in each applicable therapeutic disease area.

B3.2.2 Attending physicians shall each have had a minimum of one year of supervised training in the management of patients in the applicable therapeutic disease area throughout the continuum of care.

B3.2.3 Clinical Programs treating pediatric recipients or donors shall have a team trained in the management of pediatric patients.

~~B3.2.4 Clinical Programs treating adult recipients or donors shall have a team trained in the management of adult patients.~~

B3.2.4 Attending physicians shall participate in a minimum of ten (10) hours annually of educational activities related to cellular therapy.

~~B3.2.5.1 Continuing education shall include, but is not limited to, activities related to the specific cellular therapy administered within the Clinical Program.~~

B3.3 TRAINING FOR CLINICAL PROGRAM DIRECTORS AND ATTENDING PHYSICIANS

B3.3.1 Clinical Program Directors and attending physicians shall have received specific training in each of the following areas as applicable to the Clinical Program's services:

B3.3.1.1 Indications for cellular therapy.

B3.3.1.2 Selection of suitable recipients and appropriate cellular therapy products and preparative regimens.

B3.3.1.3 Donor selection, evaluation, and management.

B3.3.1.4 Donor and recipient informed consent.

~~B3.3.1.5 Administration of cellular therapy products and anticipated complications.~~

B3.3.1.~~6~~5 Selection and Administration of the preparative regimen.

B3.3.1.6 Administration of cellular therapy products.

~~B3.3.1.7 Adverse events associated with cellular therapy.~~

B3.3.1.7 Management of complications related to the administration of cellular therapy products.

B3.3.1.8 Evaluation and management of post-treatment cellular therapy outcomes.

B3.3.1.9 Evaluation of late effects of cellular therapy.

B3.3.1.10 Documentation and reporting for patients on investigational protocols.

B3.3.1.11 Reporting responsibilities for adverse events according to Applicable Law.

B3.3.2 If applicable to the cellular therapy product, specific training required for physicians in Clinical Programs requesting accreditation for allogeneic cellular therapy shall include:

B3.3.2.1 Identification, evaluation, and selection of cell source, including use of donor registries.

B3.3.2.2 Donor eligibility determination.

B3.3.2.3 Methodology and implications of HLA typing.

B3.3.2.4 Methodology and implications of testing for chimerism.

B3.3.2.5 Management of patients receiving ABO-incompatible cellular therapy products.

B3.3.25.6 Diagnosis and management of acute and chronic Graft versus Host Disease (GVHD).

B3.3.3 The attending physicians shall be knowledgeable in the following procedures ~~for cellular therapy products~~:

B3.3.3.1 Cellular therapy product collection, including apheresis and bone marrow harvest.

B3.3.3.2 Cellular therapy product processing, including washing and diluting.

B3.3.3.3 Genetic modification of cells and impact on patient care.

B3.3.3.4 Cellular therapy product cryopreservation.

B3.3.3.5 Extracorporeal photopheresis (ECP) for GVHD.

B3.3.3.6 Therapeutic apheresis.

B3.4 PHYSICIANS-IN-TRAINING

B3.4.1 Physicians-in-training shall be licensed to practice in the jurisdiction of the Clinical Program and shall be limited to a scope of practice within the parameters of their training and licensure and shall be appropriately supervised.

~~B3.4.2 Physicians-in-training shall receive specific training and develop competence in patient management and cellular therapy-related skills included within, but not limited to, those listed in B3.3.1 and B3.3.2.~~

B3.5 ADVANCED PRACTICE PROVIDERS/PROFESSIONALS (APPs)

B3.5.1 APPs shall be licensed to practice in the jurisdiction of the Clinical Program and shall be limited to a scope of practice within the parameters of their training and licenses.

B3.5.2 APPs shall have received specific training and maintain competence in patient management and cellular therapy-related skills included within, but not limited to, those listed in B3.3.1 and B3.3.2.

B3.5.3 APPs shall participate in a minimum of ten (10) hours annually of educational activities related to cellular therapy.

~~B3.5.3.1 Continuing education shall include, but is not limited to, activities related to the specific cellular therapy administered within the Clinical Program.~~

B3.6 NURSES

B3.6.1 The Clinical Program shall have nurses formally trained and experienced in the management of patients receiving cellular therapy~~in the therapeutic disease areas~~.

B3.6.1.1 Nurses shall be trained in age-specific management of patients receiving cellular therapy.

B3.6.1.2 Clinical Programs treating pediatric recipients or donors shall have nurses formally trained and experienced in the management of pediatric patients receiving cellular therapy.

B3.6.2 Nurses shall have received specific training and maintain competence in the cellular therapy-related skills that they practice, including:

B3.6.2.1 Care of patients in the therapeutic disease area.

B3.6.2.2 Administration of preparative and lymphodepletion regimens ~~medications~~.

B3.6.2.3 Administration of cellular therapy products, including IEC, genetically modified cells, and other cellular therapies.

B3.6.2.4 Administration of blood products, growth factors, cytokines, and other supportive therapies.

B3.6.2.5 Recognition of cellular therapy-related complications and emergencies requiring rapid notification of the clinical team.

B3.6.2.6 Care interventions to manage cellular therapy-related complications.

B3.6.2.7 Palliative and end of life care.

B3.6.3 There shall be an adequate number of nurses experienced in the care of patients in the applicable therapeutic disease areas.

B3.6.4 There shall be a nurse/recipient ratio satisfactory to manage the severity of the recipients' clinical status.

B3.7 PHARMACISTS

B3.7.1 Pharmacists shall be licensed to practice in the jurisdiction of the Clinical Program and shall be limited to a scope of practice within the parameters of their training and licensure.

B3.7.2 Training and knowledge of designated pharmacists shall include:

B3.7.2.1 An overview of the process of cellular therapy.

B3.7.2.2 Pharmacological management of expected complications, if applicable.

B3.8 CONSULTING SPECIALISTS

B3.8.1 The Clinical Program shall define and have access to certified or trained consulting specialists or specialist groups from key disciplines who are capable of assisting in the management of recipients or donors requiring medical care.

B3.8.2 A Clinical Program treating pediatric recipients or donors shall define and have access to consultants qualified to manage pediatric patients.

B3.9 QUALITY MANAGER

B3.9.1 There shall be a Clinical Program Quality Manager to establish and maintain systems to review, modify, and approve all policies and Standard Operating Procedures intended to monitor compliance with these Standards, Applicable Law, or the performance of the Clinical Program.

B3.9.2 The Clinical Program Quality Manager should have a reporting structure that is independent of clinical program operations.

B3.9.3 The Clinical Program Quality Manager shall participate in a minimum of ten (10) hours annually of educational activities related to cellular therapy, cell collection, or quality management.

B3.10 DATA MANAGEMENT STAFF

B3.10.1 There shall be data management staff sufficient to comply with B9.

B3.10.2 Defined data management staff shall participate annually in a minimum of five (5) hours of continuing education related to cellular therapy and data management.

B3.11 SUPPORT SERVICES STAFF

B3.11.1 The Clinical Program shall have ~~one or more designated~~access to support services ~~staff~~ with appropriate training and education to assist in the provision of pre-cellular therapy recipient evaluation, treatment, and post-cellular therapy follow-up. Support services shall include: ~~product administration, and follow-up care.~~

B3.11.1.1 Social services.

B3.11.1.2 Psychosocial services.

B3.11.1.3 Physical therapy services.

~~B3.10.1.1 Designated staff shall include data management staff.~~

B4: QUALITY MANAGEMENT

B4.1 There shall be an overall Quality Management Program that incorporates key performance data from clinical, collection, and processing activities.

B4.1.1 The Clinical Program Director shall have authority over and responsibility for ensuring that the overall Quality Management Program is effectively established, documented, and maintained.

B4.2 The Clinical Program shall establish and maintain a written Quality Management Plan (QM Plan).

B4.2.1 Clinical Program activities shall be performed in compliance with a written Quality Management Plan.

B4.2.2 The Clinical Program Director shall be responsible for the overall Quality Management Plan.

B4.3 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, an organizational chart of key positions, functions, and reporting relationships within the cellular therapy program, including clinical, collection, and processing activities.

B4.3.1 The ~~Quality Management Plan~~QM Plan shall include a description of how these key positions interact to implement the quality management activities.

B4.4 The QM Plan should include or summarize and reference a listing of third-party manufacturers with whom they interact to include description of scope and services provided.

~~B4.3.23 There shall be written guidelines for communication between the Clinical Program and collection or registry personnel for the management of collection-related complications.~~

B4.5 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures addressing personnel requirements for each key position in the Clinical Program. Personnel requirements shall include at a minimum:

B4.5.1 A current job description for all staff.

B4.5.2 A system to document the following for all ~~staff~~key positions:

B4.5.2.1 Initial qualifications.

B4.5.2.2 New employee orientation.

B4.5.2.3 Initial training, competency, and retraining when appropriate for all procedures performed.

B4.5.2.4 Continued competency for each critical function performed, assessed annually at a minimum.

B4.5.2.5 Annual training in applicable current GxP appropriate to the processes performed.

B4.5.2.6 Continuing education.

B4.6 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, a comprehensive system for document control.

B4.6.1 There shall be identification of the types of documents that are considered critical and shall comply with the document control system requirements. Controlled documents shall include at a minimum:

B4.6.1.1 Policies, protocols, ~~and~~ Standard Operating Procedures, and job aids.

B4.6.1.2 Worksheets.

B4.6.1.3 Forms.

B4.6.1.4 Labels.

B4.6.2 There shall be policies or Standard Operating Procedures for development, approval, implementation, distribution, review, revision, and archival of all ~~critical~~ controlled documents.

B4.6.3 The document control system shall include:

B4.6.3.1 A standardized format for ~~critical~~ controlled documents.

B4.6.3.2 Assignment of a numeric or an alphanumeric identifier, version, and a title to each controlled document ~~and document version regulated within the system~~.

B4.6.3.3 A system for document approval, including the approval date, signature of approving individual(s), and the effective date.

B4.6.3.4 A system to protect controlled documents from accidental or unauthorized modification.

B4.6.3.5 Review of controlled documents every two (2) years at a minimum.

B4.6.3.6 A system for document change control that includes a description of the change, version, the signature of approving individual(s), approval date(s), communication or training on the change~~s~~ as applicable, effective date, and archival date.

B4.6.3.7 A system for ~~A~~archival of controlled documents, the inclusive dates of use, and their historical sequence for a minimum of ten (10) years from archival or according to governmental or institutional policy, whichever is longer.

B4.6.3.8 A system for the retraction of obsolete documents to prevent unintended use.

B4.7 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the establishment and maintenance of written agreements.

B4.7.1 Agreements shall be established with external parties providing critical services that could affect the quality and safety of the cellular therapy product or health and safety of the donor or recipient.

B4.7.2 Agreements shall include the responsibility of the external party performing any step in collection, processing, testing, storage, distribution, or administration to provide clinically relevant information, to maintain required accreditations and to comply with these Standards and Applicable Law.

~~B4.6.2.1 Agreements should include the responsibility of the external parties to provide clinically relevant information related to products or services.~~

B4.7.3 Agreements shall be dated and reviewed on a regular basis, at a minimum every two (2) years.

B4.8 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for documentation and review of outcome analysis and cellular therapy product efficacy to verify that the procedures in use consistently provide a safe and effective product.

B4.8.1 Criteria for cellular therapy product safety, efficacy, and the clinical outcome, as appropriate, shall be determined for each type of cellular therapy product, recipient diagnosis, and donor type and shall be reviewed at regular time intervals.

B4.8.2 Investigation should be performed when key outcomes are not met to include processing and collection facility review.

B4.8.3 Both individual cellular therapy product data and aggregate data shall be evaluated for each type of cellular therapy product ~~and recipient type shall be evaluated~~.

B4.8.4 Review of outcome analysis and~~/or~~ product efficacy shall include at a minimum:

B4.8.4.1 An endpoint of clinical function as approved by the Clinical Program Director.

B4.8.4.2 Overall and treatment-related morbidity and mortality at thirty (30) days, one hundred (100) days, and one (1) year after cellular therapy product administration or in accordance with Applicable Law.

B4.8.5 Data on outcome analysis and cellular therapy product efficacy, including adverse events related to the recipient, donor, or product, shall be provided in a timely manner to entities involved in the collection, processing, or distribution of the cellular therapy product.

B4.9 The Quality Management Plan shall include, or summarize and reference, policies, Standard Operating Procedures for, and a schedule of, audits of the Clinical Program's activities to verify compliance with the Quality Management Program, operational policies and Standard Operating Procedures, these Standards, and Applicable Law.

B4.9.1 Clinical Program ~~A~~audits shall be conducted by an individual with ~~sufficient~~ knowledge ~~of~~in the process and competence in auditing to identify problems, but who is not solely responsible for the process being audited.

B4.9.2 An audit plan for each audit shall include the elements listed in Appendix IV.

~~B4.8.2.1 Title.~~

~~B4.8.2.2 Role of the individual(s) to complete the audit.~~

~~B4.8.2.3 Audit purpose.~~

~~B4.8.2.4 Audit scope.~~

~~B4.8.2.5 Documentation of review and approval by the Clinical Program Director and the Quality Manager.~~

B4.9.3 An audit report shall include the elements listed in Appendix IV.

~~B4.8.3.1 Approved audit plan.~~

~~B4.8.3.2 Identification of auditor.~~

~~B4.8.3.3 Date started and completed.~~

~~B4.8.3.4 Records or processes audited.~~

~~B4.8.3.5 Summary of results to include findings, assessment of the underlying cause of errors, recommendations, and conclusions.~~

~~B4.8.3.6 Plan for follow-up, if appropriate, including a timeline.~~

~~B4.8.3.7 Documentation of review and approval by the Clinical Program Director and Quality Manager.~~

B4.9.4 The results of Clinical Program audits shall be used to recognize problems, detect trends, identify improvement opportunities, implement corrective and preventive actions (CAPAs) when necessary, and follow up on the effectiveness of these actions in a timely manner.

B4.9.5 Clinical Program A~~a~~udits shall be performed annually at a minimum, and shall include at least the following:

B4.9.5.1 Accuracy of clinical data.

B4.9.5.2 ~~Documentation of proper donor eligibility and suitability~~ Donor screening and testing~~determination~~according to, or Applicable Law~~.~~.

B4.9.5.3 Management of cellular therapy products with positive microbial culture results.

~~B4.8.3.4 Infectious disease resulting from cellular therapy product collection or administration.~~

B4.9.5.4 Documentation that each external facility~~ies~~ performing critical contracted services has met the requirements of the written agreements.

B4.9.5.5 Chain of I~~i~~dentity and C~~c~~hain of C~~c~~ustody of cellular therapy products.

B4.9.6 Additional audits shall be performed as part of a risk-based approach to the follow-up of occurrences.

B4.10 The QM ~~p~~Plan shall include, or summarize and reference, ~~re shall be~~ policies or Standard Operating Procedures for the management of external audits requested by the commercial manufacturer or applicable regulatory agency.

B4.11 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the management of cellular therapy products with positive microbial culture results and responsibility for the following activities at a minimum:

B4.11.1 Criteria for the administration of cellular therapy products with positive microbial culture results.

B4.11.2 Identification of individuals authorized to approve release, including the responsible physician at a minimum.

B4.11.3 Notification of the recipient, recipient's physician, collection staff, processing staff, any other facility in receipt of the cellular therapy product, and, if relevant, the donor and the sponsor according to Applicable Law.

B4.11.4 Recipient follow-up.

B4.11.5 ~~Follow-up of the donor~~Donor follow-up, if relevant.

B4.11.6 Documentation and investigation of cause.

B4.11.7 Reporting to regulatory agencies~~,~~ as required by Applicable Law.

B4.12 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for occurrences (errors, accidents, deviations, adverse events, adverse reactions, and complaints). The following activities shall be included at a minimum:

B4.12.1 Detection.

B4.12.2 Investigation.

B4.12.2.1 A thorough and timely investigation shall be conducted by the Clinical Program in collaboration with all entities involved in the collection, manufacture, testing, or administration of the cellular therapy product, as appropriate.

B4.12.2.2 Investigations shall identify the root cause and a plan for short- and long-term corrective and preventive actions as warranted.

B4.12.2.3 Occurrences shall be tracked and trended.

B4.12.3 Documentation.

B4.12.3.1 Documentation shall include a description of the occurrence, date and time of the occurrence, the involved individuals and cellular therapy product(s) including unique identifiers, when and to whom the occurrence was reported, and the immediate actions taken.

B4.12.3.2 All investigation reports shall be reviewed in a timely manner by the Clinical Program Director or Medical Director and Quality Manager.

B4.12.3.3 Cumulative files of occurrences shall be maintained ~~and shall include written investigation reports containing conclusions, follow-up, corrective and preventive action~~CAPAs~~, and a link to the records of the involved cellular therapy products, donors, and recipients, if applicable~~.

B4.12.4 Reporting.

B4.12.4.1 When it is determined that a cellular therapy product has resulted in an adverse event or reaction, the Occurrence Report and results of the investigation shall be reported to the donor's and recipient's physician(s), as applicable, to other facilities participating in the manufacturing of the cellular therapy product, registries, grant agencies, sponsors, IBCs, IRBs, Ethics Committees, accrediting bodies, and governmental agencies as required by Applicable Law.

B4.12.4.2 Occurrences shall be reported to other facilities performing cellular therapy product functions on the affected cellular therapy product.

~~B4.10.4.1 When it is determined that a cellular therapy product has resulted in an adverse event or reaction, the event and results of the investigation shall be reported to the donor's and recipient's physician(s), as applicable, other facilities participating in the manufacturing of the cellular therapy product, registries, and governmental agencies as required by Applicable Law.~~

~~B4.10.4.2 Occurrences shall be reported as required to other facilities performing cellular therapy product functions on the affected cellular therapy product.~~

~~B4.10.4.3 Occurrences shall be reported as required to the appropriate regulatory and accrediting agencies, registries, grant agencies, and Institutional Review Boards or Ethics Committees.~~

B4.12.5 Corrective and preventive action.

B4.12.5.1 Appropriate action shall be implemented if indicated, including both short-term action to address the immediate problem and long-term action to prevent the problem from recurring.

B4.12.5.2 Follow-up ~~audits~~ of the effectiveness of corrective and preventive actions shall be performed in a timeframe as indicated in the investigative report.

B4.13 The ~~Quality Management~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for cellular therapy product C~~c~~hain of I~~i~~dentity and C~~c~~hain of C~~c~~ustody that allow tracking from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.

B4.14 The ~~Quality Management~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for actions to take in the event the Clinical Program's operations are interrupted.

B4.15 The ~~Quality Management~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for qualification of critical manufacturers, vendors, equipment, software, supplies, reagents, facilities, and services relevant to the cellular therapy product.

B4.15.1 Qualification plans shall include minimum acceptance criteria for performance.

B4.15.2 Qualification shall be required following any significant changes to these items.

B4.15.3 Qualification plans, results, reports, and conclusions shall be reviewed and approved by the Quality Manager and Clinical Program Director.

B4.16 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for validation or verification of critical procedures.

B4.16.1 Critical procedures to be validated shall include at least collection procedures, labeling, storage, distribution, preparation for administration, and ~~administration~~infusion, as applicable.

B4.16.2 Each validation or verification shall include at a minimum the elements listed in Appendix IV.~~:~~

~~B4.14.2.1 An approved plan approved by the Clinical Program Director and Quality Manager prior to initiation of data collection or testing., The plan is to include:~~

~~1. Purpose and risk assessment.~~

~~2. Conditions to be assessed.~~

~~3. Number of test events.~~

~~B4.14.2.24. Acceptance criteria.~~

~~B4.14.2.2 A report approved by the Clinical Program Director and Quality Manager prior to implementation. The plan is to include:~~

~~B4.14.2.13 Data collection.~~

~~B4.14.2.24 Evaluation of data.~~

~~B4.14.2.35 Summary of results.~~

~~B4.14.2.46 References, if applicable.~~

~~B4.14.2.7 Review and approval of the plan, report, and conclusion by the Clinical Program Director and Quality Manager.~~

~~B4.14.3 Significant changes to critical procedures shall be validated or verified as appropriate.~~

B4.17 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the evaluation of risk in changes to a critical process or procedure to assess the effect of the change elsewhere in the operation.

B4.18 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for obtaining and reviewing feedback and taking action when appropriate.

B4.18.1 Feedback shall be obtained from associated Collection and Processing Facilities.

B4.18.2 Feedback shall be obtained from donors and recipients or legally authorized representatives.

~~B4.15.1 Evaluation of risk shall be completed for changes in critical procedures.~~

B4.19 The Clinical Program Director shall review the quality management activities with representatives in key positions in all areas of the cellular therapy program~~,~~ at a minimum~~,~~ quarterly.

B4.19.1 Meetings shall have defined attendees, documented minutes, and assigned actions.

B4.19.2 Performance data and review findings shall be reported to key positions and staff.

B4.19.3 The Clinical Program Director shall not approve their own work.

B4.20 The Clinical Program Director shall ~~annually~~ review the effectiveness of the ~~overall~~ Quality Management Program annually.

B4.20.1 The annual report and documentation of the review findings shall be made available to key personnel, the Collection Facility ~~Director~~overseeing physician, the Processing Facility Director, and staff of the program.

B5: POLICIES AND STANDARD OPERATING PROCEDURES

B5.1 The Clinical Program shall establish and maintain policies or Standard Operating Procedures addressing critical aspects of operations and management in addition to those required in B4. These documents shall include all elements required by these Standards and shall address at a minimum:

B5.1.12 Donor and recipient confidentiality.

B5.1.2 Recipient evaluation, selection, and treatment across the continuum of care related to cellular therapy.

~~B5.1.2 Donor and recipient confidentiality.~~

B5.1.3 Donor and recipient informed consent related to treatment and ~~for~~ cellular therapy product collection, ~~and~~ manufacturing, storage, distribution, and disposition.

B5.1.4 Donor search and selection, including screening, testing, eligibility determination, and management.

~~B5.1.5 Preparation of the recipient prior to cellular therapy product administration.~~

B5.1.5 Management of donors and recipients who require central venous access.

B5.1.6 Administration of preparative regimens.

B5.1.7 Administration of cellular therapy products, including products under exceptional release.

B5.1.8 Management of ABO incompatible products, if applicable.

B5.1.9 Administration of blood products.

B5.1.10 ~~Detection and m~~Management of complications that include toxicities related to preparative medications or cellular therapy product administration.

B5.1.11 Monitoring patients following cellular therapy product administration, including recognition of cellular therapy complications and emergencies requiring rapid notification of the responsible clinical team.

B5.1.12 Provision of appropriate long-term follow-up care for recipients.

B5.1.13 Duration and conditions of cellular therapy product storage and indications for disposal.

~~B5.1.12 Hygiene and use of personal protective equipment and attire.~~

B5.1.14 Data management.

B5.1.15 Handling and ~~D~~disposal of medical and biohazard waste.

B5.1.16 Clinical Programs utilizing genetically modified cells shall incorporate or reference institutional or regulatory requirements related to biosafety, including disposal.

B5.1.17 Cellular therapy emergency and disaster plan, including the Clinical Program response.

B5.1.18 Chain of Identity.

B5.1.19 Chain of Custody.

