

Summary of Changes

Eighth Edition FACT-JACIE Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration

This document summarizes the major changes proposed for the draft *Eighth Edition FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration*. This summary does not list all changes made to the Standards. Reorganization or clarified verbiage is not included unless considered to be a significant change in the intent of the Standard. Refer to the draft Standards for all proposed revisions.

To clearly identify new requirements, changes to the standards listed have been redlined.

Major Changes

1. A4 Definitions

- a. “Applicable Law” was introduced in the Eighth Edition Standards to replace “applicable law and regulations”.
 - i. The phrase “Applicable Law” is defined as: “Any local, national, or international statute, regulation, or other governmental law that is applicable to hematopoietic cellular therapy product collection, processing, and administration that is relevant to the location or activities of the Clinical Program, Collection Facility, or Processing Facility.”
- b. **Cellular Therapy:**
Somatic cell-based product (e.g., mobilized HPC, mononuclear cells, cord blood cells, mesenchymal stromal cells, T cells, natural killer cells) that is procured from a donor and intended for processing and administration, to include IECs, gene-modified cells, and other cellular therapies.
- c. **Designee:**
The concept of designee was added to the document as a tenet to reflect the opinion of the Standards Committee that any activity can be delegated to an appropriate designee as that term is defined. The phrase “or designee” was removed from individual standards throughout.

A2.2 Designee is defined as an individual with appropriate education, experience, or expertise who is given the authority to assume a specific responsibility. The person appointing a designee retains ultimate responsibility.

A4 Definition: 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.

- d. 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.
- e. 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.
NOTE: This term is not used in Standards, but will be used in the accompanying Accreditation Manual.

2. Risk management plan standards

Significant specific standards were added to address risk management plan requirements for Clinical Programs utilizing licensed (or equivalent regulatory approval) cellular therapy products. Related requirements were also added in the Apheresis, Marrow, and Laboratory sections.

Clinical

- a. Clinical Programs administering cellular therapy products shall have risk minimization processes in place appropriate to the product. (B7.9)
- b. Clinical Programs administering licensed (or equivalent regulatory approval) cellular therapy products with a mandated risk management program shall have policies and Standard Operating Procedures in place for the following: (B7.10)
 - i. There shall be a designated person for each applicable cellular therapy product with a mandated risk management program. This person shall be responsible for: (B7.10.1)
 - 1. Verification that enrollment requirements of the manufacturer are met. (B7.10.1.1)
 - 2. Implementation of and compliance with the risk management program requirements. (B7.10.1.2)
 - ii. There shall be policies and Standard Operating Procedures requiring the designated person and all physicians and staff involved in the prescribing, dispensing, or administering of the cellular therapy product to complete the following: (B7.10.2)
 - 1. Training for each applicable cellular therapy product including prescribing information and medication guides, and patient management including preparative regimens and adverse event management. (B7.10.2.1)
 - 2. Assessment of knowledge for each applicable cellular therapy product. (B7.10.2.2)
 - 3. Retraining and reassessment of knowledge if the Clinical Program has not administered that cellular therapy product for a period of time specified by the manufacturer. (B7.10.2.3)
 - iii. For each patient receiving an IEC product the clinical facility shall have immediate access to targeted therapies to manage severe adverse events per manufacturer's requirements. (B7.10.3)