~~B5.1.15 Response to emerging disease agents, including recipient care, donor evaluation and management, and personnel safety.~~

B5.2 The Clinical Program shall maintain a detailed list of all controlled documents, including title and identifier.

B5.3 Standard Operating Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to follow and complete the procedures successfully. Each individual Standard Operating Procedure shall include:

B5.3.1 A clearly written description of the objectives.

B5.3.2 A description of equipment~~, reagents,~~ and supplies used.

B5.3.3 Acceptable endpoints and the range of expected results.

B5.3.4 A stepwise description of the procedure.

B5.3.5 Reference to other Standard Operating Procedures or policies required to perform the procedure.

B5.3.6 Issues related to age, sex, height, and weight, as applicable~~Age-specific issues where relevant~~.

B5.3.7 A reference section listing appropriate and current literature.

B5.3.8 Documented approval of each Standard Operating P~~p~~rocedure by the Clinical Program Director or designated physician prior to implementation and every two (2) years thereafter.

B5.3.9 Documented approval of each procedural modification ~~to a Standard Operating Procedure~~ by the Clinical Program Director or designated physician prior to implementation.

B5.3.10 Reference to a current version of orders, worksheets, reports, labels, and forms.

B5.4 Controlled documents relevant to processes being performed shall be readily available to the facility staff.

B5.5 Staff review and, if appropriate, training and competency shall be documented before performing a new or revised Standard Operating Procedure.

B5.6 All personnel shall follow the policies and Standard Operating Procedures related to their positions.

B5.7 Planned deviations shall be pre-approved by the Clinical Program Director and reviewed by the Quality Manager.

B6: ALLOGENEIC AND AUTOLOGOUS DONOR SELECTION, EVALUATION, AND MANAGEMENT

B6.1 There shall be written criteria for allogeneic and autologous donor selection, evaluation, and management by trained medical personnel.

B6.1.1 Written criteria shall include criteria for the selection of allogeneic donors who are minors or older donors.

B6.1.2 Allogeneic and autologous donors shall be collected at a collection site with the appropriate capabilities to manage the level of acuity and risks from comorbidities.

B6.2 ALLOGENEIC AND AUTOLOGOUS DONOR INFORMATION AND CONSENT ~~TO DONATE~~FOR COLLECTION

B6.2.1 The collection procedure shall be explained in terms the donor can understand~~,~~ and shall include the following information at a minimum:

B6.2.1.1 The risks and benefits of the procedure.

B6.2.1.2 The ~~i~~intent of the collection for treatment or research.

B6.2.1.3 Tests and procedures performed on the donor or donor's specimens to protect the health of the donor and the recipient.

B6.2.1.4 The rights of the donor or legally authorized representative to review the results of such tests according to Applicable Law.

B6.2.1.5 Protection of medical information and confidentiality.

B6.2.1.6 Alternative collection methods.

B6.2.2 If the Clinical Program is the entity obtaining consent for the collection procedure, the informed consent for the cellular therapy product donation shall be obtained and documented by a licensed health care professional knowledgeable in the collection procedure and the intended use of the product.

B6.2.2.1 Informed consent from the allogeneic donor shall be obtained by a licensed health care professional who is not the primary health care professional overseeing care of the recipient.

B6.2.2.2 Interpretation and translation shall be performed by individuals qualified to provide these services in the clinical setting.

B6.2.2.3 Family members and legally authorized representatives shall not serve as interpreters or translators.

B6.2.2.4 The donor shall have an opportunity to ask questions.

B6.2.2.5 The donor shall have the right to refuse to donate or withdraw consent.

B6.2.2.6 The allogeneic donor shall be informed of the potential consequences to the recipient of such refusal in the event that consent is withdrawn after the recipient has begun the preparative regimen.

~~B6.2.5 Donor informed consent for the cellular therapy product donation shall be obtained and documented by a licensed health care professional familiar with the collection procedure and intended use of the product.~~

~~B6.2.6 For directed cellular therapy product donations, informed consent of the recipient for the cellular therapy shall be obtained before cellular therapy product collection.~~

B6.2.2.7 In the case of a donor who is a minor or who does not have the capacity to give consent, informed consent shall be obtained from the donor's legally authorized representative in accordance with Applicable Law and shall be documented.

B6.2.2.8 There should be a process to obtain appropriate assent from minor donors.

B6.2.2.9 The allogeneic donor shall give informed consent and authorization prior to release of the donor's health or other information to the recipient~~'s physician~~ or the recipient's physician.

B6.2.2.10 The donor shall be informed of the policy for cellular therapy product storage, discard, or disposal, including actions taken when an intended recipient no longer requires the cellular therapy product.

B6.2.2.11 Documentation of consent shall be ~~made~~ available to the ~~c~~Collection Facility staff prior to the collection procedure.

B6.3 SUITABILITY DETERMINATION FOR ALLOGENEIC AND AUTOLOGOUS DONORS ~~Suitability for Cellular Therapy Product Collection~~

B6.3.1 There shall be criteria and evaluation policies or Standard Operating Procedures in place to protect the safety of donors during the process of cellular therapy product collection.

B6.3.1.1 The Clinical Program shall confirm that clinically significant findings are reported to the prospective donor with documentation in the donor's record of recommendations made for follow-up care.

B6.3.1.2 Allogeneic donor suitability shall be evaluated by a licensed health care professional who is not the primary health care professional overseeing care of the recipient.

B6.3.1.3 Autologous donors shall be evaluated and tested as required by Applicable Law.

B6.3.2 The risks of donation shall be evaluated and documented, including:~~.~~

B6.3.2.1 Possible need for central venous access.

B6.3.2.2 Anesthesia for cell or tissue collection.

B6.3.2.3 Mobilization for cell collection, if used.

B6.3.2.4 Other donor-specific risks.

B6.3.3 A pregnancy test shall be performed for all ~~female~~ donors with childbearing potential:

B6.3.3.1 For collections with mobilization, ~~-~~within seven (7) days prior to starting the donor mobilization regimen or ~~cellular therapy product collection,~~ undergoing anesthesia~~,~~ and, as applicable, within seven (7) days prior to the initiation of ~~preparation of~~ the recipient's preparative regimen~~for administration~~.

B6.3.3.2 For collections without mobilization, ~~a pregnancy test shall be performed~~ within seven (7) days prior to cellular therapy collection and, as applicable, within seven (7) days prior to the initiation of the ~~mobilization~~ recipient's preparative regimen.

B6.3.4 Laboratory testing of all donors shall be performed by a laboratory that is accredited, registered, certified, or licensed in accordance with Applicable Law.

B6.3.5 The Clinical Program shall inform the ~~c~~Collection Facility ~~staff~~ and ~~the~~ Processing Facility of donor test results or if any testing was not performed.

B6.3.6 There shall be a written order from a physician specifying, at a minimum, ~~an~~ anticipated date and goals of collection and processing.

B6.3.7 Collection from a donor who does not meet ~~Clinical Program collection safety~~ donor suitability criteria shall require documentation of the rationale for ~~their~~ donor selection by the ~~administering~~ donor's physician and approval by the Collection Facility Medical Director.

B6.3.7.1 Issues of donor health that pertain to the safety of the collection procedure shall be communicated in writing to the ~~c~~Collection Facility staff prior to collection.

B6.3.8 There shall be written guidelines for communication between the Clinical Program and the C~~c~~ollection Facility or registry ~~personnel~~ for the management of collection-related complications.

B6.3.9 There shall be ~~a~~ polic~~iesy~~ or Standard Operating Procedures for the management of collection-associated adverse events and follow-up of donors ~~that includes routine management~~.

B6.3.9.1 There shall be a process to track and trend collection-associated adverse events.

B6.4 ADDITIONAL REQUIREMENTS FOR ALLOGENEIC DONORS

B6.4.1 Written criteria shall include criteria for the selection of allogeneic donors when more than one (1) donor is available and suitable.

B6.4.2 Information regarding the donation process, including the considerations for donation, should be provided to the potential allogeneic donor prior to HLA typing.

B6.4.3 A donor advocate shall be available to represent allogeneic donors who are minors or who ~~are mentally incapacitated~~ do not have the capacity to give consent, as those terms are defined by Applicable Law.

B6.4.4 Allogeneic donor infectious disease testing shall be performed using donor screening tests ~~that are~~ licensed, approved, or cleared by the governmental authority.

B6.4.4.1 Hemodilution in the donor prior to collection of blood samples for infectious disease testing should be assessed, and acceptance criteria ~~shall~~ should be ~~assessed and documented~~defined.

B6.4.5 ~~For allogeneic products containing red blood cells sufficient to cause a transfusion reaction,~~ Allogeneic donors and allogeneic recipients shall be tested for ABO group and Rh type using two (2) independently collected samples. D~~D~~iscrepancies shall be resolved and documented prior to issue of the cellular therapy product.

B6.4.6 When relevant, a red blood cell antibody screen shall be performed on allogeneic recipients.

B6.4.7 Allogeneic donors shall be evaluated for risk factors that might result in disease transmission from the cellular therapy product by medical history, physical examination, examination of relevant medical records, and laboratory testing.

B6.4.8 ~~When appropriate for the cellular therapy product, T~~the medical history for allogeneic donors shall include at least the following:

B6.4.8.1 Vaccination history.

B6.4.8.2 Travel history.

B6.4.8.3 Blood transfusion history.

B6.4.8.4 Questions to identify persons at increased risk for transmission of ~~relevant~~ communicable disease ~~agents~~ as defined by the applicable governmental authority.

B6.4.8.5 Questions to identify persons at risk of transmitting inherited conditions.

B6.4.8.6 Questions to identify persons at ~~increased~~ risk of transmitting a hematologic~~al,~~ or immunologic~~al, or genetic conditions~~ disease.

B6.4.8.7 Questions to identify a ~~past~~ history of malignant disease.

B6.4.8.8 ~~The a~~Allogeneic donors shall confirm that all the information provided is true to the best of their knowledge.

B6.4.9 Allogeneic donors shall be tested for evidence of clinically relevant infection by the following communicable disease agents using tests as required by Applicable Law:

B6.4.9.1 Human immunodeficiency virus, type 1.

B6.4.9.2 Human immunodeficiency virus, type 2.

B6.4.9.3 Hepatitis B virus.

B6.4.9.4 Hepatitis C virus.

B6.4.9.5 *Treponema pallidum* (syphilis).

B6.4.10 If required by Applicable Law, allogeneic donors shall also be tested for evidence of clinically relevant infection by the following disease agents:

B6.4.10.1 Human T cell- Llymphotropic Vvirus I.

B6.4.10.2 Human T cell- Llymphotropic Vvirus II.

B6.4.10.3 West Nile Virus.

B6.4.10.4 *Trypanosoma cruzi* (Chagas Disease).

B6.4.11 Blood samples for testing for evidence of clinically relevant infection shall be drawn and tested within timeframes required by Applicable Law.

B6.4.11.1 For viable, lymphocyte-rich cells, including mononuclear cells and other cellular therapy products, blood samples from allogeneic donors shall be obtained within seven (7) days prior to or after collection, in the U.Sor in accordance with Applicable Law.

B6.4.12 Allogeneic donors shall be tested for cytomegalovirus unless previously documented to be positive.

B6.4.13 Additional tests shall be performed as required to assess the possibility of transmission of other infectious and non-infectious diseases.

B6.4.14 When appropriate for the cellular therapy product, allogeneic donors and recipients shall be tested for HLA loci alleles determined by the Clinical Program Director to be of importance to the cellular therapy product by a laboratory accredited by ASHI, EFI, CAP, or other appropriate organization.

B6.4.14.1 DNA high--resolution molecular typing shall be used for HLA typing, if indicated.

B6.4.14.2 Verification typing shall be performed on the recipient and selected allogeneic donor using independently collected samples. Results shall be confirmed prior to administration of the preparative regimen, mobilization, or cellular therapy product collection, whichever is earliest.

B6.4.14.3 ~~When relevant to the cellular therapy product, T~~there shall be a policy or Standard Operating Procedure for anti-HLA antibody testing for mismatched donors and recipients.

B6.4.15 Allogeneic donor eligibility, as defined by Applicable Law, shall be determined by a licensed health care provider after history, exam, medical record review, and testing. The donor eligibility determination shall be documented in the recipient's medical record before the recipient is prepared for administration and before the allogeneic donor begins the mobilization regimen, if applicable.

B6.4.16 Records required for donor eligibility determination shall be in English or translated into English when crossing international borders.

B6.4.17 The use of an ineligible allogeneic donor, or an allogeneic donor for whom donor eligibility determination is incomplete, shall require documentation of ~~urgent medical need that includes~~ the rationale for their selection by the administering physician, urgent medical need ~~and~~ documentation, and ~~of~~ the informed consent of the donor and the recipient.

B6.4.18 Allogeneic donor eligibility ~~and suitability~~ shall be communicated in writing to the ~~c~~Collection ~~personnel~~ and Processing Facilities.

~~B6.4.17 There shall be a policy covering the creation and retention of allogeneic donor records.~~

B6.4.19 Allogeneic donor records shall include donor suitability and eligibility determination, including the name of the responsible person who made the determination and the date of the determination.

B6.5 Allogeneic Cellular Therapy Products Manufactured for Multiple Recipients

B6.5.1 At the time of selection for administration, the Clinical Program ~~shall~~ should request all critical technical data from the cellular therapy product manufacturing facility regarding the product after processing and prior to cryopreservation, including ~~at a minimum~~as applicable:

B6.5.1.1 Total count or dose of the relevant cell or product.

B6.5.1.2 Viability and/or potency~~, if applicable~~.

B6.5.1.3 Microbial cultures from the cellular therapy product after processing prior to cryopreservation.

B6.5.1.4 ABO group and Rh type~~, if applicable~~.

B6.5.1.5 All HLA Class I and II typing results~~, if applicable~~.

B6.5.1.6 Communicable disease testing results performed on the donor.

B6.5.1.7 Final donor eligibility determination and risks of communicable or genetic diseases disclosed by the donor, medical, and genetic screening or clinical chart review, and the results of any investigation or further testing performed.

B6.5.1.8 The method of processing.

B6.5.1.9 Any variances in collection, processing, testing, cryopreservation, storage, or transport or shipping procedures that may influence the integrity or quality of the cellular therapy product.

B6.5.1.10 Physical characteristics of the cellular therapy product, including at a minimum the number and type of bags or compartments used for storage.

B7: RECIPIENT CARE

B7.1 Recipient informed consent for the cellular therapy shall be obtained and documented by a licensed healthcare professional knowledgeable in~~of~~ the proposed cellular therapy.

B7.1.1 The ~~Clinical Program~~informed consent process shall ~~provide~~include information regarding the risks and benefits of the proposed cellular therapy.

B7.1.2 For ~~directed~~ a cellular therapy product ~~donations~~collected for a designated recipient, informed consent of the recipient for the therapy shall be obtained before collection of the product ~~collection~~.

B7.2 The attending physician shall ~~confirm~~ verify the availability and suitability of a donor or cellular therapy product prior to ~~preparing~~ initiating the recipient's preparative regimen ~~for cellular therapy~~.

B7.2.1 The Clinical Program shall notify the Processing Facility prior to requesting a cellular therapy product from a cord blood bank, registry, or other facility.

B7.2.2 The Clinical Program should obtain relevant information regarding the cellular therapy product from the manufacturer.

B7.3 Records shall be made concurrently with each step of recipient care in such a way that all steps may be accurately traced.

B7.3.1 Records shall identify the person immediately responsible for each significant step, including dates and~~, if appropriate,~~ times, where appropriate of various steps.

B7.4 There shall be policies or Standard Operating Procedures addressing safe administration of the preparative regimen, if applicable.

B7.4.1 The treatment orders shall include the patient's current height and weight, specific dates of administration, daily doses ~~(~~if appropriate~~)~~, and route of administration of each agent.

B7.4.2 Preprinted orders or electronic equivalents shall be used for protocols and standardized regimens. These orders shall be verified and documented by an attending physician.

B7.5 There shall be policies or Standard Operating Procedures addressing safe administration of cellular therapy products.

B7.5.1 ~~The cellular therapy product shall be administered by a licensed healthcare professional trained in the procedure.~~ There shall be policies or Standard Operating Procedures for preparation and administration of cellular therapy products according to manufacturer specifications.

B7.5.2 Two (2) qualified persons shall verify the identity of the recipient and the product and the order for administration prior to the administration of the cellular therapy product.

B7.5.3 There shall be documentation in the recipient's medical record of the unique identifier of each cellular therapy product and~~the administered cellular therapy product,~~ dose administered, initiation and completion times of administration, and any adverse events related to administration.

B7.5.4 A ~~c~~Circular of ~~i~~Information, ~~or~~ Investigator's Brochure, or other product-specific information for cellular therapy products shall be available to staff.

B7.6 There shall be policies or Standard Operating Procedures addressing appropriate follow-up of recipients after administration of preparative regimens, if applicable, and cellular therapy products.

B7.7 There shall be policies or Standard Operating Procedures in place for ~~the~~ planned discharges and the provision of post-cellular therapy~~follow-up~~ care.

B7.7.1 The Clinical Program shall provide appropriate instructions to recipients prior to discharge.

B7.7.1.1 There shall be a process to provide cellular therapy-specific instructions for post-discharge care to the recipient, caregivers, and other health care providers who may provide care.

B7.8 There shall be policies or Standard Operating Procedures in place for provision of appropriate long-term follow-up, treatment, and plans of care ~~to recipients~~.

B8: CLINICAL RESEARCH

B8.1 Clinical Programs shall have formal review of investigational ~~treatment~~ protocols and ~~patient~~ consent forms by a process that is approved under institutional policies and Applicable Law.

B8.1.1 Those Clinical Programs utilizing investigational treatment protocols shall have ~~in place~~ a pharmacy in place that is equipped for research activities, including a process for tracking, inventory, and secured storage of investigational drugs.

B8.1.2 There shall be a process to manage investigational cellular therapy products.

B8.2 Clinical research protocols shall be performed in accordance with institutional policies and Applicable Law.

B8.2.1 The Clinical Program shall maintain:

B8.2.1.1 Documentation of approval by the Institutional Review Board (IRB), Ethics Committee, or equivalent.

B8.2.1.2 If applicable, documentation of approval by the Institutional Biosafety Committee (IBC) or equivalent.

B8.2.1.3 Correspondence with regulatory agencies.

B8.2.1.4 Audits and any adverse events, including their resolution.

B8.3 For clinical research, informed consent shall be obtained from each research subject or legally authorized representative, in a language ~~he or she~~they can understand, and under circumstances that minimize the possibility of coercion or undue influence.

B8.3.1 The research subject~~s~~ or legally authorized representative~~s~~ shall be given the opportunity to ask questions, ~~and to~~ have their questions answered to their satisfaction, and ~~to~~ withdraw from the research without prejudice.

B8.3.2 Informed consent for a research subject shall contain the following elements at a minimum and comply with Applicable Law:

B8.3.2.1 An explanation of the research purposes, a description of the procedures to be followed, and the identification of investigational procedures.

B8.3.2.2 The expected duration of the subject's participation.

B8.3.2.3 A description of the reasonably expected risks, discomforts, benefits to the subject and others, and alternative procedures.

B8.3.2.4 A statement of the extent to which confidentiality will be maintained.

B8.3.2.5 A statement of whether the participant will receive compensation for participating in the study or if it will cost the participant to be in the study.

B8.3.2.6 An explanation of the extent of compensation for injury.

B8.3.2.7 A statement of sponsorship.

B8.3.2.8 A statement of whether there is a potential conflict of interest.

~~B8.3.2.6 Contact information for the person research subjects can contact in case of questions or concerns.~~

B8.4 There shall be a process in place to address the disclosure of any issues that may represent a conflict of interest in clinical research.

B9: DATA MANAGEMENT

B9.1~~2~~ The Clinical Program shall define staff responsible for collecting and reporting data ~~specified in B9.1.~~

B9.2 The Clinical Program ~~shall~~ should collect and maintain complete and accurate data necessary to complete the Cellular Therapy Essential Data forms of the Center for International Blood and Marrow Transplant Research (CIBMTR). ~~Cellular Immunotherapy Data Resource (CIDR) forms, Cellular Therapy Med-A forms, or other appropriate forms of the EBMT.~~

B9.2.1 Clinical Programs ~~shall~~ should submit the data specified in B9.2~~1~~ to a national or international database ~~if required by Applicable Law~~.

B9.2.2 Clinical Programs should collect the data specified in B9.2~~1~~ for all patients for at least one (1) year following administration of the cellular therapy product.

~~B9.2 The Clinical Program shall define staff responsible for collecting and reporting data specified in B9.1.~~

~~B9.2.1 Defined data management staff should participate in continuing education annually.~~

B10: RECORDS

B10.1 There shall be a records management system for cellular therapy product record creation, assembly, review, storage, archival, and retrieval.

B10.1.1 A records management system shall be established and maintained to facilitate the review of records.

B10.1.2 The records management system shall facilitate tracking of the cellular therapy product from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.

B10.1.3 Records shall be maintained to ensure their integrity, preservation, and retrieval.

B10.1.4 Records shall be accurate and legible.

B10.1.5 Written records shall be indelible.

B10.1.6 Safeguards to secure the confidentiality of all records and communications among the clinical, collection, and processing staff and with donors and recipients shall be established and followed in compliance with Applicable Law.

B10.2 The Clinical Program shall define and follow good documentation practices.

B10.3 RECORDS TO BE MAINTAINED

B10.3.1 Clinical Program records related to quality control, personnel training and competency, facility maintenance, facility management, complaints, or other general facility issues shall be retained for a minimum of ten (10) years after the creation of the record or according to ~~by the Clinical Program, or longer in accordance with~~ Applicable Law.

B10.3.2 Records of validation studies for a clinical procedure shall be retained at a minimum until the procedure is no longer in use.

B10.3.3 Employee records shall be maintained ~~by the Clinical Program~~ in a confidential manner and ~~for~~ as long as required by Applicable Law.

B10.3.4 Cleaning and sanitation records shall be retained for ~~a minimum of~~at least three (3) years or longer in accordance with Applicable Law~~,~~ or by a defined program or institution policy.

~~B10.1.3 Validation study records for a procedure shall be retained at a minimum until the procedure is no longer in use.~~

B10.3.5 Records to allow tracking and tracing of cellular therapy products shall be maintained for a minimum of ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, or as required by Applicable Law, whichever is latest.

B10.3.5.1 These records should include the product code and unique numeric or alphanumeric identifier.

B10.3.6 Recipient and donor records including, but not limited to, consents and records of care, shall be maintained in a confidential manner as required by Applicable Law for a minimum of ten (10) years after the administration of the cellular therapy product, or, if not known, ten (10) years after the date of the cellular therapy product's distribution, disposition, or expiration, whichever is latest.

B10.3.7 Research records shall be maintained in a confidential manner as required by Applicable Law for a minimum of ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, whichever date is latest.

B10.4 ELECTRONIC RECORDS

B10.4.1 The Clinical Program shall maintain a current listing of all critical electronic record systems. Critical electronic record systems~~,~~ shall include at a minimum~~,~~ systems ~~under the control of the Clinical Program~~ that are used as a substitute for paper, to make decisions, to perform calculations, or to create or store information used in critical procedures. For all critical electronic record systems:

B10.4.1.1 ~~For all critical electronic record systems, t~~There shall be policies, Standard Operating Procedures, and system elements to maintain the accuracy, integrity, identity, and confidentiality of all records.

B10.4.1.2 There shall be a means by which access ~~to electronic records~~ is limited to authorized individuals.

B10.4.1.3 A method shall be established or the system shall provide for the unambiguous identification of the individual responsible for each record entry.

B10.4.1.4 There shall be written policies and Standard Operating Procedures for record entry, verification, and revision.

B10.4.1.5 A method shall be established or the system shall provide for review of data before final acceptance.

B10.4.1.6 There shall be documented training of personnel in the system's use.

B10.4.1.7 There shall be a defined process for continued competency of personnel in the system's use.

B10.4.1.8 There shall be a defined process for the use of electronic signatures.

B10.4.1.9 ~~The critical electronic record system~~ Unique identifiers shall be maintained ~~unique identifiers~~.

B10.4.1.10 There shall be the ability to generate true copies of the records in both human-readable and electronic format suitable for inspection and review.

B10.4.1.11 There shall be protection of the records to enable their accurate and ready retrieval throughout the period of record retention.

B10.4.1.12 All system modifications shall be authorized, documented, and validated prior to implementation.

~~B10.4.6 For each critical electronic record system, there shall be an alternative system for all electronic records to allow for continuous operation in the event that a critical electronic record system is not available. The alternative system shall be validated, and Clinical Program staff shall be trained in its use.~~

~~B10.4.7 For all critical electronic record systems, there shall be written Standard Operating Procedures for record entry, verification, and revision.~~

~~B10.4.7.1 A method shall be established or the system shall provide for review of data before final acceptance.~~

~~B10.4.7.2 A method shall be established or the system shall provide for the unambiguous identification of the individual responsible for each record entry.~~

~~B10.4.8 For all critical electronic record systems, there shall be the ability to generate true copies of the records in both human-readable and electronic format suitable for inspection and review.~~

B10.4.2 For all critical electronic record systems under the control of the Clinical Program, there shall be validated procedures for and documentation of:

~~B10.4.9.1 Training and continued competency of personnel in systems use.~~

B10.4.2.1 Prospective validation of systems, including hardware, software, and databases.

B10.4.2.2 Installation of the system.

B10.4.2.3 Numerical designation of system versions, if applicable.

B10.4.2.4 Authorization and validation of all system modifications prior to implementation.

B10.4.2.5 Systems development including the verification of calculations and algorithms.

B10.4.2.6 System maintenance and operations.

B10.4.2.7 Monitoring of data integrity.

B10.4.2.8 Back-up of the electronic records system on a regular schedule.

~~B10.4.9.4 System assignment of unique identifiers.~~

B10.4.3 For each critical electronic record system, there shall be an alternative system to allow for continuous operation of the Clinical Program if the critical electronic record system is not available. The alternative system shall be validated, and clinical personnel shall be trained in its use.

B10.5 RECORDS IN CASE OF DIVIDED RESPONSIBILITY

B10.5.1 If two (2) or more facilities participate in the collection, processing, or administration of the cellular therapy product, the records of each facility shall show plainly the extent of its responsibility.

B10.5.2 The Clinical Program shall furnish outcome data~~,~~ related to the safety, purity, or potency of the cellular therapy product ~~involved~~, to other facilities involved in the collection or processing of the cellular therapy product.

PART C: COLLECTION STANDARDS

C1: General

C2: Collection Environment

C3: Personnel

C4: Quality Management

C5: Policies and Standard Operating Procedures

C6: Allogeneic and Autologous Donor Evaluation and Management

C7: Coding and Labeling of Cellular Therapy Products

C8: Equipment, Supplies, and Reagents

C9: Process Controls

C10: Cellular Therapy Product Storage

C11: Cellular Therapy Product Transportation and Shipping

C12: Records

PART C: COLLECTION STANDARDS

C1: GENERAL

Throughout the Collection section of the FACT Common Standards, the term "Collection Facility" is used to describe the entity responsible for performing cellular therapy product collection activities. The use of this term is intended to be inclusive and recognizes that collection activities may be conducted within a defined physical location *or* through an organized service or program that coordinates and performs collections across one or more sites. Accordingly, a Collection Facility is not required to be a single, fixed physical location, provided that the organizational structure, oversight, policies, procedures, and personnel collectively meet the applicable Standards and ensure the quality and safety of collection activities.

C1.1 These Standards apply to all collection, storage, and distribution services performed on cellular therapy products.

~~C1.2 Collected cellular therapy products shall be distributed to facilities that meet FACT Standards with respect to their role in cellular therapy.~~

C1.2 Collection of cellular therapy products shall comply with Applicable Law.

C1.2.1 Collections shall be performed in a facility licensed, registered, or accredited as required by the appropriate governmental authority for the activities performed.

C1.3 Cellular collection services shall be overseen by a designated ~~Medical Director~~overseeing physician, a Quality Manager, and a minimum of one (1) additional designated staff member. This team shall have been in place and performing cellular therapy product collections for at least twelve (12) months preceding initial accreditation.

C1.4 The Collection Facility shall use cell processing facilities that meet FACT Standards with respect to their interactions with the Collection Facility.

C1.5 A minimum of ~~five~~one (1~~5~~) cellular therapy product~~s~~ shall have been collected prior to initial accreditation, and a minimum ~~average~~ of ~~five~~ one (1~~5~~) cellular therapy product~~s~~ shall have been collected per year within each accreditation cycle.

C1.6 There shall be a process to qualify the sites for cellular collections.

C1.7 There shall be written criteria for each collection site that defines the level of donor risk that can be safely managed.

C2: COLLECTION ENVIRONMENT

C2.1 There shall be secured and controlled access to designated areas appropriate for collection of cellular therapy products and for storage of cellular therapy products, equipment, supplies, and reagents.

C2.1.1 The collection area shall be divided into defined areas of adequate size to prevent improper labeling, mix-ups, contamination, or cross-contamination of cellular therapy products.

C2.1.2 There shall be a process to control storage areas to prevent mix-ups, contamination, and cross-contamination.

C2.1.3 There shall be suitable space for confidential donor examination and evaluation.

C2.2 During the collection process, ~~T~~there shall be adequate lighting, ventilation, and access to sinks for handwashing and to toilets ~~during collection~~ to prevent the introduction, transmission, or spread of communicable disease.

C2.3 Environmental conditions shall be controlled to protect the safety and comfort of donors and personnel.

C2.4 There shall be a written assessment of critical parameters of the facility in which collection is performed that may affect cellular therapy product viability, integrity, contamination, or cross-contamination during collection.

C2.4.1 The written assessment shall include temperature and humidity at a minimum.

C2.4.2 Critical ~~P~~parameters identified to be a risk to the cellular therapy product shall be controlled, monitored, and recorded.

C2.4.3 If using collection methods that may result in contamination or cross-contamination of cellular therapy products, critical environmental conditions shall be controlled, monitored, and recorded for air quality and surface contaminants.

C2.5 The facility shall document facility cleaning and sanitation and maintain order sufficient to achieve adequate conditions for operations.

~~C2.6 There shall be adequate equipment and materials for the procedures performed.~~

~~C2.7 There shall be access to an intensive care unit or emergency services.~~

C2.6 The facility in which collection is performed shall be operated in a manner designed to minimize risks to the health and safety of employees, donors, visitors, caregivers, and volunteers.

C2.7 There shall be a written safety manual that includes instructions for action in case of exposure to communicable disease and to chemical, biological, radiological, electrical, or fire hazards.

C2.8 All waste generated by collection activities shall be disposed of in a manner that minimizes any hazard to facility personnel and to the environment in accordance with Applicable Law.

C2.9 There shall be a written policy for personal hygiene and the use of p~~P~~ersonal protective equipment and attire.~~, including gloves and protective clothing, shall be used while handling biological specimens. Such protective equipment shall not be worn outside the work area.~~

C2.9.1 The policy shall define the protective clothing to be worn upon entering the work area and while working within it.

C2.9.2 The policy shall define personal protective equipment appropriate for the activities and classification of the environment to be worn while handling biological specimens.

C2.9.3 Such personal protective equipment shall not be worn outside the designated work area.

~~C2.13 When a collection kit is prepared and sent to collection staff, there shall be adequate instructions and materials to collect, label, store, pack, and transport or ship the cellular therapy product and associated samples to the Processing Facility.~~

~~C2.13.1 The collection kit shall be transported or shipped under conditions validated to maintain the designated temperature range from the time it leaves the shipping facility until it is received by the collection staff.~~

C2.10 There shall be access to an intensive care unit or emergency services as appropriate for the collection procedure, the donor, and the collected material.

C3: PERSONNEL

C3.1 MEDICAL ~~DIRECTOR~~ OVERSIGHT OF COLLECTION SERVICES

C3.1.1 There shall be a ~~Medical Director who is a~~ licensed physician overseeing each type of product collected with ~~postgraduate~~ training in the methods required for cellular therapy product collection or the therapeutic disease areas.

C3.1.2 The Collection Facility overseeing physician ~~Medical Director~~ shall be responsible for the following elements:

C3.1.2.1 All technical procedures.

C3.1.2.2 Performance of the collection procedures.

C3.1.2.3 Supervision of staff.

C3.1.2.4 Administrative operations.

C3.1.2.5 The medical care of donors undergoing cell collections.

C3.1.2.6 Pre-collection evaluation of donors at the time of donation.

C3.1.2.7 Care of any complications resulting from the collection procedure.

C3.1.2.8 Compliance with the Quality Management Program, these Standards, and Applicable Law.

C3.1.3 The ~~Medical Director~~overseeing physician shall have at least one (1) year of experience in performing or supervising the collection~~cellular therapy product collection procedures~~.

C3.1.4 The ~~Medical Director~~overseeing physician ~~shall~~ should participate in ~~a minimum of ten (10) hours~~ annual~~ly of~~ continuing educational activities related to ~~cellular therapy product collection or the applicable therapeutic disease areas~~their collection process.

C3.2 QUALITY MANAGER

C3.2.1 There shall be a Quality Manager for collection activities to establish and maintain systems to review, modify, and approve all policies and Standard Operating Procedures intended to monitor compliance with these Standards, Applicable Law, or the performance of the collection activities.

C3.2.2 The Quality Manager of collection activities should have a reporting structure independent of ~~cellular therapy product collections~~the collection process.

C3.2.3 The Quality Manager shall participate in a minimum of ten (10) hours annually of educational activities related to cellular therapy, cell collection, or quality management.

C3.3 STAFF

C3.3.1 The number of trained and competent collection personnel shall be adequate for the number of procedures performed and shall include a minimum of one (1) designated trained individual with an identified trained and competent backup individual to maintain sufficient coverage.

C3.3.2 For collection activities involving pediatric donors, physicians and collection staff shall have documented training and experience with pediatric donors.

C3.3.3 There shall be attending physician oversight if general medical physicians, physicians in training, or APPs provide care to the cellular therapy donors. The scope of responsibility of general medical physicians or APPs shall be defined.

C4: QUALITY MANAGEMENT

C4.1 There shall be a Quality Management Program that incorporates key performance data.

C4.1.1 The ~~Medical~~ Collection Facility overseeing physician ~~Director~~ shall have authority over and responsibility for ensuring that the Quality Management Program is effectively established and maintained.

C4.2 The Collection Facility shall establish and maintain a written Quality Management Plan.

~~C4.2.1 Collection activities shall be performed in compliance with a written Quality Management Plan.~~

C4.2.1 The ~~Medical~~ Collection Facility overseeing physician ~~Director~~ shall be responsible for the Quality Management Plan as it pertains to collection activities.

C4.3 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, an organizational chart of key positions, functions, and reporting relationships required for collection.

C4.3.1 The ~~Quality Management Plan~~QM Plan shall include a description of how these key positions interact to implement the quality management activities.

C4.4 The QM Plan should include or summarize and reference a listing of third-party manufacturers and clinical programs supported to include description of scope and services provided.

~~C4.3.2 There shall be written guidelines for communication between the collection or registry personnel and the Clinical Program for the management of collection-related complications.~~

C4.5 The ~~Quality Management Plan~~QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures addressing personnel requirements for each key position required for cellular therapy product collection. Personnel requirements shall include at a minimum:

C4.5.1 A current job description for key positions~~all staff~~.

C4.5.2 A system to document the following for all staff:

C4.5.2.1 Initial qualifications.

C4.5.2.2 New employee orientation.

C4.5.2.3 Initial training, competency, and retraining when appropriate for all procedures performed~~, and in accordance with Applicable Law~~.

C4.5.2.4 Continued competency for each critical function performed, assessed annually at a minimum.

C4.5.2.5 Annual training in applicable current GxP appropriate to the processes performed ~~in accordance with Applicable Law~~.

C4.5.2.6 Continuing education.

C4.6 The ~~Quality Management~~QM Plan shall include, or summarize and reference, a comprehensive system for document control.

C4.6.1 There shall be identification of the types of documents that are considered critical and shall comply with the document control system requirements. Controlled documents shall include at a minimum:

C4.6.1.1 Policies, protocols, ~~and~~ Standard Operating Procedures, and job aids.

C4.6.1.2 Worksheets.

C4.6.1.3 Forms.

C4.6.1.4 Labels.

C4.6.2 There shall be policies or Standard Operating Procedures for development, approval, implementation, distribution, review, revision, and archival of all ~~critical~~ controlled documents.

C4.6.3 The document control system shall include:

C4.6.3.1 A standardized format for ~~critical~~ controlled documents.

C4.6.3.2 Assignment of a numeric or an alphanumeric identifier, version, and a title to each controlled document ~~and document version regulated within the system~~.

C4.6.3.3 A system for document approval, including the approval date, signature of approving individual(s), and the effective date.

C4.6.3.4 A system to protect controlled documents from accidental or unauthorized modification.

C4.6.3.5 Review of controlled documents every two (2) years at a minimum.

C4.6.3.6 A system for document change control that includes a description of the change, version, the signature of the approving individual(s), approval date(s), communication or training on the changes as applicable, effective date, and archival date.

C4.6.3.7 A system for Aarchival of controlled documents, the inclusive dates of use, and their historical sequence for a minimum of ten (10) years from archival or according to governmental or institutional policy, whichever is longer.

C4.6.3.8 A system for the retraction of obsolete documents to prevent unintended use.

C4.7 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the establishment and maintenance of written agreements.

C4.7.1 Agreements shall be established with external parties providing critical services that could affect the quality and safety of the cellular therapy product or health and safety of the donor or recipient.

C4.7.2 Agreements shall include the responsibility of the external party performing any step in collection, processing, testing, storage, distribution, or administration to maintain required accreditations, and to comply with these Standards and Applicable Law.

C4.7.3 Agreements shall be established when the Collection Facility providescollections or other critical services are performed forto external parties.

C4.7.4 Agreements shall be dated and reviewed on a regular basis, at a minimum every two (2) years.

C4.87 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for documentation and review of outcome analysis and cellular therapy product efficacy to verify that the procedures in use consistently provide a safe and effective product.

C4.8.1 Criteria for cellular therapy product safety, efficacy, and the clinical outcome, as appropriate, shall be determined for each type of product collected and shall be reviewed at regular time intervals.

~~C4.7.2 Both individual cellular therapy product data and aggregate data for each type of cellular therapy product or recipient type shall be evaluated.~~

~~C4.7.3 Review of outcome analysis and/or product efficacy shall include at a minimum:~~

~~C4.7.3.1 An endpoint of clinical function as approved by the Clinical Program Director.~~

~~C4.7.3.2 Overall and treatment-related morbidity and mortality at thirty (30) days, one hundred (100) days, and one (1) year after cellular therapy product administration or in accordance with Applicable Law.~~

C4.8.2 Data on outcome analysis and cellular therapy product efficacy, including adverse events related to the recipient, donor, or product, shall be provided in a timely manner to entities involved in the collection, processing, or distribution of the cellular therapy product.

C4.9 The Quality Management Plan shall include, or summarize and reference, policies, Standard Operating Procedures for, and a schedule of, audits of the collection activities to verify compliance with the Quality Management Program, operational policies and Standard Operating Procedures, these Standards, and Applicable Law.

C4.9.1 Collection Facility ~~A~~audits shall be conducted by an individual with ~~sufficient~~ knowledge of the process and competence in auditing to identify problems, but who is not solely responsible for the process being audited.

C4.9.2 An audit plan for each audit shall include the elements listed in Appendix IV.~~XX...~~

C4.9.3 An audit report shall include the elements listed in Appendix IV~~XX...~~.

C4.9.4 The results of Collection Facility audits shall be used to recognize problems, detect trends, identify improvement opportunities, implement corrective and preventive actions when necessary, and follow up on the effectiveness of these actions in a timely manner.

C4.9.5 Collection Facility ~~A~~audits shall be performed annually at a minimum~~,~~ and shall include at least the following:

C4.9.5.1 Documentation of daily assessment of ~~the review of~~ donor suitability as required in C9.5~~proper donor eligibility and suitability determination~~.

C4.9.5.2 Management of cellular therapy products with positive microbial culture results.

~~C4.8.3.3 Infectious disease resulting from cellular therapy product collection and administration.~~

C4.9.5.3 Documentation that external facilities performing critical contracted services have met the requirements of the written agreements.

~~C4.8.3.5 Chain of identity and chain of custody of cellular therapy products.~~C4.9.5.4 Environmental monitoring as defined in the facility assessment to include environmental parameters, including storage areas, that may affect cellular therapy product viability, integrity, contamination, or cross-contamination during collection.

C4.9.5.5 Chain of Identity and Chain of Custody of cellular therapy products.

C4.9.6 Additional audits shall be performed as part of a risk-based approach to the follow-up of occurrences.

C4.10 There shall be policies or Standard Operating Procedures for the management of external audits requested by the commercial manufacturer or applicable regulatory agency.

C4.11 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the management of cellular therapy products with positive microbial culture results ~~and responsibility for the following activities~~and responsibility for the following activities ~~-~~at a minimum:

C4.11.1 Notification of ~~the recipient, the~~ recipient's physician, ~~p~~Processing ~~staff~~Facility, and any other facility in receipt of the cellular therapy product~~.; and if relevant, the donor and the sponsor.~~

~~C4.9.2 Recipient follow-up.~~

C4.11.2 ~~Follow-up of the donor, if relevant.~~ Donor follow-up, if relevant.

C4.11.3 Documentation and investigation of cause.

C4.11.4 Reporting to regulatory agencies, as required by Applicable Law.

C4.12 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for occurrences (errors, accidents, deviations, adverse events, adverse reactions, and complaints). The following activities shall be included at a minimum:

C4.12.1 Detection.

C4.12.2 Investigation.

C4.12.2.1 A thorough and timely investigation shall be conducted by the collection staff in collaboration with all entities involved in the collection, manufacture, testing, or administration of the cellular therapy product, as appropriate.

C4.12.2.2 Investigations shall identify the root cause and a plan for short- and long-term corrective and preventive actions as warranted.

C4.12.2.3 Occurrences shall be tracked and trended.

C4.12.3 Documentation.

C4.12.3.1 Documentation shall include a description of the occurrence, date and time of the occurrence, the involved individuals and cellular therapy product(s) to include unique identifiers, when and to whom the occurrence was reported, and the immediate actions taken.

C4.12.3.2 All investigation reports shall be reviewed in a timely manner by the ~~Collection Facility Director or Medical Director~~Collection ~~Service~~Facility overseeing physician and Quality Manager.

C4.12.3.3 Cumulative files of occurrences shall be maintained and include written investigation reports containing conclusions, follow-up, corrective and preventive actions, and a link to the records of the involved cellular therapy products, donors, and recipients, if applicable.

C4.12.4 Reporting.

C4.12.4.1 When it is determined that a cellular therapy product has resulted in an adverse event or reaction, the ~~event~~ Occurrence Report ~~and~~ and results of the investigation shall be reported to the donor's and recipient's physician(s), as applicable, to other facilities participating in the manufacturing of the cellular therapy product, registries, grant agencies, sponsors, IBCs, IRBs, Ethics Committees, accrediting bodies, and governmental agencies as required by Applicable Law.

C4.12.4.2 Occurrences shall be reported to other facilities performing cellular therapy product functions on the affected cellular therapy product.

~~C4.10.4.2 Occurrences shall be reported as required to other facilities performing cellular therapy product functions on the affected cellular therapy product.~~

~~C4.10.4.3 Occurrences shall be reported as required to the appropriate regulatory and accrediting agencies, registries, grant agencies, and Institutional Review Boards or Review Boards or Ethics Committees.~~

C4.12.5 Corrective and preventive action.

C4.12.5.1 Appropriate action shall be implemented if indicated, including both short-term action to address the immediate problem and long-term action to prevent the problem from recurring.

C4.12.5.2 Follow-up ~~audits~~ of the effectiveness of corrective and preventive actions shall be performed in a timeframe as indicated in the investigative report.

C4.13 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for cellular therapy product ~~c~~Chain of ~~i~~Identity and ~~c~~Chain of ~~c~~Custody that allow tracking from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.

C4.14 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for actions to take in the event collection operations are interrupted.

C4.15 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for qualification of critical manufacturers, vendors, equipment, software, supplies, reagents, facilities, and services relevant to the cellular therapy product.

C4.15.1 Qualification plans shall include minimum acceptance criteria for performance.

C4.15.2 Qualification shall be required following any significant changes to these items.

C4.15.3 Reagents that are not of the appropriate grade shall undergo qualification for the intended use.

C4.15.4 Qualification plans, results, reports, and conclusions shall be reviewed and approved by the Quality Manager and ~~Medical~~ Collection Facility overseeing physician~~Director~~.

~~C4.13.4 Reagents that are not the appropriate grade shall undergo qualification for the intended use.~~

C4.16 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for validation or verification of critical procedures.

C4.16.1 Critical procedures to be validated shall include ~~at least~~ collection procedures, testing, labeling, storage, and distribution as applicable.

C4.16.2 Each validation or verification shall include at a minimum the elements listed in Appendix IV.~~:~~

~~C4.14.2.1 An approved plan, including conditions to be assessed.~~

~~C4.14.2.2 Acceptance criteria.~~

~~C4.14.2.3 Data collection.~~

~~C4.14.2.4 Evaluation of data.~~

~~C4.14.2.5 Summary of results.~~

~~C4.14.2.6 References, if applicable.~~

~~C4.14.2.7 Review and approval of the plan, report, and conclusion by the Medical Director and Quality Manager.~~

C4.16.3 Significant changes to critical procedures shall be validated or verified as appropriate.

C4.17 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the evaluation of risk in changes to a critical process or procedure to assess the effect of the change elsewhere in the operation.

~~C4.15.1 Evaluation of risk shall be completed for changes in critical procedures.~~

C4.18 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for obtaining and reviewing feedback and taking action when appropriate.

C4.18.1 Feedback shall be obtained from associated Clinical Programs and Processing Facilities.

C4.18.2 Feedback shall be obtained from donors or legally authorized representatives.

C4.19 The ~~Medical~~ Collection Facility overseeing physician~~Director~~ shall review the quality management activities with representatives in key positions in all areas of the cellular therapy program, at a minimum, quarterly.

C4.19.1 Meetings shall have defined attendees, documented minutes, and assigned actions.

C4.19.2 Performance data and review findings shall be reported to key positions and staff.

C4.19.3 The ~~Medical~~ Collection Facility overseeing physician ~~Director~~ shall not approve their own work.