- iv. A patient alert card shall be provided to recipients or their caregivers with the following instructions: (B7.10.4)
 - 1. The recipient or caregiver shall carry the patient alert card at all times. (B7.10.4.1)
 - 2. The recipient or caregiver shall provide the patient alert card to any healthcare provider treating the patient. (B7.10.4.2)
 - 3. The recipient shall be given instructions related to expectations on remaining within the proximity of the clinical program for follow-up care as medically indicated. (B7.10.4.3)
 - 4. The recipient shall be made aware of the risks of cytokine release syndrome, neurologic toxicities, or other known potential adverse events, and the need to monitor for these events and to seek immediate medical attention if they occur. (B7.10.4.4)
 - 5. The recipient shall refrain from driving and other hazardous activities following IEC administration per manufacturer's instructions. (B7.10.4.5)
- v. Adverse events of cytokine release syndrome or neurologic toxicities shall be reported in accordance with regulatory requirements. (B7.10.5)
- vi. The Clinical Program shall maintain written guidelines for the management of complications that comply with the mandated risk management plan. (B7.10.6)
 - 1. Following administration of an IEC product, the recipient shall be monitored in accordance with the manufacturer's requirements. (B7.10.6.1)
- vii. Documentation of training and compliance with the risk management plan shall be established and maintained for review by the commercial manufacturer or applicable regulatory agency upon request. (B7.10.7)
- viii. There shall be policies or Standard Operating Procedures for the management of external audits requested by the commercial manufacturer or applicable regulatory agency. (B7.10.8)

Collection and Processing

- a. Facilities collecting cellular therapy products for further manufacturing shall have risk minimization processes in place appropriate to the product. (CM/C8.16)
- b. Processing Facilities providing service to a Clinical Program shall have risk minimization processes in place appropriate to the product. (D8.16)
- c. Facilities providing service to a Clinical Program that administers licensed (or equivalent regulatory approval) cellular therapy products with a mandated risk management program, shall document implementation and compliance with applicable requirements of the risk management program. (CM/C/D8.17)
 - i. Risk management program requirements shall include at a minimum: (CM/C/D8.17.1)
 - 1. Training for each applicable cellular therapy product. (CM/C/D8.17.1.1)
 - 2. Assessment of knowledge for each applicable cellular therapy product. (CM/C/D8.17.1.2)

3. Retraining and reassessment of knowledge if the Collection Facility has not collected a cellular therapy product for a period of time specified by the manufacturer. (CM/C/D8.17.1.3)
 - ii. Documentation of training and compliance with the risk management program shall be established and maintained for review by the commercial manufacturer or applicable regulatory agency upon request. (CM/C/D8.17.2)
 - iii. There shall be policies or Standard Operating Procedures for the management of external audits requested by the commercial manufacturer or applicable regulatory agency. (CM/C/D8.17.3)
- d. Personnel involved in the dispensing of licensed (or equivalent regulatory approval) cellular therapy products shall comply with the mandated risk management program, if applicable. (D3.4.2)

3. Addition of standards related to gene-modified cells

The FACT Gene-modified Cell Task Force ~~reviewed the draft Standards and~~ proposed the following additional standards:

- a. There shall be a biosafety plan consistent with the institutional biosafety committee that addresses gene-modified products. (D2.8)
 - b. Continuing education shall include, but is not limited to, activities related to the field of cellular therapy, including HPC, IEC, gene-modified cells, and other cellular therapies~~HPC~~. (B3.1.6.1, B3.2.2.1, B3.5.3.1, B3.8.4.1, B3.10.3.1, C3.1.4.1, C3.2.4.1, C3.3.3.1, D3.1.4.1, D3.2.4.1, D3.3.3.1)
 - c. Administration of cellular therapy products, including HPC, IEC, gene-modified cells, and other cellular therapies. (B3.3.4.7, B3.7.2.3)
 - d. Review of outcome analysis and/or product efficacy shall include at a minimum: (B4.7.3) For gene-modified HPC products, an endpoint of clinical function as approved by the Clinical Program Director. (B4.7.3.3)
 - e. Clinical Programs utilizing gene therapy shall incorporate or reference institutional or regulatory requirements related to the disposal of genetic material when gene-modified cellular therapy products are utilized on the clinical unit. (B5.1.17.1, C5.1.17.1, D5.1.19.1)
 - f. Agreements for storage of gene-modified cellular therapy products should include information regarding the discard procedure. (D12.1.1.1)
4. Addition of training requirements in applicable good manufacturing practices as required by applicable law for Collection and Processing Facilities.
- a. For Marrow Collection Facilities collecting cellular therapy products for further manufacturing, physicians and collection staff shall have annual training in current GMP appropriate to the processes performed in accordance with Applicable Law. (CM3.3.4)
 - b. Annual training in applicable current GMP appropriate to the processes performed in collection of cellular therapy products for further manufacturing in accordance with Applicable Law. (C4.4.2.5)

- c. Annual training in applicable current GMP appropriate to the processes performed in accordance with Applicable Law. (D4.4.2.5)
5. Accreditation of HLA Typing Laboratories
The College of American Pathologists (CAP) has been approved as an accrediting organization providing histocompatibility services appropriate for hematopoietic cellular therapy, and is expressly listed in the Standards. (See B2.13; B6.4.14)

Changes Made to the Quality Management Standards

In addition to revising standards to explicitly and consistently state requirements, the following changes and additions were made:

1. Agreements should include the responsibility of the external parties to provide clinically relevant information related to products or services. (B4.6.2.1)
2. For HPC products intended for hematopoietic reconstitution, time to neutrophil and platelet engraftment following cellular therapy product administration. (B4.7.3.1, C4.7.3, D4.7.3)
3. Audits shall be conducted by an individual with sufficient expertise and competence to identify problems, but who is not solely responsible for the process being audited. (B/C/D4.8.1)
4. Periodic-Annual audit of the accuracy of clinical data. (B4.8.3.1)
5. Periodic-Annual audit, at a minimum, of the accuracy of the data contained in the Transplant Essential Data Forms of the CIBMTR or the Minimum Essential DataMed-A Forms of the EBMT. (B4.8.3.2)
6. A thorough investigation shall be conducted by the Apheresis Collection Facility in collaboration with the Processing Facility, and the Clinical Program, and other entities involved in the manufacture of the cellular therapy product, as appropriate. (C/D4.10.2.1)
7. Cumulative files of occurrences shall be maintained, tracked, and trended. (B/C/D4.10.3.4)
8. 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. Qualification shall be required following any significant changes to these items. (B/C/D4.13)
 - a. Critical equipment, software, supplies, reagents, and facilities used for the marrow collection procedure and other cellular collections shall be qualified. (B4.13.1)
9. Critical procedures to be validated shall include at least the following: marrow collection procedures, other cellular collections, labeling, storage, and distribution, and preparation for administration. (B4.14.1)
10. Critical procedures to be validated shall include at least the following: processing techniques, cryopreservation procedures, testing, labeling, storage, and distribution, and preparation for administration. (D4.14.1)
11. Each validation and verification shall include at a minimum: (B/C/D4.14.2)
 - a. An approved validation plan, including conditions to be validatedassessed. (B/C/D4.14.2.1)
 - b. Review and approval of the validation plan, validation report, and conclusion by the Quality Manager or designee and the Clinical Program Director. or designee. (B/C/D4.14.2.7)

12. Evaluation of risk shall be completed for changes in critical procedures. (C/D4.15.1)
13. Meetings ~~should~~shall have defined attendees, documented minutes, and assigned actions. (B/C/D4.17.1)
14. Key performance data and review findings shall be reported to key personnel and staff. (B/C/D4.17.2)
15. The annual report and documentation of the review findings shall be made available to ~~the~~ key personnel, the Collection Facility Director, ~~and~~ the Processing Facility Director, and all staff of the program, as appropriate. (B/C/D4.18.1)

Changes to Clinical Program Standards

In addition to revising standards to explicitly and consistently state requirements, the following changes and additions were made:

1. General
 - a. The Clinical Program shall consist of an integrated medical team that includes a Clinical Program Director (s) housed in a defined location(s). (B1.1)
 - i. These Standards apply to all services of the Clinical Cellular Therapy Program. (B1.1.1)
 - b. If the Clinical Program or an intermediary facility receives cellular therapy products directly from a third-party provider, the following responsibilities ~~shall~~should be defined, ~~at a minimum,~~ by a written agreement: (B1.2.1)
2. Clinical Unit
 - a. There shall be 24-hour availability of CMV-appropriate and irradiated blood products or equivalent needed for the care of cellular therapy recipients. (B2.12)
 - b. 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, ~~or~~ radiological, electrical, or fire hazards. (B2.16)
3. Personnel and Policies and SOPs

Several changes were made to this section to provide clarity and improve the requirements as the field evolves.