C4.20 The ~~Medical~~ Collection Facility overseeing physician ~~Director~~ shall ~~annually~~ review the effectiveness of the Quality Management Program annually.

C4.20.1 The annual report and documentation of the review findings shall be made available to key personnel, the Clinical Program Director, the Processing Facility Director, and staff of the program.

C5: POLICIES AND STANDARD OPERATING PROCEDURES

C5.1 The Collection Facility shall establish and maintain ~~P~~policies or Standard Operating Procedures addressing critical aspects of operations and management in addition to those required in C4 ~~shall be established and maintained~~. These documents shall include all elements required by these Standards and shall address at a minimum:

C5.1.1 Donor and recipient confidentiality.

C5.1.2 Donor informed consent for cellular therapy product collection~~, processing and manufacturing, storage, distribution, and disposition~~.

C5.1.3 Donor screening, testing, eligibility and suitability determination, and management.

C5.1.4 Donor-specific issues related to age, sex, height, and weight.

C5.1.5 Management of donors who require central venous access.

C5.1.6 Cellular therapy product collection.

C5.1.7 Prevention of mix-ups and cross-contamination.

C5.1.8 Labeling ~~(~~including associated forms and samples~~)~~.

C5.1.9 Cellular therapy product expiration dates.

C5.1.10 Cellular therapy product storage.

C5.1.11 Release and exceptional release.

C5.1.12 Chain of Identity.

C5.1.13 Chain of Custody.

C5.1.14 Packaging, transportation, and shipping~~.~~ including ~~C5.1.11.1 m~~Methods and conditions to be used within the Collection Facility and for distribution to external facilities.

~~C5.1.11.2 Use of additives for long duration of shipment.~~

C5.1.15 Critical equipment, reagent, and supply management, including recalls and corrective actions in the event of failure.

C5.1.16 Equipment operation, maintenance, and monitoring including corrective actions in the event of malfunction or failure.

C5.1.17 Cleaning and sanitation procedures including identification of the individuals responsible for the activities.

C5.1.18 Hygiene and use of personal protective equipment and attire.

C5.1.19 Handling and ~~D~~disposal of medical and biohazard waste.

C5.1.20 Cellular therapy emergency and disaster plan, including the collection staff response and product management.

~~C5.1.18 Response to emerging disease agents, including donor evaluation and management and personnel safety.~~

C5.2 The Collection facility shall maintain a~~A~~ detailed list of all controlled documents, including title and identifier, ~~shall be maintained~~ for collection activities.

C5.3 Standard Operating Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to follow and complete the procedures successfully. Each individual Standard Operating Procedure shall include:

C5.3.1 A clearly written description of the objectives, scope, and responsibilities.

C5.3.2 A description of equipment, reagents, and supplies used.

C5.3.3 Acceptable endpoints and the range of expected results.

C5.3.4 A stepwise description of the procedure.

~~C5.3.5 Donor age-specific issues where relevant.~~

C5.3.5 Reference to other Standard Operating Procedures or policies required to perform the procedure.

C5.3.6 A reference section listing appropriate and current literature.

C5.3.7 Documented approval of each Standard Operating ~~p~~Procedure by the Collection Facility Director ~~or Medical Director~~overseeing physician, as appropriate, prior to implementation and every two (2) years thereafter.

C5.3.8 Documented approval of each procedural modification ~~to a Standard Operating Procedure~~ by the Collection Facility ~~Director or Medical Director~~overseeing physician, as appropriate, prior to implementation.

C5.3.9 Reference to the current version of orders, worksheets, reports, labels, and forms.

C5.4 Controlled documents relevant to processes being performed shall be readily available to the Collection F~~f~~acility staff.

C5.5 Staff review and, if appropriate, training and competency shall be documented before performing a new or revised ~~Standard Operating P~~procedure.

C5.6 All personnel shall follow the policies and Standard Operating Procedures related to their positions.

C5.7 Planned deviations shall be pre-approved by the Collection Facility ~~Director~~overseeing physician and ~~or Medical Director and~~ reviewed by the Quality Manager.

C6: ALLOGENEIC AND AUTOLOGOUS DONOR EVALUATION AND MANAGEMENT

C6.1 There shall be written criteria for allogeneic and autologous donor evaluation and management by trained medical personnel.

C6.1.1 The donor shall undergo the collection procedure as a site with the appropriate capabilities to manage the level of acuity and risk.

C6.2 ALLOGENEIC AND AUTOLOGOUS DONOR INFORMATION AND CONSENT FOR COLLECTION

C6.2.1 The collection procedure shall be explained in terms the donor can understand~~,~~ and shall include the following information at a minimum:

C6.2.1.1 The risks and benefits of the procedure.

C6.2.1.2 The ~~I~~intent of the collection for treatment or research.

C6.2.1.3 Tests and procedures performed on the donor or donor's specimens to protect the health of the donor and the recipient.

C6.2.1.4 The rights of the donor or legally authorized representative to review the results of such tests according to Applicable Law.

C6.2.1.5 Protection of medical information and confidentiality.

C6.2.1.6 Alternative collection methods.

C6.2.2 Interpretation and translation shall be performed by individuals qualified to provide these services in the clinical setting.

C6.2.2.1 Family members and legally authorized representatives shall not serve as interpreters or translators.

C6.2.3 The donor shall have an opportunity to ask questions.

C6.2.4 The donor shall have the right to refuse to donate or withdraw consent.

C6.2.4.1 The allogeneic donor shall be informed of the potential consequences to the recipient of such refusal in the event that consent is withdrawn after the recipient has begun the preparative regimen.

C6.2.5 Donor informed consent for ~~the~~ cellular therapy product collection, including use, storage, and discard, shall be obtained and documented by a licensed health care professional knowledgeable in the collection procedure and intended use of the product.

C6.2.5.1 Informed consent from the allogeneic donor shall be obtained by a licensed health care professional who is not the primary health professional overseeing care of the recipient.

~~C6.2.6 For directed cellular therapy product donations, informed consent of the recipient for the cellular therapy shall be obtained before cellular therapy product collection.~~

C6.2.6 In the case of a donor who is a minor or who does not have the capacity to give consent, informed consent shall be obtained from the donor's legally authorized representative in accordance with Applicable Law and shall be documented.

C6.2.6.1 There should be a process to obtain appropriate assent from minor donors.

C6.2.7 The allogeneic donor shall give informed consent and authorization prior to release of the donor's health or other information to the recipient or the recipient's physician ~~or the recipient~~.

C6.2.8 The donor shall be informed of the policy for cellular therapy product storage, discard, or disposal, including actions taken when an intended recipient no longer requires the cellular therapy product.

C6.2.9 Documentation of consent shall be verified by the ~~c~~Collection Facility staff prior to the collection procedure.

C6.3 SUITABILITY DETERMINATION FOR ALLOGENEIC AND AUTOLOGOUS DONORS ~~Suitability for Cellular Therapy Product Collection~~

C6.3.1 There shall be criteria and evaluation policies or Standard Operating Procedures in place to protect the safety of donors during the process of cellular therapy product collection.

C6.3.1.1 The collection staff shall confirm that clinically significant findings are reported to the ~~prospective~~ donor with documentation in the donor's record of recommendations made for follow-up care.

C6.3.1.2 Allogeneic donor suitability shall be evaluated by a licensed health care professional who is not the primary health care professional overseeing care of the recipient.

C6.3.1.3 Autologous donors shall be evaluated and tested as required by Applicable Law.

C6.3.2 The risks of the ~~cellular therapy product~~ collection procedure shall be evaluated and documented, including: ~~.~~

C6.3.2.1 Possible need for central venous access.

C6.3.2.2 Anesthesia for cell or tissue collection.

C6.3.2.3 Mobilization for cell collection, if used.

C6.3.2.4 Other donor-specific risks.

C6.3.3 Administration of appropriate mobilization agents if required shall be under the supervision of a licensed health care professional experienced in their administration and management of complications in persons receiving these agents.

C6.3.4 A pregnancy test shall be performed for all ~~female~~ donors with childbearing potential~~: within seven (7) days prior to cellular therapy product collection, undergoing anesthesia, and, as applicable, within seven (7) days prior to the preparation of the recipient for administration.~~

C6.3.4.1 For collections with mobilization, ~~a pregnancy test shall be performed~~ within seven (7) days prior to ~~the initiation of~~starting the donor mobilization regimen or undergoing anesthesia and, as applicable, within seven (7) days prior to the initiation of the recipient's preparative regimen.

C6.3.4.2 For collections without mobilization, within seven (7) days prior to cellular therapy collection and, as applicable, within seven (7) days prior to the initiation of the recipient's preparative regimen.

C6.3.5 The donor shall be evaluated for the risk of hemoglobinopathy, and if indicated, tested.

C6.3.5.1 The evaluation shall be verified prior to collection or administration of the mobilization regimen, if used.

C6.3.6 Laboratory testing of all donors shall be performed by a laboratory that is accredited, registered, certified, or licensed in accordance with Applicable Law.

C6.3.7 The Collection Facility shall verify that appropriate donor suitability has been determined.

C6.3.8 Collection from a donor who does not meet ~~Clinical Program~~ collection ~~safety~~ suitability criteria shall require documentation of the rationale for ~~their~~ selection by the ~~administering~~ donor's physician and approval by the Collection Facility Medical Director. Collection staff shall document review of these donor suitability issues.

~~C6.3.5.1 Issues of donor health that pertain to the safety of the collection procedure shall be available to the collection staff. Collection staff shall document review of these issues prior to collection.~~

C6.3.9 If central venous access is required:

C6.3.9.1 The rationale shall be documented in the donor's records.

C6.3.9.2 Adequacy of central line placement shall be verified and documented by the Collection Facility staff prior to initiating each collection procedure.

C6.3.10 There shall be a policy or Standard Operating Procedure for the management of collection-associated adverse events and follow-up of donors ~~that includes routine management~~.

C6.3.10.1 There shall be a process to track and trend collection-associated adverse events.

C6.4 ADDITIONAL REQUIREMENTS FOR ALLOGENEIC DONORS

C6.4.1 A donor advocate shall be available to represent allogeneic donors who are minors or who ~~are mentally incapacitated~~do not have the capacity to consent, as those terms are defined by Applicable Law.

C6.4.2 Allogeneic donor infectious disease testing shall be performed using donor screening tests licensed, approved, or cleared by the governmental authority.

C6.4.2.1 Hemodilution in the donor prior to collection of blood samples for infectious disease testing ~~and acceptance criteria shall~~should be assessed, and acceptance criteria ~~documented~~should be defined.

C6.4.3 Collection staff shall comply with B6.4.8~~6~~ through B6.4.8~~6~~.8~~7~~ when primarily responsible for donor screening for transmissible disease.

C6.4.4 Collection staff shall comply with B6.4.9~~7~~ through B6.4.13~~1~~ when primarily responsible for infectious and non-infectious disease testing of donors.

C6.4.5 Collection staff shall comply with B6.4.4, B6.4.5,~~2~~ and ~~-~~B6.4.14 ~~and~~ through B6.4.14.3~~2~~ when primarily responsible for testing for the selection of allogeneic donors.

C6.4.6 Collection staff shall confirm that allogeneic donor eligibility determination was performed prior to collection, starting the donor mobilization regimen, or initiation of the recipient's preparative regimen.

C6.4.7 Collection of a cellular therapy product from an ineligible allogeneic donor, or from an allogeneic donor for whom donor eligibility determination is incomplete, shall require documentation of urgent medical need that includes the rationale for the selection and documentation of the informed consent of the donor and the recipient.

C6.4.8 Records required for donor eligibility determination shall be in English or translated into English when crossing international borders.

C6.4.9 Allogeneic donor eligibility shall be communicated in writing to the Processing Facility.

C6.5 There shall be policies covering the creation and retention of donor records, including at a minimum:

C6.5.1 Allogeneic donor eligibility and suitability determination, including the name of the responsible person who made the determination and the date of the determination.

C6.5.2 Donor identification including at minimum name and date of birth.

C6.5.3 Age, ~~gender~~sex at birth, medical history, and, for allogeneic donors, behavioral history.

C6.5.4 Consent to donate.

C6.5.5 Results of laboratory testing.

C7: CODING AND LABELING OF CELLULAR THERAPY PRODUCTS

C7.1 ISBT 128 CODING AND LABELING

C7.1.1 Cellular therapy products shall be identified by name according to ISBT 128 standard terminology or relevant regulatory labeling requirements.

C7.1.2 Coding and labeling technologies shall be implemented using ISBT 128.

C7.2 LABELING OPERATIONS

C7.2.1 Labeling operations shall be conducted in a manner adequate to prevent mislabeling or misidentification of cellular therapy products, product samples, and associated records.

C7.2.1.1 Stocks of unused labels representing different cellular therapy products shall be stored in a controlled manner to prevent errors.

C7.2.1.2 Obsolete labels shall be restricted from use.

C7.2.2 Pre-printed labels shall be ~~held~~ quarantined upon receipt from the manufacturer pending review and proofing against a copy or template approved by the ~~Medical~~ Collection Facility ~~Director~~ overseeing physician to confirm accuracy regarding identity, content, and conformity.

~~C7.2.2.1 Stocks of unused labels representing different products shall be stored in a controlled manner to prevent errors.~~

C7.2.3 A system of label reconciliation shall be used to ensure the final disposition of all labels allocated to a specific product is documented.

C7.2.4 Label systems shall be validated to confirm accuracy regarding identity, content, and conformity of labels to templates approved by the ~~Medical~~ Collection Facility ~~Director~~overseeing physician.

C7.2.5 A system for label version control shall be employed.

C7.2.5.1 Representative obsolete labels with inclusive dates of use shall be archived ~~minimally~~ for a minimum of ten (10) years after the last cellular therapy product was distributed ~~with inclusive dates of use~~ or as defined by Applicable Law, whichever is longer.

C7.2.6 A system of checks in labeling procedures shall be used to prevent errors in transferring information to labels.

C7.2.6.1 The information entered on a container label shall be verified by one (1) qualified staff member using a validated process or two (2) qualified staff members ~~prior to distribution of the cellular therapy product~~.

C7.2.6.2 A controlled labeling procedure consistent with Applicable Law shall be defined and followed if container label information is transmitted electronically during a labeling process. This procedure shall include a verification step.

C7.2.6.3 Cellular therapy products that are subsequently re-packaged into new containers shall be labeled with new labels before they are detached from the original container.

C7.2.7 When the label has been affixed to the container, a sufficient area of the container shall remain uncovered to permit inspection of the contents.

C7.2.8 Labeling elements required by Applicable Law shall be present.

C7.2.9 All data fields on labels shall be completed.

C7.2.10 All labeling shall be clear, legible, and completed using ink that is indelible to all relevant agents.

C7.2.11 Labels affixed directly to a cellular therapy product bag or ~~–~~container shall be applied using appropriate materials as defined by the applicable regulatory authority.

C7.2.12 The label shall be validated as reliable for storage under the conditions in use.

C7.3 PRODUCT IDENTIFICATION

C7.3.1 Each cellular therapy product collection shall be assigned a unique numeric or alphanumeric donation identifier by which it will be possible to trace any cellular therapy product to its donor, its recipient or final disposition, and all ~~accompanying~~ records~~, and its recipient or final disposition~~.

C7.3.1.1 The cellular therapy product, product samples, concurrent plasma, and concurrently collected donor samples shall be labeled with the same identifier.

C7.3.1.2 If a single cellular therapy product is stored in more than one (1) container, there shall be a system to identify each container.

C7.3.1.3 If cellular therapy products from the same donor are pooled, the ~~identifier on the pooled product~~pool identifier shall allow tracing to the original products.

C7.3.2 Supplementary identifiers shall not obscure the original identifier.

C7.3.3 The facility associated with each identifier shall be named in the documents to accompany the cellular therapy product.

C7.3.4 If the original identifier is replaced, documentation shall link the new identifier to the original.

C7.4 LABEL CONTENT

C7.4.1 ~~At all stages of collection, t~~The cellular therapy product shall be labeled with the proper name of the product and the unique numeric or alphanumeric identifier, at a minimum.

C7.4.2 Labeling at the end of collection shall occur before the cellular therapy product is removed from the proximity of or disconnected from the donor.

C7.4.2.1 The content of the label shall be verified prior to removing the cellular therapy product from the proximity of the donor.

C7.4.3 At the end of the cellular therapy product collection, the cellular therapy product label on the primary product container and concurrent plasma container shall bear the information in the Cellular Therapy Product Labeling table in Appendix I.

C7.4.4 Each label shall bear the appropriate biohazard and warning labels as found in the *Circular of Information for the Use of Cellular Therapy Products*, ~~"~~Table 2~~. Biohazard and Warning Labels on Cellular Therapy Products Collected, Processed, and/or Administered in the United States" or other appropriate labels as required by Applicable Law.~~

C7.4.5 A cellular therapy product collected in or designated for use in the U.S. shall be accompanied by the elements listed in the Accompanying Documentations ~~at Distribution~~ table in Appendix III at the time ~~of distribution~~it leaves the control of the Collection Facility.

C7.4.6 Any container bearing a partial label at the time of distribution shall be accompanied by the information required by the Cellular Therapy Product Labeling table in Appendix I. Such information shall be attached securely to the cellular therapy product on a tie tag or enclosed in a sealed package to accompany the product.

C7.4.7 For allogeneic cellular therapy products distributed before completion of donor eligibility determination, there shall be documentation that donor eligibility determination was completed during or after distribution of the cellular therapy product and that the physician using the product shall be~~was~~ informed of the results of that determination.

C7.4.8 Cellular therapy products for third-party manufacturers shall be labeled with product labels that conform to FACT requirements or Applicable Law.

C7.4.9 Cellular therapy products distributed for nonclinical purposes shall be designated and labeled with the statement, "For Nonclinical Use Only."~~as not for clinical use.~~

C8: EQUIPMENT, SUPPLIES, AND REAGENTS

C8.1 Equipment, supplies, and reagents used to collect cellular therapy products shall be qualified and used in a manner that maintains product function and integrity and minimizes risks of product mix-ups, contamination, and cross-contamination.

C8.2 There shall be adequate equipment and materials for the procedures performed.

C8.3 There shall be a process for inventory control that encompasses equipment, containers for transport and shipping, supplies, reagents, and labels.

C8.3.1 There shall be a system to uniquely identify and track and trace all critical equipment, supplies, reagents, and labels used in the collection of cellular therapy products.

C8.3.2 Each supply and reagent used to collect cellular therapy products shall be visually examined at receipt and prior to use for damage or evidence of contamination.

C8.3.2.1 Supplies and reagents shall be quarantined prior to use until verified to have met acceptance criteria.

C8.3.3 Records of receipt shall include the supply or reagent type, quantity, manufacturer, lot number, date of receipt, acceptability, and expiration date.

C8.3.4 Materials shall be stored under the appropriate environmental conditions in a secure, sanitary, and orderly manner to prevent mix-up or unintended use.

C8.3.5 Supplies and reagents coming into contact with cellular therapy products during collection shall be qualified, sterile, and ~~of the appropriate grade~~meet predetermined specifications for the intended use.

C8.3.6 Non-disposable supplies or instruments shall be cleaned and sterilized using a procedure verified to remove infectious agents and other contaminants.

C8.3.7 Supplies and reagents shall be used in a manner consistent with manufacturer instructions.

C8.3.8 There shall be a process to prevent the use of expired reagents and supplies.

C8.3.9 Equipment, supplies and reagents for the collection procedure shall conform to Applicable Law.

C8.4 There shall be a process for equipment management that encompasses maintenance, cleaning, and calibration.

C8.4.1 Equipment used in the collection of cellular therapy products shall be maintained in a clean and orderly manner. Equipment shall be located to facilitate cleaning, calibration, and maintenance according to established schedules, as described in Standard Operating Procedures, and in accordance with the manufacturer's recommendations.

C8.4.1.1 The equipment shall be inspected for cleanliness and verified to be in compliance with the maintenance schedule prior to use.

C8.4.2 The equipment shall be standardized and calibrated on a regularly scheduled basis and after a critical repair or move as described in Standard Operating Procedures and in accordance with the manufacturer's recommendations.

C8.4.2.1 All equipment with a critical measuring function shall be calibrated against a traceable standard, if available. Where no traceable standard is available, the basis for calibration shall be described and documented.

C8.4.2.2 Calibration shall be performed according to established schedules as described in Standard Operating Procedures and in accordance with the manufacturer's recommendations.

C8.4.2.3 When equipment is found to be out of calibration or specification, there shall be a defined process for action required for cellular therapy products collected since the last calibration.

C8.5 Lot numbers, expiration dates, manufacturers of critical reagents and supplies, and key equipment used in each procedure shall be documented.

C9: PROCESS CONTROLS

C9.1 Collection of cellular therapy products shall be performed according to written Standard Operating Procedures.

C9.2 Autologous or CMV-appropriate and irradiated (or equivalent) blood products shall be available during the collection procedure for all donors.

C9.3 There shall be a written order from a physician specifying, at a minimum, an anticipated date and goals of collection.

C9.4 There shall be peripheral blood count criteria to proceed with collection including the timing of sample collection.

C9.4.1 The peripheral blood count criteria shall be met and documented prior to each collection.

C9.4.1.1 A complete blood count, including platelet count, shall be performed within 24 hours prior to each subsequent cellular therapy product collection.

~~C8.2 There shall be a process for inventory control that encompasses equipment, containers for transport and shipping, supplies, reagents, and labels.~~

~~C8.2.1 There shall be a system to uniquely identify and track and trace all critical equipment, supplies, reagents, and labels used in the collection of cellular therapy products.~~

~~C8.2.2 Each supply and reagent used to collect cellular therapy products shall be visually examined at receipt and prior to use for damage or evidence of contamination.~~

~~C8.2.2.1 Supplies and reagents shall be quarantined prior to use until verified to have met acceptance criteria.~~

~~C8.3 There shall be a process for equipment management that encompasses maintenance, cleaning, and calibration.~~

~~C8.3.1 Equipment shall be maintained in a clean and orderly manner.~~

~~C8.3.1.1 Cleaning shall be performed according to established schedules as described in Standard Operating Procedures and in accordance with the manufacturer's recommendations.~~

~~C8.3.1.2 Equipment shall be inspected for cleanliness and documented to be clean prior to use.~~

~~C8.3.2 Maintenance shall be performed according to established schedules as described in Standard Operating Procedures and in accordance with the manufacturer's recommendations.~~

~~C8.3.2.1 The equipment shall be verified and documented to be in compliance with the maintenance schedule prior to use.~~

~~C8.4 All equipment with a critical measuring function shall be calibrated against a traceable standard, if available. Where no traceable standard is available, the basis for calibration shall be described and documented.~~

~~C8.4.1 Calibration shall be performed according to established schedules as described in Standard Operating Procedures and in accordance with the manufacturer's recommendations.~~

~~C8.4.2 When equipment is found to be out of calibration or specification, there shall be a defined process for action required for cellular therapy products collected since the last calibration.~~

~~C8.5 Equipment, supplies and reagents for the collection procedure shall conform to Applicable Law.~~

C9.5 There shall be written documentation of a daily~~n~~ assessment of donor suitability for the collection procedure performed by a qualified person immediately prior to each collection procedure.

~~C8.8 There shall be a written order from a physician specifying, at a minimum, an anticipated date and goals of collection.~~

C9.6~~8~~ Collection procedures shall include a process for assessing the quality of cellular therapy products to ensure ~~confirm~~ product safety and integrity and to document that products meet predetermined release specifications. Results of all such assessments and procedures shall become part of the permanent record of the product collected.

C9.6.1 Methods for collection shall employ procedures that minimize the risk of microbial contamination and are validated to result in acceptable cell viability and collection yield.

C9.7 There shall be a process to verify the donor's identity and the intended collection procedure prior to initiating the collection procedure.

C9.8 Collection methods shall employ appropriate age, sex, height, and weight~~size~~ adjustments to the procedures when required.

C9.9 Cellular therapy products shall be ~~packaged~~ collected in ~~closed~~ sterile containers appropriate for the product ~~collected~~.

C9.9.1 Containers shall be securely closed to prevent leakage or contamination prior to distribution.

C9.10 Records shall be made concurrently with each step of collection of each cellular therapy product in such a way that all steps may be accurately traced.

C9.10.1 Records shall identify the person immediately responsible for each significant step, including dates and times, where appropriate.

C9.11 The Collection Facility shall provide the Clinical Facility, Processing Facility, or manufacturer with a summary of all cellular therapy product records relating to the collection procedure and storage procedures performed as required.

C9.12 When a collection kit is prepared and sent to collection staff, there shall be adequate instructions and materials to collect, label, store, pack, and transport or ship the cellular therapy product and associated samples to the Processing Facility.

C9.12.1 The collection kit shall be transported or shipped under conditions validated to maintain the designated temperature range from the time it leaves the shipping facility until it is received by the collection staff.

~~C8.11 Marrow Cellular therapy products that may contain particulate material shall be filtered to remove particulate material prior to final packaging, distribution, or administration using filters that are non-reactive with blood.~~

C10: CELLULAR THERAPY PRODUCT STORAGE

C10.1 Collection Facilities shall control and secure ~~S~~storage areas ~~shall be secure and controlled~~ in a manner to prevent mix-ups, deterioration, contamination, cross-contamination, and improper release or distribution of cellular therapy products.

C10.2 STORAGE DURATION

~~C9.2 Collection policies or Standard Operating Procedures shall include the duration and conditions of short-term storage prior to distribution to a Processing Facility or Clinical Program.~~

C10.2.1 Conditions and duration of storage, including temperature of ~~for~~ all cellular therapy products, shall be defined and validated.

C10.2.2 ~~When~~ Collection Facilities collecting, storing, or releasing cellular therapy products for administration, processing, or further manufacturing~~,~~ shall assign an expiration date and time ~~shall be assigned~~.

C10.3 STORAGE TEMPERATURE

C10.3.1 Storage temperatures shall be defined in Standard Operating Procedures.

C10.3.2 Cellular therapy products shall be maintained within a specific temperature range to maintain viability and function.

C10.4 STORAGE MONITORING

C10.4.1 Storage devices shall have a system to monitor the temperature continuously and to record the temperature at least every four (4) hours.

C11~~0~~: CELLULAR THERAPY PRODUCT TRANSPORTATION AND SHIPPING

C11.1 Standard Operating Procedures for transportation and shipping of the cellular therapy product shall be designed to protect the integrity of the product and the health and safety of individuals ~~in the immediate area~~in the immediate area.

C11.2 The primary cellular therapy product container shall be placed in a secondary container ~~that is~~and sealed to prevent leakage.

C11.3 Conditions shall be established and maintained to preserve the integrity and safety of cellular therapy products during transport or shipping.

C11.4 Cellular therapy products transported internally shall be packaged in a qualified, closed, and rigid outer container.

C11.4.1 The outer container for internal transport shall be labeled as defined in Appendix II B.

C11.5 Cellular therapy products that are shipped to another facility or transported on public roads shall be packaged in an outer container.

C11.5.1 The outer container shall conform to the applicable regulations regarding the mode of transportation or shipping.

C11.5.2 The outer container shall be made of material adequate to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling during transport or shipping.

C11.5.3 The outer container shall be secured to prevent unauthorized access.

C11.5.3.1 A mechanism should be in place to allow detection if the shipping container was opened. If opened, the shipping facility should be notified.

C11.5.4 The outer container shall be labeled as defined in the Cellular Therapy Product Labels for Shipping and Transport on Public Roads table in Appendix II A.

C11.5.5 There shall be a document inside the outer container that includes all the information required on the outer container in conformity with the Cellular Therapy Product Labels for Shipping and Transport on Public Roads table in Appendix II A.

C11.6 C~~The c~~ellular therapy product~~s shall be~~ transported or shipped over an extended period of time shall be transported or shipped ~~to the Processing Facility~~ in a ~~validated~~ container within a temperature range defined in a Standard Operating Procedure or written agreement and according to manufacturer instructions.

C11.6.1 Additives to the cellular therapy product should be used for shipping or transporting over a prolonged duration of time.

~~C10.3.1 Cellular therapy products that are transported or shipped from the collection site to a processing facility shall be in an outer container made of material adequate to withstand leakage of contents, impact shocks, pressure changes, temperature changes, puncture, and other conditions incident to ordinary handling.~~

~~C10.3.2 The outer container shall conform to the applicable regulations regarding the mode of transportation or shipping.~~

~~C10.3.3 When a cellular therapy product is transported or shipped on public roads the outer container shall be secured.~~A mechanism should be in place to allow detection if the shipping container was opened. If opened, the shipping facility should be notified.

~~C10.4 When a cellular therapy product is transported or shipped on public roads, the outer container shall be labeled as defined in the Cellular Therapy Product Labels for Shipping and Transport on Public Roads table in Appendix II A.~~

~~C10.4.1 There shall be a document inside the outer container that includes all the information required on the outer container.~~

~~C10.4.2 The cellular therapy product shall be transported or shipped with required accompanying records as defined in the transportation and shipping Standard Operating Procedures and in compliance with C7.4.5 and C7.4.6.~~

~~C10.4.3 The outer container shall be labeled in accordance with Applicable Law regarding the cryogenic material used and the transport or shipment of biological materials.~~

~~C10.5 There shall be a record of the date and time of cellular therapy product distribution.~~

~~C10.6 Cellular therapy products transported internally shall be packaged in a qualified, closed, and protective outer container.~~

~~C10.6.1 The outer container for internal transport shall be labeled as defined in Appendix II B.~~

C11.7 There shall be a risk assessment to evaluate the need for continuous temperature monitoring during transportation or shipment of cellular therapy products.

C11.8 If the intended recipient has received high-dose therapy, the cellular therapy product shall be transported.

C11.9 The transit time shall be within time limits determined by the distributing facility in consultation with the receiving facility to maintain cellular therapy product safety.

C11.10 There shall be contingency plans for alternative means of transport or shipping in an emergency.

C11.11 The cellular therapy product shall be transported or shipped with required accompanying records as defined in ~~the transportation and shipping~~ Standard Operating Procedures and in compliance with C7.4 ~~.5 and C7.4.6~~as applicable.

C11.12 There shall be a record of the date and time of cellular therapy product distribution.

C11.13 ~~The c~~Cellular therapy products should not be passed through X-~~R~~ray irradiation devices designed to detect metal objects. If inspection is necessary, the contents of the container should be inspected manually.

~~C10.10 A mechanism should be in place to allow detection if the shipping container was opened. If opened, the shipping facility should be notified.~~

C12: RECORDS

C12.1 There shall be a records management system for quality and cellular therapy product record creation, assembly, review, storage, archival, and retrieval.

C12.1.1 A records management system shall be established and maintained to facilitate the review of records.

C12.1.2 The records management system shall facilitate tracking of the cellular therapy product from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.

C12.1.3 For cellular therapy products that are to be distributed for use at another institution, the ~~c~~Collection Facility~~staff~~ shall inform the receiving institution of the tracking system and ~~the~~ requirement for tracking the product in writing or electronic format at or before the time of product distribution.

C12.1.4 Records shall be maintained ~~in such a way as~~ to ensure their integrity, preservation, and retrieval.

C12.1.5 Records shall be accurate and legible.

C12.1.6 Written records shall be indelible.

C12.1.7 Safeguards to secure the confidentiality of all records and communications among the clinical, collection, and processing staff~~, processing facilities and clinical facilities, and health care providers~~ and ~~their~~with donors and recipients ~~and donors~~ shall be established and followed in compliance with Applicable Law.

C12.2 The Collection Facility shall define and follow ~~G~~good documentation practices ~~shall be defined and used~~.

C12.3 RECORDS TO BE MAINTAINED

~~C11.2.1Records shall be accurate and legible.~~

~~C11.2.2Written records shall be indelible.~~

~~C11.3 Records shall be maintained in such a way as to ensure their integrity, preservation, and retrieval.~~

~~C11.4 Safeguards to secure the confidentiality of all records and communications among the collection staff, processing facilities and clinical facilities, and health care providers and their recipients and donors shall be established and followed in compliance with Applicable Law.~~

C12.3.1 Collection Facility records related to quality control, personnel training and competency, facility maintenance, facility management, complaints, or other general facility issues shall be retained for a minimum of ten (10) years ~~or~~ after the creation of the cellular therapy product record, date of the cellular therapy product's distribution, disposition, or expiration, whichever is latest, or ~~longer in~~ according to ~~ance with~~ Applicable Law.

C12.3.2 Records of ~~V~~validation studies for a collection procedure shall be retained at a minimum until the procedure is no longer in use and no products remain in storage that were collected using that procedure~~for the duration of the use of the procedure~~.

C12.3.3 Employee records shall be maintained in a confidential manner, as required by Applicable Law.

C12.3.4 Cleaning and sanitation records shall be retained for a minimum of three (3) years or longer in accordance with Applicable Law or by a defined program or institutional policy.

C12.3.5 Records to allow tracking and tracing of cellular therapy products shall be maintained in a confidential manner for a minimum of ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, or as required by Applicable law, whichever is latest.

C12.3.5.1 These records shall include the identity of the Collection Facility, ~~product code,~~ unique numeric or alphanumeric identifier, ~~and~~ collection date and time, product code,~~;~~ and donor and recipient identification as found on the original container~~far as known~~.

C12.4 Recipient and donor records including, but not limited to, consents and records of care shall be maintained in a confidential manner as required by Applicable Law for a minimum of ten (10) years after the administration of the cellular therapy product, or, if not known, ten (10) years after the date of the distribution, disposition, or expiration of the product, whichever is latest.

C12.5 Research records shall be maintained in a confidential manner as required by Applicable Law or for a minimum of ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, whichever is latest.

C12.6 ELECTRONIC RECORDS

C12.6.1 The~~re~~ Collection Facility shall ~~be~~ maintain a current listing of all critical electronic record systems. Critical electronic record systems shall include at a minimum~~,~~ systems ~~under the control of the cellular therapy program~~ that are used as a substitute for paper, to make decisions, to perform calculations, or to create or store information used in critical procedures. For all critical electronic recording systems:

C12.6.1.1 ~~For all critical electronic record systems, t~~There shall be policies, Standard Operating Procedures, and system ~~controls~~ elements to maintain the accuracy, integrity, identity, and confidentiality of all records.

C12.6.1.2 There shall be a means by which access to electronic records is limited to authorized individuals.

C12.6.1.3 A method shall be established or the system shall provide for the unambiguous identification of the individual responsible for each record entry.

C12.6.1.4 ~~For all critical electronic record systems, t~~There shall be written policies and Standard Operating Procedures for record entry, verification, and revision.

C12.6.1.5 A method shall be established or the system shall provide for review of data before final acceptance.

C12.6.1.6 There shall be documented ~~T~~training ~~and continued competency~~ of personnel in the system's use.

C12.6.1.7 There shall be a defined process for continued competency of personnel in the system's use.

C12.6.1.8 There shall be a defined process for the use of electronic signatures.

C12.6.1.9 ~~The critical electronic record system shall maintain u~~Unique identifiers shall be maintained.

C12.6.1.10 ~~For all critical electronic record systems, t~~There shall be the ability to generate true copies of the records in both human-readable and electronic format suitable for inspection and review.

C12.6.1.11 There shall be protection of ~~the~~ records to enable their accurate and ready retrieval throughout the period of record retention.

C12.6.1.12 ~~For all critical electronic record systems, t~~All system modifications shall be authorized, documented, and validated prior to implementation.

~~C11.9.7.1 A method shall be established or the system shall provide for review of data before final acceptance.~~

C12.6.2 For all critical electronic record systems under the control of the Collection Facility, there shall be ~~validated~~ additional ~~procedures~~ processes for and documentation of:

C12.6.2.1 Prospective validation of systems, including hardware, software, and databases.

C12.6.2.2 Installation of the system.

C12.6.2.3 Numerical designation of system versions, if applicable.

C12.6.2.4 Authorization and validation of all system modifications prior to implementation.

C12.6.2.5 Systems development, including the verification of calculations and algorithms.

C12.6.2.6 System maintenance and operations.

C12.6.2.7 Monitoring of data integrity.

C12.6.2.8 Back-up of the electronic records system on a regular schedule.

C12.6.3 For each critical electronic record system, there shall be an alternative system ~~for all electronic records~~ to allow for continuous operation of the Collection Facility ~~in the event that~~ if the critical electronic record system is not available. The alternative system shall be validated, and collection staff shall be trained in its use.

~~C11.9.9.9 System assignment of unique identifiers.~~

~~C11.9.10 All system modifications shall be authorized, documented, and validated prior to implementation.~~

C12.7 RECORDS IN CASE OF DIVIDED RESPONSIBILTY

C12.7.1 If two (2) or more facilities participate in the collection, processing, or administration of the cellular therapy product, the records of each facility shall show plainly the extent of its responsibility.

C12.7.2 ~~A copy of all cellular therapy product records relating to the collection procedure~~ The Collection Facility shall ~~be~~ furnish~~ed~~ to the facility of final disposition a copy of all cellular therapy product collection~~s~~ records defined in the agreement, policies, or Standard Operating Procedures.

~~C11.10.2 If two (2) or more facilities participate in the collection, processing, or administration of the cellular therapy product, the records of each facility shall show plainly the extent of its responsibility.~~

PART D: PROCESSING FACILITY STANDARDS

D1: General

D2: Processing Facility

D3: Personnel

D4: Quality Management

D5: Policies and Standard Operating Procedures

D6: Equipment, Supplies, and Reagents

D7: Coding and Labeling of Cellular Therapy Products

D8: Process Controls

D9: Cellular Therapy Product Storage

D10: Cellular Therapy Product Transportation and Shipping

D11: Receipt and Distribution

D12: Disposal

D13: Records

PART D: PROCESSING FACILITY STANDARDS

D1: GENERAL

D1.1 These Standards apply to all processing, storage, and distribution activities performed in the Processing Facility on cellular therapy products.

D1.2 The Processing Facility shall abide by Applicable Law.

D1.2.1 The Processing Facility shall be licensed, registered, or accredited as required by the appropriate governmental authorities for the activities performed.

D1.3 The Processing Facility shall have a Processing Facility Director, a Processing Facility Medical Director, a Quality Manager, and a minimum of one (1) additional designated staff member. ~~This~~ The designated team shall have been in place and actively performing cellular therapy product processing for at least twelve (12) months preceding initial accreditation.

D2: PROCESSING FACILITY

D2.1 There shall be secured and controlled access to designated areas appropriate for the processing procedure(s) and for storage of equipment, supplies, reagents, cellular therapy products, and ~~reagents~~records.

D2.1.1 The designated area for processing shall be in an appropriate location of adequate space and design to minimize the risk of airborne or surface microbial contamination.

D2.1.2 The Processing Facility shall be divided into defined areas of adequate size to prevent improper labeling, mix-ups, contamination, or cross-contamination of cellular therapy ~~or genetically modified~~ products.

D2.1.3 There shall be a process to control storage areas to prevent mix-ups, contamination, and cross-contamination of cellular therapy products.

D2.2 The Processing Facility shall provide adequate lighting, ventilation, and access to sinks for hand-washing and to toilets to prevent the introduction, transmission, or spread of communicable disease.

~~D2.3 Oxygen sensors shall be appropriately placed and utilized in areas where liquid nitrogen is present.~~

D2.3 ~~Processing Facility parameters and e~~Environmental conditions shall be controlled to protect the safety and comfort of personnel.

D2.4 There shall be a written assessment of critical Processing Facility environmental parameters that may affect cellular therapy product viability, integrity, ~~or~~ contamination or cross-contamination during processing, storage, or distribution.

D2.4.1 The written assessment shall include temperature, humidity, air quality, and surface contaminants at a minimum.

D2.4.2 Critical facility parameters identified to be a risk to the cellular therapy product shall be controlled, monitored, and recorded.

D2.4.3 The Processing Facility shall qualify environmental control systems and validate cleaning and sanitation procedures appropriate for the environmental classification and degree of manipulation performed.

D2.5 The Processing Facility shall document facility cleaning and sanitation and shall maintain order sufficient to achieve adequate conditions for operations.

D2.6 The Processing Facility shall be operated in a manner designed to minimize risks to the health and safety of employees, visitors, and volunteers.

D2.7 The Processing Facility shall have a written safety manual that includes instructions for action in case of exposure~~, as applicable~~, to liquid nitrogen; communicable disease; and to chemical, biological, radiological, electrical, or fire hazards.

~~D2.89 There shall be a biosafety plan, if applicable, consistent with the Institutional Biosafety Committee (IBC) requirements that addresses genetically modified products in compliance with Applicable Law.~~

D2.8 All waste generated by the Processing Facility's activities shall be disposed of in a manner that minimizes any hazard to facility personnel and to the environment in accordance with Applicable Law.

~~D2.103 Oxygen sensors shall be appropriately placed and utilized in areas where liquid nitrogen is present.~~

~~D2.10.1 Oxygen sensors shall have visible and audible alarms with appropriate settings to ensure safety of personnel.~~

~~D2.10.2 In areas where liquid nitrogen is present, oxygen sensors shall be placed to alert staff working in the area to evacuate, and to notify any staff responding to the alarm not to enter the area.~~

~~D2.10.3 Instructions for staff responding to the alarm shall be posted at the entrances of areas where liquid nitrogen is present.~~

D2.9 There shall be a written policy for personal hygiene and the use of personal protective equipment and attire.

D2.9.1 The policy shall define the protective clothing to be worn upon entering the work area and while working within it.

D2.9.2 The policy shall define personal protective equipment appropriate for the activities and classification of the environment to be worn while handling biological specimens.

D2.9.3 Such personal protective equipment shall not be worn outside the designated work area.

D2.10 There shall be a biosafety plan, if applicable, consistent with the Institutional Biosafety Committee (IBC) requirements that addresses genetically modified products in compliance with Applicable Law.

D2.11 Oxygen sensors shall be appropriately placed and utilized in areas where liquid nitrogen is present.

D2.11.1 Oxygen sensors shall have visible and audible alarms with appropriate settings to ensure safety of personnel.

D2.11.2 In areas where liquid nitrogen is present, oxygen sensors shall be placed to alert staff working in the area to evacuate, and to notify any staff responding to the alarm not to enter the area.

D2.11.3 Instructions for staff responding to the alarm shall be posted at the entrances of areas where liquid nitrogen is present.

~~D2.11 Personal protective equipment, including gloves and protective clothing, shall be used while handling biological specimens. Such protective equipment shall not be worn outside the work area.~~

D2.12 When a collection kit is prepared and sent to collection staff, there ~~The Processing Facility~~ shall ~~provide~~~~When a collection kit is prepared and sent to collection staff, there shall be~~ be adequate instructions and materials to collect, label, store, pack, and transport or ship the cellular therapy product and associated samples to the Processing Facility.

D2.12.1 The~~The~~ collection kit shall be transported or shipped under conditions validated to maintain the designated temperature range from the time it ~~leaves the Processing Facility~~is distributed until it is received by the ~~collection~~ processing staff.

~~D2.12.2 Identity of the supplies and reagents including manufacturer, lot number, and expiration date shall be documented for each collection.~~

~~D2.12.3 Supplies and reagents shipped to the collection staff from the Processing Facility shall be in an outer container validated to maintain the designated temperature range.~~

D3: PERSONNEL

D3.1 PROCESSING FACILITY DIRECTOR

D3.1.1 There shall be a Processing Facility Director with a medical ~~degree,~~ or doctoral degree and a minimum of two (2) years of experience, or an Advanced Degree as defined in these Standards, with a minimum of ten (10) years of experience. Experience shall be in the field of cellular therapy and in the management and oversight of~~, or equivalent degree in a relevant science, qualified by a minimum of two (2) years training and experience for~~ the scope of activities carried out by~~in~~ the Processing Facility.

D3.1.2 The Processing Facility Director shall be responsible for all Standard Operating Procedures, technical procedures, performance of the processing procedure(s), supervision of staff, administrative operations, and ~~compliance with~~ the Quality Management Program ~~of the Processing Facility~~, including compliance with these Standards and Applicable Law.

D3.1.3 The Processing Facility Director shall have performed or supervised a minimum of five (5) cellular therapy product processing procedures in the twelve (12) months preceding initial accreditation and a minimum average of five (5) cellular therapy product processing procedures per year within each accreditation cycle.

D3.1.4 The Processing Facility Director shall participate in a minimum of ten (10) hours of educational activities annually.

~~D3.1.3.1 Continuing education shall includinge, but is not limited to, activities related to the cellular therapy product processing or the applicable therapeutic disease area.~~

D3.2 PROCESSING FACILITY MEDICAL DIRECTOR

D3.2.1 There shall be a Processing Facility Medical Director who is a licensed physician with a minimum of two (2) years of postgraduate education, including training and practical and relevant experience for the scope of activities carried out in the preparation and clinical use of cellular therapy products.

D3.2.2 The Processing Facility Medical Director shall be directly responsible for all medical aspects related to the Processing Facility.

D3.2.3 The Processing Facility Medical Director shall have performed, supervised, or reviewed a minimum of five (5) cellular therapy product processing procedures in the twelve (12) months preceding initial accreditation and a minimum average of five (5) cellular therapy product processing procedures per year within each accreditation cycle.

D3.2.4 The Processing Facility Medical Director shall participate in a minimum of ten (10) hours of educational activities annually.

~~D3.2.3.1 Continuing education shall includinge, but is not limited to, activities related to cellular therapy product processing or the applicable therapeutic disease area.~~

D3.3 QUALITY MANAGER

D3.3.1 There shall be a Processing Facility Quality Manager to establish and maintain systems to review, modify, and approve all policies and Standard Operating Procedures intended to monitor compliance with these Standards and the performance of the Processing Facility~~, these Standards, or Applicable Law~~.

D3.3.2 The Processing Facility Quality Manager should have a reporting structure independent of cellular therapy product manufacturing.

D3.3.3 The Processing Facility Quality Manager shall participate in a minimum of ten ~~—~~(10) hours of education activities annually.~~—annually of educational activities.of~~

~~D3.3.3.1 Continuing education shall include, but is not limited to, activities related to cellular therapy, cell processing, and Quality Management.~~

D3.4 STAFF

D3.4.1 The number of trained and competent processing personnel shall be adequate for the number of procedures performed and shall include a minimum of one (1) designated trained individual with an identified trained and competent backup individual to maintain sufficient coverage.

D4: QUALITY MANAGEMENT

D4.1 There shall be a Quality Management Program that incorporates key performance data.