The section for nursing SOPs (B3.7.4) was integrated into Clinical Program SOPs (B5).
4. Donor Selection, Evaluation, and Management
 - a. Family members and legally authorized representatives ~~shall~~should not serve as interpreters or translators. (B6.2.2.1)
 - b. Donor informed consent for the cellular therapy product donation shall be obtained and documented by a licensed health care professional ~~familiar~~ knowledgeable inwith the collection procedure. (B6.2.5)
 - c. 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 ~~and~~ or the recipient. (B6.2.7)

- d. 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. (B6.2.8)
- e. Appropriate mobilization should be used for the disease being treated. (B6.3.4)

5. Recipient Care

- a. Recipient informed consent for the cellular therapy shall be obtained and documented by a licensed health care professional knowledgeable in ~~familiar with~~ the proposed cellular therapy. (B7.1)
- b. The ~~Clinical Program~~ informed consent process shall ~~provide~~ include information regarding the risks and benefits of the proposed cellular therapy. (B7.1.1)
- c. There shall be policies for the infusion of ABO-~~incompatible-mismatched~~ red cells in allogeneic cellular therapy products. (B7.6.2)
- d. ~~For transplants~~ When utilizing cellular therapy products from more than one (1) donor or with multiple lots, ~~the first~~ each cellular therapy product shall be administered safely prior to administration of the ~~second~~ subsequent cellular therapy product. (B7.6.5)

6. Clinical Research

- a. ~~Documentation for all~~ All clinical research protocols ~~performed by the Clinical Program~~ shall be ~~maintained~~ performed in accordance with institutional policies and ~~applicable laws and regulations~~ Applicable Law, ~~including audits; approvals by the Institutional Review Board, Ethics Committee, or equivalent; correspondence with regulatory agencies; and any adverse events and the resolution.~~ (B8.2)
- b. Documentation of approvals by the Institutional Review Board, Ethics Committee, or equivalent; and if applicable, the Institutional Biosafety Committee or equivalent; correspondence with regulatory agencies; audits; and any adverse events and the resolution shall be maintained. (B8.2.1)

7. Data Management

- a. The Clinical Program shall collect and maintain complete and accurate ~~all the~~ data necessary to complete the Transplant Essential Data Forms of the CIBMTR or the Minimum Essential Data-A forms of the EBMT. (B9.1)
 - i. Clinical Programs ~~should~~ shall submit the data specified in B9.1 for allogeneic and autologous transplants to a national or international database. (B9.1.1)
 - ii. Clinical Programs ~~should~~ shall collect the data specified in B9.1 for all patients for at least one (1) year following administration of the cellular therapy product. (B9.1.2)
 - iii. Clinical Programs should meet accuracy benchmarks established by the CIBMTR, EBMT, FACT, or JACIE. (B9.1.3)

- b. The Clinical Program should collect all data elements included in the Cellular Immunotherapy Data Resource (CIDR) forms or the Cellular Therapy Med-A forms of the EBMT. (B9.2)
8. Records
- a. Validation studies for a current procedure shall be retained at a minimum until no products manufactured using that procedure remain in inventory. (B10.1.3)