D4.1.1 The Processing Facility Director shall have authority over and responsibility for ensuring that the Quality Management Program is effectively established and maintained.

D4.2 The Processing Facility shall establish and maintain a written Quality Management Plan.

~~D4.2.1 Processing activities shall be performed in compliance with a written Quality Management Plan.~~

D4.2.1 The Processing Facility Director shall be responsible for the Quality Management Plan as it pertains to the Processing Facility.

D4.3 The Quality Management Plan shall include, or summarize and reference, an organizational chart of key positions, functions, and reporting relationships within the Processing Facility.

D4.3.1 The Quality Management Plan shall include a description of how these key positions interact to implement the quality management activities.

D4.4 The Quality Management Plan should include or summarize and reference a listing of third-party manufacturers and clinical programs supported to include description of scope and services provided.

D4.5 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures addressing personnel requirements for each key position in the Processing Facility. Personnel requirements shall include at a minimum:

D4.5.1 A current job description for all ~~staff~~~~key positions~~each position.

D4.5.2 A system to document the following ~~for all staff~~:

D4.5.2.1 Initial qualifications.

D4.5.2.2 New employee orientation.

D4.5.2.3 Initial training, competency, and retraining when appropriate for all procedures performed~~, and in accordance with Applicable Law~~.

D4.5.2.4 Continued competency for each critical function performed, assessed annually at a minimum.

D4.5.2.5 Annual training in applicable ~~current~~ GxP ~~appropriate to the processes performed in accordance with Applicable Law~~.

D4.5.2.6 Continuing education.

D4.6 The Quality Management Plan shall include, or summarize and reference, a comprehensive system for document control.

D4.6.1 There shall be identification of the types of documents that are considered critical, and these shall comply with the document control system requirements. Controlled documents shall include at a minimum:

D4.6.1.1 Policies, protocols, ~~and~~ Standard Operating Procedures, and job aids.

D4.6.1.2 Worksheets.

D4.6.1.3 Forms.

D4.6.1.4 Labels.

D4.6.2 There shall be policies or Standard Operating Procedures for the development, approval, implementation, distribution, review, revision, and archival of all ~~critical~~ controlled documents.

D4.6.3 The document control system shall include:

D4.6.3.1 A standardized format for ~~critical~~ controlled documents.

D4.6.3.2 Assignment of a numeric or ~~an~~ alphanumeric identifier, version, and ~~a~~ title to each controlled document ~~and document version regulated within the system~~.

D4.6.3.3 A system for document approval, including the approval date, signature of approving individual(s), and ~~the~~ effective date.

D4.6.3.4 A system to protect controlled documents from accidental or unauthorized modification.

D4.6.3.5 Review of controlled documents every two (2) years at a minimum.

D4.6.3.6 A system for document change control that includes a description of the change, version, the signature of approving individual(s), approval date(s), communication or training on the change~~s~~ as applicable, effective date, and archival date.

D4.6.3.7 A system for archival~~Archival~~ of controlled documents, ~~including policies and Standard Operating Procedures, the inclusive dates of use, and their historical sequence~~ for a minimum of ten (10) years from archival or according to governmental requirements or institutional policy, whichever is longer. The system shall include the inclusive dates of use and their historical sequence.

D4.6.3.8 A system for the retraction of obsolete documents to prevent unintended use.

D4.7 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the establishment and maintenance of written agreements.

D4.7.1 Agreements shall be established with external parties providing critical services that could affect the quality and safety of the cellular therapy product or the health and safety of the donor or recipient.

D4.7.2 Agreements shall include the responsibility of the external party performing any step in collection, processing, testing, storage, distribution, or administration to maintain required accreditations and to comply with these Standards and Applicable Law.

D4.7.3 Agreements shall be established when the Processing Facility provides critical services to external parties.

D4.7.4 Agreements shall be dated and reviewed on a regular basis, at a minimum every two (2) years.

D4.8 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for documentation and review of outcome analysis and cellular therapy product efficacy to verify that the procedures in use consistently provide a safe and effective product.

D4.8.1 Criteria for cellular therapy product safety, efficacy, and the clinical outcome, as appropriate, shall be determined for each type of product processed and shall be reviewed at regular time intervals.

D4.8.2 Both individual cellular therapy product data and aggregate data shall be evaluated for each type of cellular therapy product, recipient diagnosis, ~~or recipient~~and donor type ~~shall be evaluated~~.

~~D4.7.3 Review of outcome analysis and/or product efficacy shall include at a minimum:~~

~~D4.7.3.1 An endpoint of clinical function as approved by the Clinical Program Director.~~

~~D4.7.3.2 Overall and treatment-related morbidity and mortality at thirty (30) days, one hundred (100) days, and one (1) year after cellular therapy product administration or in accordance with Applicable Law.~~

~~D4.7.34~~ ~~Data on outcome analysis and cellular therapy product efficacy, including adverse events related to the recipient, donor, or product, shall be provided in a timely manner to entities involved in the collection, processing, or distribution of the cellular therapy product.~~

D4.9 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for, and a schedule of, audits of the Processing Facility's activities to verify compliance with the Quality Management Program, ~~operational~~ policies and Standard Operating Procedures, these Standards, and Applicable Law.

D4.9.1 Processing Facility ~~A~~audits shall be conducted by an individual with sufficient knowledge ~~of~~ in the process and competence in auditing to identify problems, but who is not solely responsible for the process being audited.

D4.9.2 An audit plan for each audit shall include the elements listed in Appendix IV.

D4.9.3 An audit report shall include the elements listed in Appendix IV.

D4.9.4 The results of Processing Facility audits shall be used to recognize problems, detect trends, identify improvement opportunities, implement corrective and preventive actions when necessary, and follow-up on the effectiveness of these actions in a timely manner.

D4.9.5 Processing Facility ~~A~~audits shall be performed annually at a minimum, and shall include at least the following:

~~D4.8.5.1 Confirmation that product labeling matches documentation of eligibility determination accompanying the product and receipt and at distribution.~~

D4.9.5.1 Documentation that each external facility performing critical contracted services has met the requirements of the written agreement.

D4.9.5.2 Management of cellular therapy products with positive microbial culture results.

D4.9.5.3 Environmental monitoring as defined in the facility assessment to include environmental parameters, that may affect cellular therapy product viability, integrity, contamination, or cross-contamination during processing, storage, or distribution.

~~D4.8.53.32 Infectious disease resulting from a cellular therapy product collection, processing, or administration.~~

~~D4.8.3.3 Documentation that external facilities performing critical contracted services have met the requirements of the written agreements.~~

D4.9.5.4 Chain of ~~i~~Identity and ~~c~~Chain of Custody of ~~custody of~~ cellular therapy products.

D4.9.6 Additional audits shall be performed as part of a risk-based approach to the follow-up of occurrences.

D4.10 There shall be policies or Standard Operating Procedures for the management of external audits requested by the commercial manufacturer or applicable regulatory agency.

D4.11 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the management of cellular therapy products with positive microbial culture results and responsibility for the following activities at a minimum:

D4.11.1 Notification of the recipient, recipient's physician, collection staff, and any other facility in receipt of the cellular therapy product~~; and if relevant, the donor and the sponsor according to Applicable Law~~.

D4.11.2 Documentation and product labeling.

D4.11.3 ~~Cellular therapy p~~Product quarantine.

D4.11.4 Criteria for the release of cellular therapy products with positive microbial culture results ~~release~~.

D4.11.5 Identification of individuals authorized to approve release, including at a minimum the Processing Facility Medical Director ~~at a minimum~~.

~~D4.9.5 Notification of the recipient, recipient's physician, collection staff, and any other facility in receipt of the cellular therapy product; and if relevant, the donor and the sponsor according to Applicable Law.~~

~~D4.9.6 Recipient follow-up.~~

~~D4.9.7 Follow-up of the donor, if relevant.~~

D4.11.6 Documentation and investigation of cause.

D4.11.7 Reporting to regulatory agencies, as required by Applicable Law.

D4.12 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for occurrences (errors, accidents, deviations, adverse events, adverse reactions, and complaints). The following activities shall be included at a minimum:

D4.12.1 Detection.

D4.12.2 Investigation.

D4.12.2.1 A thorough and timely investigation shall be conducted by the p~~P~~rocessing ~~Facility~~ staff in collaboration with ~~all~~ the Collection Facility, the Clinical Program, and other entities involved in the ~~collection,~~ manufacture~~, testing, or administration~~ of the cellular therapy product, as appropriate.

D4.12.2.2 Investigations shall identify the root cause and a plan for short- and long-term corrective and preventive action as warranted.

D4.12.2.3 Occurrences shall be tracked and trended.

D4.12.3 Documentation.

D4.12.3.1 Documentation shall include a description of the occurrence, the date and time of the occurrence, the involved individuals and cellular therapy product(s) ~~to include~~including the unique identifier~~s~~ for the product involved as applicable, when and to whom the occurrence was reported, and the immediate actions taken.

D4.12.3.2 All investigati~~on~~ve reports shall be reviewed in a timely manner by the Processing Facility Director, ~~or~~, Medical Director~~,~~ and ~~the~~ Quality Manager.

D4.12.3.3 Cumulative files of occurrences shall be maintained and include written investigati~~on~~ve reports containing conclusions, root cause analysis, follow-up, corrective and preventive actions, and a link to the records of the involved cellular therapy products, donors, and recipients, if applicable.

D4.12.4 Reporting.

D4.12.4.1 When it is determined that a cellular therapy product has resulted in an adverse event or reaction, the Occurrence Report and results of the investigation shall be reported to the donor's and recipient's physician(s), as applicable, to other facilities participating in the manufacturing of the cellular therapy product, registries, grant agencies, sponsors, IBCs, IRBs, Ethics Committees, accrediting bodies, and governmental agencies as required by Applicable Law.

D4.12.4.2 Occurrences shall be reported to other facilities performing cellular therapy product functions on the affected cellular therapy product.

~~D4.10.4.1 When it is determined that a cellular therapy product has resulted in an adverse event or reaction, the event and results of the investigation shall be reported to the donor's and recipient's physician(s), as applicable, to other facilities participating in the manufacturing of the cellular therapy product, registries, and governmental agencies as required by Applicable Law.~~

~~D4.10.4.2 Occurrences shall be reported as required to other facilities performing cellular therapy product functions on the affected cellular therapy product.~~

~~D4.10.4.3 Occurrences shall be reported as required to the appropriate regulatory and accrediting agencies, registries, grant agencies, and Institutional Review Boards or Ethics Committees.~~

D4.12.5 Corrective and preventive action.

D4.12.5.1 Appropriate action shall be implemented if indicated, including both short-term action to address the immediate problem and long-term action to prevent the problem from recurring.

D4.12.5.2 Follow-up ~~audits~~ of the effectiveness of corrective and preventive actions shall be performed in a timeframe as indicated in the investigative report.

D4.13 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for cellular therapy product ~~c~~Chain of ~~i~~Identity and ~~c~~Chain of ~~c~~Custody that allow tracking from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.

D4.14 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for actions to take in the event th~~e~~at Processing operations ~~Facility's operations~~ are interrupted.

D4.15 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for qualification of critical manufacturers, vendors, equipment, software, supplies, reagents, facilities, and services ~~relevant to the cellular therapy product~~.

D4.15.1 Critical equipment, software, supplies, reagents, and facilities used for cellular therapy product manufacturing procedures shall be qualified.

~~D4.13.1 Qualification plans shall include minimum acceptance criteria for performance.~~

D4.15.1.1 Qualification shall be required following any significant changes to these items.

D4.15.2 Reagents that are not the appropriate grade shall undergo qualification for the intended use.

D4.15.3 Qualification plans shall include minimum acceptance criteria for performance.

D4.15.4 Qualification plans, results, reports, and conclusions shall be reviewed and approved by the Quality Manager and Processing Facility Director.

~~D4.13.4 Reagents that are not the appropriate grade shall undergo qualification for the intended use.~~

D4.16 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for validation or verification of critical procedures.

D4.16.1 Critical procedures to be validated shall include ~~at least~~ processing ~~techniques~~procedures, cryopreservation procedures, testing, labeling, storage, distribution, and preparation for administration, as applicable.

D4.16.2 Each validation or verification shall include at a minimum~~:~~ the elements listed in Appendix IV.

~~D4.14.2.1 An approved plan including conditions to be assessed. approved plan, including~~

~~4. Acceptance criteria.~~

~~1. Data collection.~~

~~2. Evaluation of data.~~

~~3. Summary of results.~~

~~4. References, if applicable.~~

~~5. Review and approval of the plan, report, and conclusion by the Processing Facility Director and Quality Manager.~~

~~1. Purpose and risk assessment.~~

~~2. Cconditions to be assessed.~~

~~3. Number of test events.~~

~~4. Acceptance criteria.~~

~~D4.14.2.3 Data collection.~~

~~D4.14.2.4 Evaluation of data.~~

~~D4.14.2.5 Summary of results.~~

~~D4.14.2.6 References, if applicable.~~

~~D4.146.2.7 Review and approval of the plan, report, and conclusion by the Processing Facility Director and Quality Manager.~~

~~6. Validation studies for a procedure shall be retained at a minimum until the procedure is no longer in use.~~

D4.16.3 Significant changes to critical procedures shall be validated or verified as appropriate.

D4.17 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the evaluati~~on~~ng the risk of ~~of risk in~~ changes to ~~a~~ critical ~~process or~~ procedures to assess the effect(s) ~~confirm that the changes do not create an adverse impact or inherent risk~~ elsewhere in the operation.

~~D4.15.1 Evaluation of risk shall be completed for changes in critical procedures.~~

D4.18 The QM Plan shall include, or summarize and reference, policies and Standard Operating Procedures for obtaining and reviewing feedback and taking action when appropriate.

D4.18.1 Feedback shall be obtained from associated Clinical Programs and Collection Facilities.

D4.19 The Processing Facility Director shall review the quality management activities with representatives in key positions in all ~~areas~~ elements of the cellular therapy program, at a minimum, quarterly.

D4.19.1 Meetings shall have defined attendees, documented minutes, and assigned actions.

D4.19.2 Performance data and review findings shall be reported to key positions and staff.

D4.19.3 The Processing Facility Director shall not ~~approve~~ have oversight of their own work if this person also performs other tasks in the Processing Facility.

D4.20 The Processing Facility Director shall ~~annually~~ review the effectiveness of the Quality Management Program annually~~-~~.

D4.20.1 The annual report and documentation of the review findings shall be made available to key personnel, the Clinical Program Director, the Collection ~~Services~~ Facility Director~~personnel~~, and staff of the program.

D5: POLICIES AND STANDARD OPERATING PROCEDURES

D5.1 The Processing Facility shall establish and maintain policies or Standard Operating Procedures addressing critical aspects of operations and management in addition to those required in D4. These documents shall include all elements required by these Standards and shall address at a minimum:

D5.1.1 Donor and recipient confidentiality.

D5.1.2 Cellular therapy product receipt.

D5.1.3 Processing and process control.

D5.1.4 Appropriate processing procedures for specific cellular therapy products, including cryopreservation and thawing.

~~D5.1.4 Processing of ABO-incompatible cellular therapy products to include a description of the indication for and processing methods to be used for plasma and red blood cell reduction.~~

D5.1.5 Prevention of mix-ups and cross-contamination.

D5.1.6 Labeling, ~~(~~including associated forms and samples~~)~~.

D5.1.7 Cellular therapy product expiration dates.

D5.1.8 Cellular therapy product storage, ~~to~~ includinge alternative storage ~~if the primary storage device fails~~.

D5.1.9 Release and exceptional release.

D5.1.10 Packaging, transportation, and shipping, including methods and conditions within the Processing Facility and to and from external facilities.

D5.1.11 Cellular therapy product recall, ~~to~~ includeing a description of responsibilities and actions to be taken, and notification of appropriate regulatory agencies.

D5.1.12 Cellular therapy product disposal.

D5.1.13 Critical equipment, reagent, and supply management, including recalls and corrective actions in the event of failure.

D5.1.14 Equipment operation, maintenance, and monitoring, including corrective actions in the event of malfunction or failure.

D5.1.15 Cleaning and sanitation procedures including identification of the individuals responsible for the activities.

D5.1.16 Environmental control ~~to~~ includinge a description of the environmental monitoring plan.

~~D5.1.17 Hygiene and use of personal protective equipment and attire.~~

D5.1.17 Handling and ~~D~~disposal of medical and biohazard waste.

D5.1.18 Processing Facilities utilizing genetically modified cellular therapy products shall incorporate or reference institutional or regulatory requirements relating to biosafety practices, including handling and disposal~~ed to the disposal of genetic material~~.

D5.1.19 Cellular therapy emergency and disaster plan, including the Processing Facility response.

~~D5.1.20 Response to emerging disease agents, including donor evaluation, product assessment and labeling, and personnel safety.~~

D5.1.20 Chain of Identity.

D5.1.21 Chain of Custody.

D5.2 The Processing Facility shall maintain a detailed list of all controlled documents, including title and identifier.

D5.3 Standard Operating Procedures shall be sufficiently detailed and unambiguous to allow qualified staff to follow and complete the procedures successfully. Each individual Standard Operating Procedure shall include:

D5.3.1 A clearly written description of the objectives.

D5.3.2 A description of equipment, reagents, and supplies used.

D5.3.3 Acceptable endpoints and the range of expected results.

D5.3.4 A stepwise description of the procedure.

D5.3.5 Reference to other policies or Standard Operating Procedures ~~or policies~~ required to perform the procedure.

D5.3.6 A reference section listing appropriate and current literature.

D5.3.7 Documented approval of each Standard Operating ~~p~~Procedure by the Processing Facility Director or Medical Director, as appropriate, prior to implementation and every two (2) years thereafter.

D5.3.8 Documented approval of each procedural modification ~~to a Standard Operating Procedure~~ by the Processing Facility Director or Medical Director, as appropriate, prior to implementation.

D5.3.9 Reference to ~~the~~ a current version of orders, worksheets, reports, labels, and forms.

D5.4 Controlled documents relevant to processes ~~being~~ performed shall be readily available to the facility staff.

D5.5 Staff review and, if appropriate, training and competency shall be documented before performing a new or revised ~~Standard Operating P~~procedure.

D5.6 All personnel shall follow the policies and Standard Operating Procedures related to their positions.

D5.7 Planned deviations shall be pre-approved by the ~~appropriate~~ Processing Facility Director or Medical Director and reviewed by the Quality Manager.

D6: EQUIPMENT, SUPPLIES, AND REAGENTS

D6.1 Equipment, supplies, and reagents used to process or store cellular therapy products shall be qualified and used in a manner that maintains product function and integrity and minimizes risks of product mix-ups, contamination, and cross-contamination.

D6.2 There shall be adequate equipment and materials for the procedures performed.

D6.3 There shall be a process for inventory control that encompasses equipment, containers for transport and shipping, supplies, reagents, and labels.~~Supplies and reagents used in processing, testing, cryopreservation, and storage shall be controlled by a materials management system that includes requirements for the following, at a minimum:~~

~~D6.3.1 Supplies and reagents shall be quarantined prior to use until verified to have met acceptance criteria.~~

D6.3.1 There shall be a system to uniquely identify, track, and trace all critical equipment used in the processing of cellular therapy products. The system shall identify each cellular therapy product for which the equipment was used.

D6.3.2 ~~Visual examination of e~~Each supply and reagent used to manufacture cellular therapy products shall be visually examined for damage or evidence of contamination ~~upon receipt and acceptance into inventory~~.

D6.3.2.1~~1~~ Supplies and reagents shall be quarantined prior to use until verified to have met acceptance criteria.

~~D6.3.2.1 Critical supplies and reagents should be visually examined at time of use.~~

D6.3.3 Records of receipt ~~that~~ shall include the supply or reagent type, quantity, manufacturer, lot number, date of receipt, acceptability, and expiration date.

D6.3.4 ~~Storage of m~~Materials shall be stored under the appropriate environmental conditions in a secure, sanitary, and orderly manner to prevent mix-up or unintended use.

D6.3.5 ~~Use of s~~Supplies and reagents coming into contact with cellular therapy products during processing, storage, or distribution shall be qualified, sterile, and meet predetermined specifications~~administration that are sterile and of the appropriate grade~~ for the intended use.

D6.3.5.1 Reagents shall undergo initial qualification and meet predetermined specifications for the intended use.

D6.3.5.2 Reagents shall undergo risk assessment as part of their initial qualification to ensure product integrity and safety.

D6.3.5.3 ~~Where there are no suitable clinical or pharmaceutical grade reagents available, R~~reagents shall undergo lot-to-lot functional verification to ensure that the new lot meets specifications.

~~D6.3.4.3 Lot-to-lot functional verification shall include acceptance criteria to confirm that new lots perform as expected compared to the previous lots.~~

D6.3.6 ~~Cleaning and sterilizing of n~~Non-disposable supplies or instruments shall be cleaned using a procedure verified to remove infectious agents and other contaminants.

D6.3.7 ~~Use of s~~Supplies and reagents shall be used in a manner consistent with manufacturer instructions.

D6.3.8 There shall be a ~~P~~process to prevent the use of expired reagents and supplies.

D6.3.9 Equipment, supplies, and reagents for processing shall conform to Applicable Law.

~~D6.4 There shall be a system to uniquely identify and track all critical equipment used in the processing of cellular therapy products. The system shall identify each cellular therapy product for which the equipment was used.~~

D6.4 There shall be a process for equipment management that encompasses maintenance, cleaning, and calibration.

D6.4.1 Equipment used in cellular therapy product processing, testing, cryopreservation, storage, and distribution shall be maintained in a clean and orderly manner. Equipment shall be ~~and~~ located to facilitate cleaning, sanitation, calibration, and maintenance according to established schedules, as described in Standard Operating Procedures, and in accordance with the manufacturer's recommendations.

D6.4.1.1 The ~~E~~equipment shall be inspected for cleanliness and verified to be in compliance with the maintenance schedule prior to each use.

D6.4.2 The ~~E~~equipment shall be standardized and calibrated on a regularly scheduled basis and after a critical repair or move as described in Standard Operating Procedures and in accordance with the manufacturer's recommendations.

D6.4.2.1 All equipment with a critical measuring function shall be calibrated against a traceable standard, if available. Where no traceable standard is available, the basis for calibration shall be described and documented.

D6.4.2.2 Calibration shall be performed according to established schedules as described in Standard Operating Procedures and in accordance with the manufacturer's recommendations.

D6.4.2.3 When equipment is found to be out of calibration or specification, there shall be a defined process for action required for cellular therapy products manufactured since the last calibration.

~~D6.8 There shall be a Standard Operating Procedure that addresses the actions to take in the event of equipment malfunction or failure.~~

~~D6.9 Equipment shall conform to Applicable Law.~~

D6.5 Lot numbers, expiration dates, manufacturers, and key equipment identifiers used in each procedure shall be documented.

D6.6 The Processing Facility shall use an inventory control system to document the availability and identity of critical reagents and supplies. This shall include at a minimum:

D6.6.1 A system to uniquely identify and track all critical reagents and supplies used to manufacture cellular therapy products.

D6.6.2 A system to identify each cellular therapy product for which each critical reagent or supply was used.

D6.6.3 A system to maintain adequate stocks of reagents and supplies for the procedures to be performed.