Changes to Collection Facility Standards

1. General
 - a. These Standards apply to all collection, storage, and distribution activities performed in the Marrow Collection Facility for cellular therapy products ~~obtained from living donors~~. (CM/C1.1)
2. Collection Facility
 - a. There shall be appropriate secure and controlled access to designated areas for collection of cellular therapy products, for collected products, and for storage of equipment, supplies, and reagents. (CM/C2.1)
 - b. The Collection Facility shall provide adequate lighting, ventilation, toilets, and access to sinks for handwashing and to prevent the introduction, transmission, or spread of communicable disease. (CM/C2.2)
 - c. 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. (CM/C2.8)
 - d. The Collection Facility shall have a written safety manual that includes instructions for action in case of exposure, as applicable, to communicable disease and to chemical, biological, ~~or~~ radiological, electrical, or fire hazards. (CM/C2.10)
3. Personnel
 - a. Medical Director qualifications were harmonized:
There shall be a Collection Facility Medical Director who is a licensed physician with a minimum of two (2) years postgraduate certification, with and training and practical and relevant experience in cellular therapy product collection and transplantation. (CM3.1.1, C3.2.1)
 - b. Continuing education shall include, but is not limited to, activities related to the field of HPC transplantation and other cellular therapies. (CM3.1.4.1, CM3.2.3.1)
4. Policies and SOPs
 - a. Donor screening, testing, eligibility and suitability determination, and management. (CM/C5.1.3)
 - b. Packaging, Transportation and shipping, including methods and conditions to be used for distribution to external facilities. (CM5.1.11)

- c. Packaging, Transportation and shipping, including methods and conditions to be used for distribution to external facilities including additives and preservatives for long distance or duration of shipment. (C5.1.12)
 - d. Cleaning and sanitation procedures ~~including identification of the individuals responsible for the activities.~~ (C5.1.15)
 - e. Donor Age-specific and size-specific issues where relevant. (CM/C5.3.5)
5. Allogeneic and Autologous Donor Evaluation and Management
- a. Family members and legally authorized representatives ~~should~~ shall not serve as interpreters or translators. (CM/C6.2.2.1)
 - b. Donor informed consent for the cellular therapy product collection shall be obtained and documented by a licensed health care professional ~~familiar knowledgeable in~~ with the collection procedure. (CM/C6.2.5)
 - c. ~~If required,~~ a central venous catheters ~~shall be~~ is placed ~~by a licensed health care professional qualified to perform the procedure, the rationale for placement shall be documented in the donor's records.~~ (C6.3.2.3)
 - d. Adequacy of central line placement shall be verified and documented by the Apheresis Collection Facility prior to initiating ~~each~~ the collection procedure. (C6.3.2.4)
 - e. For collections without mobilization, a pregnancy test shall be performed within seven (7) days prior to cellular therapy collection. (C6.3.4.1)
6. Coding and Labeling of Cellular Therapy Products
- a. A system of label reconciliation shall be used to ensure the final disposition of all labels allocated to a specific product are documented. (C7.2.2.1)
 - b. ~~Print-on-demand~~ label systems shall be validated to confirm accuracy regarding identity, content and conformity of labels to templates approved by the Marrow Collection Facility Director ~~or designee.~~ (CM/C7.2.3)
 - c. 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 table in Appendix IV at the time it leaves the control of the Apheresis Collection Facility. (C7.4.5; This was added to be consistent with Processing Facility standard.)
 - d. Cellular therapy products for third-party manufacturers shall be labeled with product labels that conform to FACT and JACIE requirements or Applicable Law. (CM/C7.4.9)
7. Process Controls
- a. There shall be a process for inventory control that encompasses equipment, transport containers, supplies, reagents, and labels. (CM/C8.2)
 - b. Supplies and reagents shall be quarantined or segregated prior to approval for use, until acceptance criteria have been met. (CM/C8.2.2.1)
 - c. Processes for equipment management in C8.3 were streamlined for clarity and added to the marrow collection section as applicable (CM8.3).
- There shall be a process for equipment management that encompasses maintenance, cleaning, and calibration. (CM/C8.3)
- i. Equipment shall be maintained in a clean and orderly manner. (CM/C8.3.1)