D7: CODING AND LABELING OF CELLULAR THERAPY PRODUCTS

D7.1 ISBT 128 CODING AND LABELING ~~OPERATIONS~~

D7.1.1 Cellular therapy products should~~all~~ be identified by name according to ISBT 128 standard terminology.

D7.1.2 Coding and labeling technologies should~~all~~ be implemented using ISBT 128.

D7.2 LABELING OPERATIONS

D7.2.1 Labeling operations shall be conducted in a manner adequate to prevent mislabeling or misidentification of cellular therapy products, product samples, and associated records.

D7.2.1.1 Stocks of unused labels representing different cellular therapy products shall be stored in a controlled manner to prevent errors.

D7.2.1.2 Obsolete labels shall be restricted from use.

D7.2.2 Pre-printed labels shall be ~~held~~ quarantined upon receipt ~~from the manufacturer~~ pending review and proofing against a copy or template approved by the Processing Facility Director to confirm accuracy regarding identity, content, and conformity.

~~D7.2.2.1 Stocks of unused labels representing different cellular therapy products shall be stored in a controlled manner to prevent errors.~~

~~D7.2.34.1 Obsolete labels shall be restricted from use.~~

D7.2.3 A system of label reconciliation shall be used to ensure the final disposition of all labels allocated to a specific product is documented.

D7.2.4 Label systems shall be validated to confirm accuracy regarding identity, content, and conformity of labels to templates approved by the Processing Facility Director.

~~D7.2.4.1 Obsolete labels shall be restricted from use.~~

D7.2.5 A system for label version control shall be employed.

D7.2.5.1 Representative obsolete labels with inclusive dates of use shall be archived ~~minimally~~ for a minimum of ten (10) years after the last cellular therapy product was distributed ~~with inclusive dates of use~~ or as defined by Applicable Law, whichever is longer.

D7.2.6 A system of checks in labeling procedures shall be used to prevent errors in transferring information to labels.

D7.2.6.1 The information entered on a container label shall be verified by one (1) qualified staff member using a validated process or two (2) qualified staff members ~~prior to distribution of the cellular therapy product~~.

D7.2.6.2 A controlled labeling procedure consistent with Applicable Law shall be defined and followed if container label information is transmitted electronically during a labeling process. This procedure shall include a verification step.

D7.2.6.3 Cellular therapy products that are subsequently re-packaged into new containers shall be labeled with new labels before they are detached from the original container.

D7.2.7 When the label has been affixed to the container, a sufficient area of the container shall remain uncovered to permit inspection of the contents.

D7.2.8 Labeling elements required by Applicable Law shall be present.

D7.2.9 All data fields on labels shall be completed.

D7.2.10 All labeling shall be clear, legible, and completed using ink that is indelible to all relevant agents.

D7.2.11 Labels affixed directly to a cellular therapy product bag shall be applied using appropriate materials as defined by the applicable regulatory authority.

D7.2.12 The label shall be validated as reliable for storage under the conditions in use.

D7.3 PRODUCT IDENTIFICATION

D7.3.1 Each cellular therapy product shall be assigned a unique numeric or alphanumeric identifier by which it will be possible to trace any cellular therapy product to its donor, ~~all accompanying records, and~~ its recipient or final disposition, and all records.

D7.3.1.1 The cellular therapy product, product samples, concurrent plasma, and concurrently collected donor samples shall be labeled with the same identifier.

D7.3.1.2 If a single cellular therapy product is stored in more than one (1) container, there shall be a system to identify each container.

D7.3.1.3 If cellular therapy products from the same donor are pooled, the ~~identifier on the~~ pool~~ed~~ identifier ~~product~~ shall ~~be assigned to~~ allow tracing to the original products.

D7.3.1.4 Supplementary identifiers shall not obscure the original identifier.

D7.3.1.5 The facility associated with each identifier shall be named in the documents to accompany the cellular therapy product.

D7.3.1.6 If the original donation identifier is replaced, documentation shall link the new identifier to the original.

D7.4 LABEL CONTENT

D7.4.1 At all stages of processing, the cellular therapy product shall be labeled with the proper name of the product and the unique numeric or alphanumeric identifier, at a minimum.

D7.4.2 The name and address of the facility that determines that the cellular therapy product meets release criteria and the name and address of the facility that makes the product available for distribution shall either appear on the product label or accompany the product at distribution.

D7.4.3 At the completion of processing and at distribution for administration, the cellular therapy product label on the primary product container and concurrent plasma container shall bear the information in the Cellular Therapy Product Labeling table in Appendix I.

D7.4.4 At distribution for administration the final cellular therapy product label shall include at a minimum two (2) identifiers which link the product to the intended recipient to maintain the Chain of Identity.

D7.4.5 Each label shall bear the appropriate biohazard and warning labels as ~~required by Applicable Law and should be described~~ found in the *Circular of Information for the Use of Cellular Therapy Products*, ~~"~~Table 2. ~~Biohazard and Warning Labels on Cellular Therapy Products Collected, Processed, and/or Administered in the United States," or other appropriate labels as required by Applicable Law.~~

D7.4.6 A cellular therapy product collected in or designated for use in the U.S. shall be accompanied by the elements listed in the Accompanying Documentation~~s at Distribution~~ table in Appendix III at the time it leaves the control of the Processing Facility.

D7.4.7 Any container bearing a partial label at the time of distribution shall be accompanied by the information required by the Cellular Therapy Product Labeling table in Appendix I. Such information shall be attached securely to the cellular therapy product on a tie tag or enclosed in a sealed package to accompany the product.

D7.4.8 For allogeneic cellular therapy products distributed before completion of donor eligibility determination, there shall be documentation that donor eligibility determination was completed during or after distribution of the cellular therapy product and that the physician using the product was informed of the results of that determination.

~~D7.4.8 Cellular therapy products for third-party manufacturers shall be labeled with product labels that conform to FACT requirements and Applicable Law.~~

D7.4.9 Cellular therapy products distributed for nonclinical purposes shall be ~~designated and~~ labeled with the statement "For Nonclinical Use Only."~~as not for clinical use.~~

D7.4.10 Cellular therapy products for third-party manufacturers shall be labeled with product labels that conform to FACT requirements and Applicable Law.

D8: PROCESS CONTROLS

D8.1 There shall be a process for controlling and monitoring the manufacturing of cellular therapy products so that products meet predetermined release specifications.

D8.1.1 The Processing Facility Director shall define tests and procedures for measuring and assaying cellular therapy products to ensure~~assure~~ their safety, viability, and integrity and to document that products meet predetermined release specifications. Results of all such tests and procedures shall become part of the permanent record of the product processed.

D8.1.2 There shall be a documented system for the identification and handling of test samples so that they are accurately related to the corresponding cellular therapy product, donor, or recipient.

D8.1.2.1 There shall be a mechanism to identify the individual obtaining the sample, the sample source, the date, and the time, if appropriate.

D8.1.2.2 Samples obtained for testing shall be representative of the cellular therapy product to be evaluated.

D8.1.3 There shall be established, appropriate, and validated assays and testing procedures for the evaluation of cellular therapy products.

D8.1.4 The following assays and testing procedures for the evaluation of cellular therapy products shall be performed:

D8.1.4.1 For all cellular therapy products, a total nucleated cell count~~enumeration~~ and viability measurement~~assays~~ shall be performed ~~for clinically relevant cell populations~~.

D8.1.4.2 For cellular therapy products undergoing manipulation that alters the final cell population, a relevant and validated assay, where available, shall be employed for evaluation of the viable target cell population before and after the processing procedures.

D8.1.5 For tests required by these Standards performed within the Processing Facility:

D8.1.5.1 There shall be a process for monitoring the reliability, accuracy, precision, and performance of laboratory test procedures and instruments.

D8.1.5.2 New reagent lots shall be verified to provide comparable results to current lots or to give results in agreement with suitable reference material before or concurrently with being placed into service.

D8.1.5.3 Where available, controls shall be used each day of testing and shown to give results within the defined range established for that material.

D8.1.5.4 Function checks shall be performed for testing instruments prior to testing donor, recipient, or cellular therapy product samples.

D8.1.5.5 There shall be documentation of ongoing proficiency testing as designated by the Processing Facility Director. The results shall be reviewed by the Processing Facility Director and outcomes reviewed with the staff.

D8.1.6 Tests required by these Standards~~,~~ ~~and~~ not performed by the Processing Facility~~,~~ shall be performed by a laboratory that is certified, licensed, or accredited by the appropriate laboratory regulatory agency.

D8.1.7 Infectious disease testing required by these Standards shall be performed using screening tests ~~that are~~ licensed, approved, or cleared by the governmental authority for cellular therapy product donors.

D8.1.8 Cellular therapy products that do not meet allogeneic donor eligibility requirements, or for which allogeneic donor eligibility determination is not yet complete, shall be distributed only if there is documented urgent medical need for the product. Documentation shall include, at a minimum, the approval of the recipient's physician and the Processing Facility Medical Director.

D8.1.9 Notification of the recipient's physician of nonconforming cellular therapy products and approval for their release shall be documented.

D8.2 There shall be a written request from the recipient's physician specifying the cellular therapy product type, recipient and donor identifiers, the type of processing that is to be performed, and the anticipated date of processing before a cellular therapy product is processed, shipped, or otherwise prepared for administration.

D8.3 For allogeneic cellular therapy products, information required by the Processing Facility prior to distribution of the product shall include:

D8.3.1 A statement of donor eligibility.

D8.3.2 For ineligible donors, the reason(s) for their ineligibility.

D8.3.3 For ineligible donors or donors for whom eligibility determination is incomplete, documentation of urgent medical need and physician approval for use.

D8.4 Processing procedures shall be validated in the Processing Facility and documented to result in acceptable target cell viability and recovery.

D8.4.1 Published validated processes shall be verified within the Processing Facility prior to implementation.

D8.4.2 The Processing Facility shall use validated methods for preparation of cellular therapy products for administration.

D8.4.3 Preparation for administration of cellular therapy products manufactured by third parties shall follow the instructions provided by the manufacturer.

D8.4.3.1 The Processing Facility should verify the preparation procedures utilizing practice ~~materials~~units similar to the cellular therapy product intended for administration when feasible.

D8.4.3.2 If relabeling of prepared third-party products is required, the label shall follow Applicable Law.

D8.5 Critical control points and associated assays shall be identified and performed on each cellular therapy product as defined in Standard Operating Procedures.

D8.6 Critical calculations shall be verified and documented where appropriate.

D8.7 Methods for processing shall employ aseptic technique and cellular therapy products shall be processed in a manner that minimizes the risk of cross-contamination.

D8.7.1 Where processing of tissues and cells involves exposure to the environment, processing shall take place in an environment with specified air quality and cleanliness.

D8.7.2 The effectiveness of measures to avoid contamination and cross-contamination shall be verified and monitored.

D8.8 The Processing Facility shall monitor and document microbial contamination of cellular therapy products after processing as specified in Standard Operating Procedures.

D8.8.1 The results of microbial cultures shall be reviewed by the Processing Facility Director in a timely manner.

D8.8.2 The recipient's physician shall be notified ~~in a timely manner~~ of any positive microbial cultures in a timely manner.

D8.9 Records shall be made concurrently with each step of the processing, testing, cryopreservation, storage, and administration or disposal/disposition/distribution of each cellular therapy product in such a way that all steps ~~may~~can be accurately traced.

D8.9.1 Records shall identify the person immediately responsible for each significant step, including dates and times, where appropriate.

D8.9.2 Records shall include~~show~~ the test results and, where appropriate, the interpretation ~~of each result, where appropriate~~.

D8.10 The Processing Facility Director shall review the processing record for each cellular therapy product prior to release or distribution.

D8.11 There shall be documented notification to the recipient's physician and the Processing Facility Medical Director of clinically relevant processing endpoints not met and remedial actions taken.

D8.12 Processing using more- than- minimal manipulation shall only be performed in accordance with institutional policies and Applicable Law and with the written informed consent of the donor, if applicable, and the recipient of the cellular therapy product.

D8.12.1 Documentation of approvals by the Institutional Review Board, Ethics Committee, or equivalent and the Institutional Biosafety Committee or equivalent shall be maintained.

D8.12.2 The Processing Facility shall adhere to Good Manufacturing Practice ~~regulations~~ appropriate for the degree of cellular therapy product manipulation.

D8.13 For allogeneic cellular therapy products containing red blood cells at the time of administration ~~sufficient to cause a transfusion reaction~~:

D8.13.1 Results for ~~donor and recipient~~ ABO group and Rh type testing shall be available from two (2) independently collected samples. Discrepancies shall be resolved and documented prior to issue of the cellular therapy product.

D8.13.2 ~~When relevant, r~~Results for a red blood cell antibody screen on the recipient shall be available.

D8.14 One (1) or more ~~retention~~ samples representing the cryopreserved cellular therapy product shall be stored under conditions that achieve a valid representation of the clinical product and in accordance with ~~institutional~~ Standard Operating Procedures.

D9: CELLULAR THERAPY PRODUCT STORAGE

D9.1 Processing and storage facilities shall ~~be secured and~~ control~~led~~ and secure storage areas to prevent mix-ups, deterioration, contamination, cross-contamination, and improper release of distribution of cellular therapy products.

D9.2 STORAGE DURATION

D9.2.1 Conditions and duration of storage of all cellular therapy products from their collection to final disposition shall be defined and validated.

D9.2.1.1 Validated procedures shall include non-cryopreserved, cryopreserved, and thawed products.

D9.2.2 Processing Facilities processing, storing, or releasing cellular therapy products for administration or further manufacturing shall assign an expiration date and time for non-cryopreserved products and for products thawed after cryopreservation.

D9.2.3 There shall be a written stability program that annually evaluates the viability and potency of cryopreserved cellular therapy products.

D9.2.3.1 Samples should include those representative of all processing methods and those representative of maximum storage duration.

D9.3 STORAGE TEMPERATURE

D9.3.1 Storage temperatures shall be defined in Standard Operating Procedures.

D9.3.2 Non-cryopreserved cellular therapy products shall be maintained within a specific temperature range to maintain viability and function~~, to inhibit infectious agents, and for a period of time not to exceed that specified in Standard Operating Procedures~~.

D9.3.3 Cryopreserved cellular therapy products shall be stored within a temperature range as defined in Standard Operating Procedures, that is appropriate for the product and cryoprotectant solution used.

D9.3.4 Prior to receipt of a cellular therapy product from an external facility, there shall be confirmation that the product can be appropriately stored.

D9.4 PRODUCT SAFETY

D9.4.1 Materials that may adversely affect cellular therapy products shall not be stored in the same refrigerators or freezers as ~~the~~ cellular therapy products.

D9.4.2 For cellular therapy products immersed in liquid nitrogen, procedures to minimize the risk of cross-contamination of products shall be employed.

D9.4.3 Processes for storing cellular therapy products in quarantine shall be defined in Standard Operating Procedures.

D9.4.3.1 Quarantined cellular therapy products shall be easily distinguishable and stored in a manner that minimizes the risks of cross-contamination and inappropriate distribution.

D9.4.3.2 All cellular therapy products with positive infectious disease test results for relevant communicable disease agents or positive microbial cultures shall be quarantined. ~~Disposition shall be documented.~~

D9.4.3.3 Processing Facilities storing cellular therapy products shall quarantine each product until completion of the donor eligibility determination as required by Applicable Law.

D9.5 STORAGE MONITORING

D9.5.1 Storage devices in which cellular therapy products are not fully immersed in liquid nitrogen shall have a system to monitor the temperature continuously and to record the temperature at least every four (4) hours.

D9.5.2 There shall be a mechanism to confirm that levels of liquid nitrogen in liquid nitrogen freezers are consistently maintained to ensure~~assure~~ that cellular therapy products remain within the specified temperature range.

D9.6 ALARM SYSTEMS

D9.6.1 Storage devices for cellular therapy products or reagents for cellular therapy product processing shall have alarm systems that are continuously active.

D9.6.2 Alarm systems shall have audible and visible signals ~~or other effective notification methods~~.

D9.6.3 Alarm systems shall be checked ~~periodically~~ for function according to the manufacturer's recommendation or annually at a minimum.

D9.6.4 If trained personnel are not always present in the immediate area of the storage device, a system shall be in place that alerts responsible personnel of alarm conditions on a 24-hour basis.

D9.6.5 Alarms shall be set to activate at a temperature or level of liquid nitrogen that will allow time to salvage products.

D9.6.6 Storage devices of appropriate temperature shall be available for cellular therapy product storage if the primary storage device fails.

D9.7 Written instructions to be followed if the storage device fails shall be displayed in the immediate area of the storage device and at each remote alarm location.

D9.7.1 Instructions shall include a procedure for notifying processing personnel.

~~D9.6.7 Storage devices of appropriate temperature shall be available for cellular therapy product storage if the primary storage device fails.~~

D9.8 ~~The S~~storage devices shall be located in a secure area and accessible only to personnel authorized by the Processing Facility Director.

D9.9 The Processing Facility shall use an inventory control system to identify the location of each cellular therapy product and associated samples. The inventory control system records shall include:

D9.9.1 Cellular therapy product unique identifier.

D9.9.2 Recipient name or unique identifier.

D9.9.3 Storage device identifier.

D9.9.4 Location within the storage device.

D10: CELLULAR THERAPY PRODUCT TRANSPORTATION AND SHIPPING

D10.1 Standard Operating Procedures for transportation and shipping of cellular therapy products shall be designed to protect the integrity of the product and the health and safety of individuals in the immediate area.

D10.2 The primary cellular therapy product container for non-frozen cellular therapy products shall be placed in a secondary container and sealed to prevent leakage.

D10.3 Conditions shall be established and maintained to preserve the integrity and safety of cellular therapy products during transport or shipping.

~~D10.3 Cellular therapy products that require a temperature-controlled environment and that are transported or shipped over an extended period of time shall be transported or shipped in a container validated to maintain the appropriate temperature range.~~

~~D10.4 Conditions shall be established and maintained to preserve the integrity and safety of cellular therapy products during transport or shipping.~~

D10.4 Cellular therapy products transported internally shall be packaged in a ~~qualified,~~ closed~~,~~ and ~~protective~~ rigid outer container.

D10.4.1 The outer container for internal transport shall be labeled as defined in Appendix II B.

D10.5 Cellular therapy products that are shipped to another facility or transported on public roads shall be packaged in an outer container.

D10.5.1 The outer container shall conform to the applicable regulations regarding the mode of transportation or shipping.

D10.5.2 The outer container shall be made of material adequate to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling during transport or shipping.

D10.5.2.1 The temperature of the shipping container shall be continuously monitored during shipment of cellular therapy products.

D10.5.2.2 The shipping facility shall maintain a record of the temperature over the period of travel.

D10.5.3 The outer container shall be secured to prevent unauthorized access.

D10.5.3.1 A mechanism should be in place to allow detection if the shipping container was opened. If opened, the shipping facility should be notified.

D10.5.4 The outer container shall be labeled as defined in the Cellular Therapy Product Labels for Shipping and Transport on Public Roads table in Appendix II A and Applicable Law.

D10.5.5 There shall be a document inside the outer container that includes all the information required on the outer container, in conformity with the Cellular Therapy Product Labels for Shipping and Transport on Public Roads table in Appendix II A.

D10.5.6 The outer container shall be labeled in accordance with Applicable Law regarding the cryogenic material used and the transport or shipment of biological materials.

~~D10.6 Cellular therapy products transported internally shall be packaged in a qualified, closed, and protective outer container.~~

~~D10.6.1 The outer container for internal transport shall be labeled as defined in Appendix II B.~~

D10.6 Cellular therapy products ~~that require a temperature-controlled environment and that are~~ transported or shipped over an extended period of time shall be transported or shipped in a container ~~validated to maintain the appropriate~~ within a temperature range defined in a Standard Operating Procedure or written agreement and according to manufacturer instructions.

D10.6.1 Additives to the cellular therapy product should be used for shipping or transporting over a prolonged duration of time.

D10.7 There shall be a risk assessment to evaluate the need for continuous temperature monitoring during transportation or shipment of cellular therapy products.

D10.8 If the intended recipient has received high-dose therapy, the cellular therapy product shall be transported.

D10.9 The transit time shall be within time limits determined by the distributing facility in consultation with the receiving facility to maintain cellular therapy product safety.

D10.10 There shall be contingency plans for alternative means of transport or shipping in an emergency.

D10.11 The cellular therapy product shall be transported or shipped with required accompanying records as defined in ~~the transportation and shipping~~ Standard Operating Procedures and in compliance with D7.4 as applicable.

D10.12 There shall be a record of the date and time of cellular therapy product distribution.

D10.13 ~~The c~~Cellular therapy products should not be passed through X-r~~R~~ay irradiation devices designed to detect metal objects. If inspection is necessary, the contents of the container should be inspected manually.

~~D10.10 A mechanism should be in place to allow detection if the shipping container was opened. If opened, the shipping facility should be notified.~~

D11: RECEIPT AND DISTRIBUTION

D11.1 RECEIPT OF CELLULAR THERAPY PRODUCTS

D11.1.1 Standard Operating Procedures shall be established and maintained for acceptance, rejection, and quarantine of cellular therapy products.

D11.1.2 The receipt of each cellular therapy product shall include inspection to verify:

D11.1.2.1 The integrity of the cellular therapy product container.

D11.1.2.2 The appearance of the cellular therapy product for evidence of mishandling or microbial contamination.

D11.1.2.3 Appropriate labeling.

D11.1.3 There shall be Standard Operating Procedures to verify that the cellular therapy product was appropriately transported or shipped.

D11.1.3.1 The receiving facility shall document the temperature inside the container upon arrival if shipped or transported on public roads.

D11.1.3.2 For cryopreserved cellular therapy products, the receiving facility records shall include documentation of the container temperature during shipping.

D11.1.4 The receiving facility shall review and verify cellular therapy product specifications provided by the manufacturer, if applicable.

D11.1.5 The receiving facility shall have readily available access to a summary of documents used to determine allogeneic donor eligibility.

D11.1.5.1 For cellular therapy products received from an external facility, there shall be documented evidence of donor eligibility screening and testing in accordance with Applicable Law.

~~D11.1.5 There shall be Standard Operating Procedures to maintain cellular therapy products in quarantine until they have been determined to meet criteria for release from quarantine.~~

D11.1.6 When cellular therapy products are returned to the Processing Facility after distribution for administration, there shall be documentation in the Processing Facility records of the events requiring return, the temporary storage temperature when at the clinical facility, the results of inspection upon return, and subsequent action taken to protect product safety and viability.

D11.1.6.1 The Processing Facility Director shall consult with the recipient's physician regarding reissue or disposal of the returned cellular therapy product.

D11.1.6.2 If the temperature of the cellular therapy product has been compromised, the Processing Facility Director shall give specific authorization to return the product to inventory.

~~D11.1.7 The receiving facility shall have readily available access to a summary of documents used to determine allogeneic donor eligibility.~~

~~D11.1.7.1 For cellular therapy products received from an external facility, there shall be documented evidence of donor eligibility screening and testing in accordance with Applicable Law.~~

~~D11.1.8 When cellular therapy products are returned to the Processing Facility after distribution for administration, there shall be documentation in the Processing Facility records of the events requiring return, the temporary storage temperature when at the clinical facility, the results of inspection upon return, and subsequent action taken to protect product safety and viability.~~

~~D11.1.8.1 The Processing Facility Director shall consult with the recipient's physician regarding reissue or disposal of the returned cellular therapy product.~~

~~D11.1.8.2 If the temperature of the cellular therapy product has been compromised, the Processing Facility Director shall give specific authorization to return the product to inventory.~~

D11.2 DISTRIBUTION CRITERIA

D11.2.1 The processing, collection, and transport or shipping records for each cellular therapy product shall be reviewed by the Processing Facility Director for compliance with Standard Operating Procedures and Applicable Law prior to product release or ~~and~~ distribution.

D11.2.1.1 Records shall demonstrate traceability from the donor to the recipient and from the recipient to the donor.

D11.2.2 Each cellular therapy product shall meet pre-determined release criteria prior to distribution from the Processing Facility. The release criteria shall include donor eligibility determination for allogeneic products.

D11.2.2.1 The Processing Facility Director shall give specific authorization for release when the cellular therapy product does not meet technical release criteria.

D11.2.2.2 The Processing Facility Medical Director shall give specific authorization for release when the cellular therapy product does not meet clinically relevant release criteria.

D11.2.2.3 Documentation of agreement between the Processing Facility Medical Director and the recipient's physician to use any non-conforming ~~cellular therapy~~ product shall be retained in the processing record if such release is allowed by policies, Standard Operating Procedures, or package inserts of licensed products.

D11.2.3 Each cellular therapy product issued for administration shall be visually inspected by two (2) trained personnel immediately before release to verify the integrity of the product container and ~~identity as indicated by~~ appropriate labeling.

D11.2.3.1 A cellular therapy product shall not be released when the container is compromised or recipient or~~,~~ donor~~, or product~~ information is not verified unless the Processing Facility Director gives specific authorization for the product's release.

D11.2.4 For each type of cellular therapy product, the Processing Facility shall maintain and distribute or make a document available to clinical staff containing the following:

D11.2.4.1 The use of the cellular therapy product, indications, contraindications, side effects and hazards, dosage, and administration recommendations.

D11.2.4.2 Instructions for handling the cellular therapy product to minimize the risk of contamination or cross-contamination.

D11.2.4.3 Appropriate warnings related to the prevention of the transmission or spread of communicable diseases.

D11.3 DISTRIBUTION RECORDS

D11.3.1 The cellular therapy product distribution records shall permit tracking and tracing of the cellular therapy product, and shall contain the following information at a minimum:

D11.3.1.1 The proper product name and identifier.

D11.3.1.2 Unique identifier of the intended recipient.

D11.3.1.3 Documentation of allogeneic donor eligibility determination, as appropriate.

D11.3.1.4 For autologous donors, results of any communicable disease testing performed.

D11.3.1.5 Identification of the facilities that requested and distributed the product.

D11.3.1.6 Identity of the receiving facility.

D11.3.1.7 Date and time the cellular therapy product was distributed.

D11.3.1.8 Date and time the cellular therapy product was received.

D11.3.1.9 Identity of the transporting or shipping facility.

D11.3.1.10 Identity of personnel responsible for cellular therapy product transportation or shipping and of personnel responsible for receiving the product.

D11.3.1.11 Identity of the courier.

D11.3.1.12 Documentation of any delay or problems incurred during transportation or shipping.

D12: DISPOSAL

D12.1 Disposal of cellular therapy products shall include the following requirements:

D12.1.1 A pre-collection written agreement between the storage facility and the designated recipient or the donor defining the length of storage and the circumstances for disposal of cellular therapy products.

D12.1.2 The option, if in accordance with Applicable Law, to transfer the cellular therapy product to another facility if the designated recipient is still alive after the agreed-upon storage interval.

D12.1.3 Documentation of no further need for the cellular therapy product before any product is discarded.

D12.1.4 Approval by the Processing Facility Medical Director in consultation with the recipient's physician for cellular therapy product discard or other disposition, and method of disposal.

D12.1.5 A method of disposal and decontamination that meets Applicable Law for disposal of biohazardous materials ~~and~~or medical waste.

D12.2 Processing Facilities, in consultation with the Clinical Program, shall establish policies or Standard Operating Procedures for the duration and conditions of storage and indications for disposal.

D12.2.1 If there is no pre-existing agreement describing conditions for cellular therapy product storage and/or discard or if the intended recipient is lost to follow-up, the storage facility shall make a documented effort to notify the donor, cellular therapy product manufacturer, or designated recipient's physician and facility about product disposition, including disposal or transfer.

D12.3 The records for discarded or transferred cellular therapy products shall indicate the ~~identity of the~~ product was discarded or transferred,~~,~~ date of discard or transfer, disposition, and method of disposal or transfer.

D13: RECORDS

D13.1 There shall be a records management system for ~~quality and~~ cellular therapy product record creation, assembly, review, storage, archival, and retrieval.

D13.1.1 A records management system shall be established and maintained to facilitate the review of records.

D13.1.2 The records management system shall facilitate tracking of the cellular therapy product from the donor to the recipient or final disposition and tracing from the recipient or final disposition to the donor.

D13.1.3 For cellular therapy products that are to be distributed for use at another institution, the Processing Facility shall inform the receiving institution of the tracking system and requirement for tracking the product in writing or electronic format at or before the time of product distribution.

D13.1.4 Records shall be maintained ~~in such a way as~~ to ensure their integrity, preservation, and retrieval.

~~D13.2 The Processing facility shall define and follow good documentation practices.~~

D13.1.5 Records shall be accurate and legible.

D13.1.6 Written ~~R~~records shall be indelible.

~~D13.3 Records shall be maintained in such a way as to ensure their integrity, preservation, and retrieval.~~

D13.1.7 Safeguards to secure the confidentiality of all records and communications among the clinical, collection, and ~~staff,~~ processing staff, ~~facilities, and clinical facilities,~~ and ~~health care providers and their recipients and~~ donors shall be established and followed in compliance with Applicable Law.

D13.2 The Processing ~~f~~Facility shall define and follow good documentation practices.

D13.3 RECORDS TO BE MAINTAINED

D13.3.1 Processing Facility records related to quality control, investigational protocols, personnel training and competency, facility maintenance, facility management, complaints, or other general facility issues shall be retained for a minimum of ten (10) years after the creation of the cellular therapy product record, ~~or~~ date of the cellular therapy product's distribution, disposition, or expiration, whichever is latest, or according to Applicable Law.

D13.3.2 Records of v~~V~~alidation studies ~~y records~~ for a processing procedure shall be retained ~~for~~at a minimum until the procedure is no longer in use and no ~~of ten (10) years after distribution of the final~~ products remain in storage that were processed~~manufactured~~ using that procedure.

D13.3.3 Employee records shall be maintained in a confidential manner, as required by Applicable Law.

D13.3.4 ~~Facility maintenance records pertaining to facility c~~Cleaning and sanitation records shall be retained for at least three (3) years or longer in accordance with Applicable Law or by a defined program or institution policy.

D13.3.5 Records to allow tracking and tracing of cellular therapy products shall be maintained in a confidential manner for a minimum of ten (10) years after administration, distribution, disposition, or expiration of the cellular therapy product, or as required by Applicable Law, whichever is latest.

D13.3.5.1 These records shall include the identities of the C~~c~~ollection and ~~p~~Processing ~~f~~Facilities~~y identity~~, unique numeric or alphanumeric identifier, collection date and time, product code, and donor and recipient information as ~~known~~found on the original container.

D13.3.6 All records pertaining to the processing, testing, storage, or distribution of cellular therapy products shall be maintained for a minimum of ten (10) years after the date of administration, or if the date of administration is not known, ~~then a minimum of~~ ten (10) years after the date of the cellular therapy product's distribution, disposition, or expiration, or the creation of the cellular therapy product record, whichever is most recent, or according to Applicable Law or institutional policy, whichever is latest.

D13.3.7 Research records shall be maintained in a confidential manner as required by Applicable Law or for a minimum of ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, whichever is latest.

D13.4 ELECTRONIC RECORDS

D13.4.1 The Processing Facility shall maintain a current listing of all critical electronic record systems. Critical electronic record systems shall include, at a minimum, systems ~~under the control of the Processing Facility~~ that are used as a substitute for paper, to make decisions, to perform calculations, or to create or store information used in critical procedures. For all critical electronic record systems:

D13.4.1.1 ~~For all critical electronic record systems, t~~There shall be policies, Standard Operating Procedures, and system ~~controls~~ elements to maintain the accuracy, integrity, identity, and confidentiality of all records.

D13.4.1.2 There shall be a means by which access ~~to electronic records~~ is limited to authorized individuals.

D13.4.1.3 A method shall be established or the system shall provide for the unambiguous identification of the individual responsible for each record entry.

D13.4.1.4 ~~For all critical electronic record systems, t~~There shall be written policies and Standard Operating Procedures for record entry, verification, and revision.

D13.4.1.5 A method shall be established or the system shall provide for review of data before final acceptance.

D13.4.1.6 There shall be documented t~~T~~raining ~~and continued competency~~ of personnel in the system's use.

D13.4.1.7 There shall be a defined process for continued competency of personnel in the system's use.

D13.4.1.8 There shall be a defined process for the use of electronic signatures.

D13.4.1.9 Unique identifiers shall be maintained.

D13.4.1.10 ~~For all critical electronic record systems, T~~there shall be the ability to generate true copies of the records in both human-~~-~~readable and electronic format suitable for inspection and review.

D13.4.1.11 There shall be protection of ~~the~~ records to enable their accurate and ready retrieval throughout the period of record retention.

D13.4.1.12 All system modifications shall be authorized, documented, and validated prior to implementation.

D13.4.2 For all critical electronic record systems under the control of the facility, there shall be validated procedures for and documentation of:

D13.4.2.1 Prospective validation of systems, including hardware, software, and databases.

D13.4.2.2 Installation of the system.

D13.4.2.3 Numerical designation of system versions, if applicable.

D13.4.2.4 Authorization and validation of all system modifications prior to implementation.

D13.4.2.5 Systems development, including the verification of calculations and algorithms.

~~D13.5.6 For each critical electronic record system, there shall be an alternative system for all electronic records to allow for continuous operation of the Processing Facility in the event that a critical electronic record system is not available. The alternative system shall be validated, and Processing Facility staff shall be trained in its use.~~

~~D13.5.7 For all critical electronic record systems, there shall be written Standard Operating Procedures for record entry, verification, and revision.~~

~~D13.5.7.1 A method shall be established or the system shall provide for review of data before final acceptance.~~

~~D13.5.7.2 A method shall be established or the system shall provide for the unambiguous identification of the individual responsible for each record entry.~~

~~D13.5.8 For all critical electronic record systems, there shall be the ability to generate true copies of the records in both human-readable and electronic format suitable for inspection and review.~~

~~D13.5.9 For all critical electronic record systems, there shall be validated procedures for and documentation of:~~

~~D13.5.9.1 Systems development.~~

~~D13.5.9.2 Numerical designation of system versions, if applicable.~~

~~D13.5.9.3 Prospective validation of systems, including hardware, software, and databases.~~

~~D13.5.9.4 Installation of the system.~~

~~D13.5.9.5 Training and continued competency of personnel in systems use.~~

D13.4.2.6 System maintenance and operations.

D13.4.2.7 Monitoring of data integrity.

D13.4.2.8 Back-up of the electronic records system on a regular schedule.

~~D13.5.9.8 System maintenance and operations.~~

D13.4.3 For each critical electronic record system, there shall be an alternative system ~~for all electronic records~~ to allow for continuous operation of the Processing Facility ~~in the event that a~~if the critical electronic record system is not available. The alternative system shall be validated, and ~~P~~processing ~~Facility~~ staff shall be trained in its use.

D13.5.9.9 System assignment of unique identifiers.

D13.5.9.10 All system modifications shall be authorized, documented, and validated prior to implementation.

D13.6 RECORDS TO BE MAINTAINED

D13.6.1 Processing Facility records related to quality control, investigational protocols, personnel training and competency, facility maintenance, facility management, complaints, or other general facility issues shall be retained for a minimum of ten (10) years after the creation of the cellular therapy product record or date of the cellular therapy product's distribution, disposition, or expiration, whichever is latest, or according to Applicable Law.

D13.6.1.1 Employee records shall be maintained in a confidential manner, as required by Applicable Law.

D13.6.1.2 Facility maintenance records pertaining to facility cleaning and sanitation shall be retained for at least three (3) years or longer in accordance with Applicable Law.

D13.6.1.3 Validation study records for a processing procedure shall be retained for a minimum of ten (10) years after distribution of the final products manufactured using that procedure.

D13.6.2 Records to allow tracing of cellular therapy products shall be maintained for a minimum of ten (10) years after administration, distribution, disposition, or expiration of the cellular therapy product, or as required by Applicable Law. These records shall include collection and processing facility identity, unique numeric or alphanumeric identifier, collection date and time, product code, and donor and recipient information as known.

D13.6.3 All records pertaining to the processing, testing, storage, or distribution of cellular therapy products shall be maintained for a minimum of ten (10) years after the date of administration, or if the date of administration is not known, then a minimum of ten (10) years after the date of the cellular therapy product's distribution, disposition, or expiration, or the creation of the cellular therapy product record, whichever is most recent, or according to Applicable Law or institutional policy, whichever is latest.

~~D13.6.4 Research records shall be maintained in a confidential manner as required by Applicable Law or for a minimum of ten (10) years after the administration, distribution, disposition, or expiration of the cellular therapy product, whichever is latest.~~

D13.5 RECORDS IN CASE OF DIVIDED RESPONSIBILITY

D13.5.1 If two (2) or more facilities participate in the collection, processing, or ~~distribution~~administration of the cellular therapy product, the records of ~~the Processing Facility~~each facility shall show plainly the extent of its responsibility.

D13.5.2 The Processing Facility shall provide to the facility of final disposition a summary of records relating to the collection, processing, and storage procedures performed related to the safety, purity, or potency of the cellular therapy product involved.

D13.5.3 The Processing Facility shall furnish~~maintain~~ a listing of the names, addresses, and responsibilities of other facilities that perform manufacturing steps on a cellular therapy product.

~~D13.7.2 The Processing Facility shall provide to the facility of final disposition a summary of all records relating to the collection, processing, and storage procedures performed and the safety, purity, or potency of the cellular therapy product.~~

~~D13.7.3 If two (2) or more facilities participate in the collection, processing, or distribution of the cellular therapy product, the records of the Processing Facility shall show the extent of its responsibility.~~

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APPENDIX I

CELLULAR THERAPY PRODUCT LABELING

Each label shall include at least the elements detailed in the following table[1]:

Element[2]	Label at completion of collection	Label at completion of processing	Partial label at distribution for administration[4]	Label at distribution for administration[3]
Unique numeric or alphanumeric identifier[3]	AF	AF	AF	AF
Proper name of product[5,6]	AF	AF	AF	AF
Product code[5]	AF	AF	AF	AF
Product attributes[5]	AC	AC	AC	AFC
Recipient name and/or identifier	AT	AT	AC	AT
Identity and address of collection facility or donor registry	AT	AC	AC	AC
Date, time collection ends, and (if applicable) time zone	AT	-	-	-
Approximate volume	AF	AF	AFC	AF
Name and quantity of anticoagulant and other additives	AF	AF	AFC	AF
Recommended storage temperature range	AF	AF	AFC	AT
Donor identifier and ~~(if applicable)~~ name (if applicable)	AT	AT	AC	AC
Biohazard and Warning Labels (as applicable, see C7.4.~~4~~, D7.4.~~4~~).	AT	AT	AC	AC
As applicable: Statement "NOT EVALUATED FOR INFECTIOUS SUBSTANCES"	AT	AT	AC	AT
Statement "WARNING: Advise Patient of Communicable Disease Risks"	AT	AT	AC	AT
Statement "WARNING: Reactive Test Results for [name of disease agent or disease]"	AT	AT	AC	AT
Identity and address of processing and distribution facility(ies)	-	AC	AC	AC
Statement "Do Not Irradiate"	-	AT	AC	AF
Expiration d~~D~~ate and time (if applicable)	AC~~-~~	AC	AC	AC~~F~~
ABO and Rh of donor (if applicable)	-	AC	AC	AC
RBC compatibility determination (if applicable)	-	-	AC	AC
Statement indicating that leukoreduction filters shall not be used	-	-	AC	AF
Statement "FOR AUTOLOGOUS USE ONLY" (if applicable)	AT	AT	AC	AF
Date of distribution	-	-	AC	AC

AF=Affix; AT=Attach or Affix; AC=Accompany, Attach, or Affix

[1]Container and full package labeling requirements for licensed products or products under Investigational New Drug (IND) application shall follow Applicable Law. In the U.S., see 21 CFR 312.6(a).

[2]Full implementation of ISBT 128 labeling requires compliance with the ISBT 128 Standard for the location of information on the label and the accompanying documentation.

[3]Overlay labels for supplementary identifiers shall not obscure the original identifier.

[4]A partial label at distribution is a label that because of the size of the product container or other constraints, does not contain all the required information.

[5]Product proper names and attributes must also be identified in words and are listed in Chapter Three of the *ISBT 128 Standard Terminology for ~~Blood, Cellular Therapy, and Tissue Product Descriptions~~Medical Products of Human Origin~~: Available at: www.isbt128.org/standard-terminology~~*. This includes all potential attributes, in addition to the core attributes referenced in this table (Anticoagulant, Volume, Storage Temperature): Intended Use, Manipulation, Cryoprotectant, Blood Component from ~~Third~~ 3rd Party

Donor, ~~Preparation~~Other Additives, Genetically Modified, Irradiation, Modification, Mobilization, Pooled Single Donor, Cultured, Enrichment, ~~and~~ Reduction, and Fluid Source Location.

[6]Proper name of product is also referred to as class name in the ISBT 128 Standard Terminology.

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APPENDIX II

A: CELLULAR THERAPY PRODUCT LABELS FOR SHIPPING AND TRANSPORT ON PUBLIC ROADS

Each container for shipping ~~and~~ or transport on public roads shall include a document on the inside of the container and a label on the exterior of the container with at least the elements detailed in the following table:

Element	Inner container document	Outer container label
Date of distribution	AC	AC
Time[1] of distribution, if appropriate	AC	AC
Statement "Do Not X-Ray" and/or "Do Not Irradiate", if applicable	AC	AF
Statements "~~Human~~ Cells or Tissue for Administration" or equivalent and "Handle with Care"	AC	AF
Shipper handling instructions	AC	AF
Shipping facility name, street address, contact person, and phone number	AC	AF
Receiving facility name, street address, contact person, and phone number	AC	AF
Biohazard and~~/or~~ Warning Labels (as applicable, see C7.4.~~4~~, D7.4.~~4~~).	AC	-
If applicable: Statement "NOT EVALUATED FOR INFECTIOUS SUBSTANCES"	AC	-
Statement "WARNING: Advise Patient of Communicable Disease Risks"	AC	
Statement "WARNING: Reactive Test Results for [name of disease agent or disease]"	AC	

AC= Accompany, AF=Affix

[1]Time shall include the time zone when shipping or transport of the cellular therapy product involves crossing time zones.

B: CELLULAR THERAPY PRODUCT LABELS FOR INTERNAL TRANSPORT

Each container for internal transport shall be ~~include an internal transport~~ labeled with at least the elements detailed in the following table:

Element	Label for Internal transport ~~label~~
Statements "~~Human~~ Cells or Tissues for Administration" or equivalent and "Handle with Care"	AF
Emergency contact person name and phone number	AF

AF=Affix

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APPENDIX III

ACCOMPANYING DOCUMENT~~S AT DISTRIBUTION~~ATION

Products collected in or designated for use in the U.S. shall be accompanied upon leaving the control of the Collection or Processing Facility with at least the elements detailed in the following table[1]:

Documentation	Allogeneic Donor-Eligible	Allogeneic Donor-Ineligible[2]	Allogeneic Donor-Incomplete[2]
Statement that the donor has been determined to be either eligible or ineligible, based upon results of donor screening and testing	X	X	-
Summary of records used to make the donor-eligibility determination[3]	X	X	-
Name and address of the establishment that made the donor-eligibility determination	X	X	-
Listing and interpretation of the results of all communicable disease testing performed	X	X	X
Statement that the communicable disease testing was performed by a laboratory meeting regulatory requirements[4]	X	If applicable	If applicable
Statement noting the reason(s) for the determination of ineligibility	-	X	-
Statement that the donor-eligibility determination has not been completed	-	-	X
Statement that the product must not be ~~transplanted or infused~~administered until completion of the donor-eligibility determination, except under condition of urgent medical need	-	-	X
Listing of any required screening or testing that has not yet been completed	-	-	X
Results of donor screening that has been performed	-	-	X
Documentation that the physician using the cellular therapy product was notified of incomplete testing or screening	-	-	X
Instructions for product use to prevent the introduction, transmission, or spread of communicable diseases[1]	X	X	X
Instructions for reporting serious adverse reactions or events to the distributing facility[1,5]	X	X	X

[1]For autologous cellular therapy products, instructions for product use to prevent the introduction, transmission, or spread of communicable diseases and for reporting serious adverse reactions or events to the distributing facility are always required. Autologous ~~D~~donor eligibility determination is not required by FDA; however, if any donor screening or testing is performed and risk factors or reactive test results are identified, accompanying documentation shall be provided.

[2]May only be distributed after release by the Processing Facility Medical Director due to urgent medical need. For ineligible cellular therapy products or incomplete donor eligibility determination, the product shall be shipped in quarantine. For products distributed prior to completion of donor eligibility, determination shall be completed and the physician shall be informed of the results.

[3]Access (electronic or otherwise) to the source documents by the distributing facility and/or receiving facility is sufficient.

[4]This includes laboratories certified to perform such testing on human specimens under the Clinical Laboratory Improvement Amendments of 1988 or those laboratories that have met equivalent requirements as determined by the Centers for Medicare and Medicaid Services, or those that have met equivalent non-U.S. requirements. If communicable disease testing is not performed by a laboratory that meets regulatory requirements, the donor is ineligible. If a donor is ineligible for other reasons, but the testing was performed in a compliant laboratory, this statement must be included in the documentation.

[5]Access to the Clinical Program SOPs and forms could suffice when the distributing and clinical facilities are within the same institution.

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APPENDIX IV

MINIMUM ELEMENTS TO INCLUDE IN AUDITS AND VALIDATIONS

Each audit plan, audit report, and validation or verification shall include:

Audit Plan	Audit Report	Validation or Verification
• Title. • ~~Name~~Name and role of individual(s) to complete the audit. • Audit purpose. • Audit scope. • Documentation of review and approval by the applicable Program Director and the Quality Manager.	• Approved audit plan. • Identification of auditor. • Date started and completed. • Records or processes audited. • Summary of results to include findings, assessment of the underlying cause of errors, recommendations, and conclusions. • Plan for follow-up, if appropriate, including timeline. • Documentation of review and approval by the applicable Program Director and Quality Manager.	• A **plan**, approved by the applicable Program Director and Quality Manager prior to the initiation of data collection or testing, to include: o Purpose and risk assessment. o Conditions to be assessed. o Number of test events. o Acceptance criteria. • A **report and** resulting **conclusion**, reviewed and approved by the applicable Program Director and Quality Manager, to include: o Data collection. o Evaluation of data. o Summary of results. o References, if applicable.

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