1. Maintenance, calibration, and cleaning shall be performed according to established schedules as described in Standard Operating Procedures and in accordance with the manufacturer's recommendations. (CM/C8.3.1.1)
2. The equipment shall be inspected for cleanliness and verified to be in compliance with the maintenance schedule prior to use. (CM/C8.3.1.2)
- ii. 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. (CM8.3.2)
 1. 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. (CM8.3.2.1)
- iii. Equipment, supplies, and reagents for the marrow collection procedure shall conform to ~~applicable laws and regulations~~Applicable Law. (CM/C8.3.3)
- d. Autologous or CMV-appropriate and irradiated blood products or equivalent components shall be available during the marrow collection procedure for all donors. (CM/C8.4)
 - i. Allogeneic blood ~~components-products~~ administered to the donor during marrow collection ~~should~~shall be CMV-appropriate and irradiated or equivalent prior to transfusion. (CM8.4.1)
 - ii. Allogeneic blood ~~components-products~~ administered to the donor during apheresis collection ~~or used during priming procedures should~~shall be CMV-appropriate and irradiated or equivalent prior to transfusion. (C8.4.1)
- e. Appropriate mobilization should be used for the disease being treated. (C8.9.1)
- f. Methods for collection shall employ procedures that minimize the risk of microbial contamination and be validated to result in acceptable cell viability, ~~sterility~~, and recovery. (CM/C8.10.1)
- g. Final product shall be assessed to ensure requirements for further manufacturing are achieved. (CM/C8.10.2)
- h. Collection methods for ~~pediatric~~ donors shall employ appropriate age and size adjustments to the procedures. (CM/C8.12)
- i. There shall be policies addressing safe treatment with ECP, if applicable. (C8.15.1)
 - i. ~~The ECP shall be performed according to written standard operating procedures of the facility performing the procedure appropriate for the clinical condition of the patient.~~ (Was C8.17.2 in the Seventh Edition Standards)
 - ii. A final report of the ~~details of the~~ ECP treatment including procedure shall~~details, shall~~ be documented in the patient's medical record. (C8.15.2)

8. Cellular Therapy Product Storage
 - a. Collection Facilities collecting, 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. (CM/C9.2.1)
 - i. Storage time, duration, and conditions of all cellular therapy products shall be validated. (CM/C9.2.1.1)
9. Cellular Therapy Product Transportation and Shipping
 - a. Preservative solutions should be added to the cellular therapy product for shipping over long distances or duration of time. (CM10.1.1)
 - b. The facility shall perform a risk assessment to evaluate the need for continuous temperature monitoring during transportation or shipment of cellular therapy products. (C10.3.2)
10. Records
 - a. Safeguards to secure the confidentiality of all records and communications between the collection, processing, ~~and~~ clinical facilities, and health care providers and their recipients and donors, shall be established and followed in compliance with ~~applicable laws and regulations~~ Applicable Law. (C11.1.4)
 - b. Validation studies for a current collection procedure shall be retained for the duration of the use of the procedure to demonstrate compliance with the validation requirements. (C11.3.3)
 - c. The Apheresis Collection Facility shall furnish to the facility of final disposition a copy of all records relating to the collection procedures performed related to the safety, purity, or potency integrity of the cellular therapy product involved. (C11.8.1)

Changes to Processing Facility Standards

1. General
 - a. These Standards apply to all processing, storage, and distribution activities performed in the Processing Facility on cellular therapy products ~~obtained from living donors~~. (D1.1)
2. Processing Facility
 - a. There shall be appropriate secured and controlled access to designated areas for processing of cellular therapy products, processed products, and for storage of equipment, supplies, and reagents. (D2.1)
 - i. There shall be a designated area for processing with the appropriate location and ~~The Processing Facility shall be of~~ adequate space, and design, and location for the intended procedures to minimize the risk of airborne microbial contamination. (D2.1.1)
 - b. The Processing Facility shall provide adequate lighting, ventilation, toilets, and access to sinks for hand washing, and to prevent the introduction, transmission, or spread of communicable disease. (D2.2)

- c. There shall be a written assessment of critical Processing Facility parameters that may affect cellular therapy product viability, integrity, or contamination or cross-contamination during processing, storage, or distribution. (D2.4)
3. Policies and Standard Operating Procedures
 - a. Processing of ABO-~~incompatible mismatched~~ cellular therapy products to include a description of the indication for and processing methods to be used for red cell and plasma ~~depletion~~reduction. (D5.1.4)
 - b. Appropriate processing procedures for specific products, including Cryopreservation and thawing. (D5.1.7)
 - c. Packaging, Transportation and shipping, including methods and conditions within the Processing Facility and to and from external facilities. (D5.1.11)
 4. Equipment, Supplies, and Reagents
 - a. There shall be adequate equipment and materials for the procedures performed. (D6.2)
 5. Coding and Labeling
 - a. A system of label reconciliation shall be used to ensure the final disposition of all labels allocated to a specific product are documented. (D7.2.2.1)
 - b. Print-on-demand label systems shall be validated to confirm accuracy regarding identity, content, and conformity of labels to templates approved by the Processing Facility Director ~~or designee~~. (D7.2.3)
 - c. Cellular therapy products from third-party manufacturers shall be labeled with product labels that conform to FACT and JACIE requirements or Applicable Law. (D7.4.8)
 6. Process Controls
 - a. ~~For tests performed within the Processing Facility, 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 or designee and outcomes reviewed with the staff.~~ (D8.1.4.5)
 - b. ~~Preparation for administration of products manufactured by third-parties. If the Processing Facility shall follow the instructions provided by the manufacturer. lacks experience with the type of cellular therapy product requested for a recipient, personnel shall obtain the manufacturer's instructions and follow these instructions to the extent possible.~~ (D8.4.5)
 - i. If relabeling of prepared third-party products is required, the label shall follow manufacturer's requirements. (D8.4.5.2)
 - ii. If the manufacturer does not provide instructions regarding preparation for administration, existing Standard Operating Procedures may be followed or adapted as appropriate under direction of the Facility Director and Medical Director. (D8.4.5.3)
 - c. Critical calculations shall be verified and documented where appropriate. (D8.6)

- d. Processing using more-than-minimal manipulation shall only be performed in accordance with institutional policies and Applicable Law; with Institutional Review Board or Ethics Committee approval, and with the written informed consent of the donor, if applicable, and the recipient of the cellular therapy product, ~~and in compliance with applicable laws and regulations.~~ (D8.12)
 - i. Documentation of approvals by the Institutional Review Board, Ethics Committee, or equivalent; and the Institutional Biosafety Committee, or equivalent; correspondence with regulatory agencies; audits; and any adverse events and the resolution shall be maintained. (D8.12.1)
7. Cellular Therapy Product Storage
- a. Storage time, duration, and conditions of all cellular therapy products shall be validated. (D9.2.1.1)
8. Cellular Therapy Product Transportation and Shipping
- a. Cellular therapy products transported internally shall be packaged in a closed and rigid outer container. (D10.6)
 - i. The outer container for internal transport shall be labeled as defined in Appendix III B. (D10.6.1)
9. Records
- a. Safeguards to secure the confidentiality of all records and communications between the collection, processing, ~~and~~ clinical facilities, and health care providers and their recipients and donors, shall be established and followed in compliance with ~~applicable laws and regulations~~ Applicable Law. (D13.1.6)
 - b. 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 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 laws and regulations~~ Applicable Law. (D13.4.1)
 - i. Validation studies for a current processing procedure shall be retained at a minimum until no products manufactured using that procedure remain in inventory. (D13.4.1.3)
 - c. The Processing Facility shall furnish to the facility of final disposition a summary ~~copy~~ of all records relating to the collection, processing, and storage procedures performed related to the safety, purity, or potency of the cellular therapy product involved. (D13.5.2)

10. Appendix III

B: CELLULAR THERAPY PRODUCT LABELS FOR INTERNAL TRANSPORT

| <u>Element</u> | <u>Internal transport label</u> |
|---|--|
| <u>Statements "Human Cells for Administration" or equivalent and "Handle with Care"</u> | <u>AF</u> |
| <u>Emergency contact person name and phone number</u> | <u>AF</u> |