PROPOSED Standards for Cellular Therapy Services
11th Edition

Effective July 1, 2023

A Note to Readers

Individuals not familiar with the standards-setting practices of AABB should be aware of the following:

• Requirements, once stated, are not repeated. For example, standard 5.0 requires that all processes and procedures be validated. Therefore, it is not necessary to require in other areas that a specific process or procedure be validated.
• Words or phrases used in a way different from their usual meaning are defined in the glossary.
• The term "specified requirements" is defined broadly to include accreditation requirements, national, state, or local laws, and any other applicable requirement.
• Please note, that the Summary of Significant Changes to the proposed 11th edition begins on page 2 and runs through page 24.

The proposed 11th edition begins on page 25 and runs through page 140.

1.1.2 The facility shall register for all applicable products and activities with the Food and Drug Administration (FDA) or relevant Competent Authority. When applicable, the facility shall obtain **regulatory approval** ~~licensure~~ for all products and activities.

The committee replaced the term "licensure" with "regulatory approval" as licensure was deemed too specific and restrictive. The new terminology ensures that the regional health authority has appropriate oversight.

1.2.3.1.1 Signatures of the individual approving all policies, processes, and procedures shall comply with the requirements of the FDA or relevant Competent Authority.

The committee felt that the inclusion of this new standard was appropriate to ensure the signature method in use meets the requirements in place for each country where these Standards are implemented.

1.2.4 Quality Representative
The facility's executive management shall appoint a member of management **who is qualified by training with relevant experience in quality management systems. The quality representative** ~~who~~ shall have defined independent authority for ensuring that the facility establishes, implements, and maintains a quality system that meets the requirements of these *CT Standards*. When the quality representative delegates these responsibilities to a designee, the quality representative shall retain ultimate responsibility.

The committee added the element in bold to ensure parallel construction with other standards that delineate the expectations for individuals who serve in the role of quality representative.

1.4.1 The facility shall have a policy to address critical supply shortages.

The committee created new standard 1.4.1 based on a similar standard in the Standards for Blood Banks and Transfusion Services. This standard complements the operational continuity standard, 1.4.

C **2.1.4 Training**
The facility shall establish and maintain policies, processes, and procedures for:
1) Orientation,
2) Initial **job specific training,**
3) Quality-systems-related training ~~needs~~**, and**
4) Ongoing job-specific **training.**

2.1.4.1 The facility shall define the qualifications **and approve subject matter experts who provide training** ~~required for trainers~~.

The committee elected to split standard 2.1.4 into two separate standards for clarity. Standard 2.1.4 was broken up into a list for legibility, however the intent of the standard has not changed.
Standard 2.1.4.1 is new and previously appeared as a part of standard 2.1.4. The committee elected to add the content in bold for clarity and to ensure that the individuals performing training are qualified to do so.

✎C **2.1.6.4** **Corrective** action shall be taken when competence has not been demonstrated.

The committee added the term "corrective" for completeness, understanding that the action taken in this case would be corrective in the event that a lack of competence is found.

2.1.7.1 The facility shall ensure that **the** medical, laboratory, procurement, and clinical program directors, **and** ~~as well as~~ the quality representative, **annually** complete 10 hours of educational activities ~~annually related~~ **relevant** to the **role and the associated** ~~accredited~~ cellular therapy activity or activities **performed in the facility***. Standards 1.1.3.1, 1.1.4.1, 1.1.4.2, and 1.1.5.2 apply.

*42 CFR 493.1413(b)(8) and 42 CFR 493.1451(b)(8).

The committee edited the standard for clarity. The intent of the standard has not changed.

2.2 Access to Ancillary Services and Direct Patient Care

The clinical facility shall **have an agreement in place to** ensure **comprehensive care** and ~~access to medical specialty services~~ **relevant** resources **required** ~~as needed~~ for patient care **in cellular therapies**, including but not limited to:

1) **Transfusion medicine** ~~Leukocyte-reduced/irradiated blood components for patients receiving hematopoietic stem cell transplants~~.
2) **Services related to** pharmacy.
3) Radiology.
4) Laboratory services.
5) **Acute care or medical facilities.**
6) **Social and psychological support.**
7) **Long term follow-up based on protocol or treatment plan.**

The committee edited the content of the first sentence of the standard to ensure it can best cover the new activities related to cellular starting materials. AABB is attempting to provide a qualification to help ensure broader aspects of patient care are also considered.
Subnumber 1 has been edited to focus only on transfusion medicine, which includes the content that previously was listed in the entry; this will be moved to guidance.
Subnumber 2 was edited to broaden the requirement while not changing its intent.
Subnumbers 5 – 7 were added to broaden the Standards to meet the needs of potential new customers and accredited facilities, and provide more comprehensive aspects of patient care.

3.1 Equipment Specifications <u>and Selection</u>

Equipment specifications shall be defined before **<u>selection and</u>** purchase.

The committee added the concept of "selection" to the standard to match other sets of AABB standards that exist.

***F* 3.2 Qualification of Equipment**

All critical equipment shall be qualified for its intended use. Equipment repairs and upgrades shall be evaluated and equipment requalified, as appropriate, based on the facility's policies, **<u>equipment maintenance or repair reports</u>** and manufacturer's **<u>written instructions</u>** ~~recommendations~~.

The committee added the clause in bold for clarity and completeness. These requirements are a part of the activities of accredited facilities and the standards are being specific to match. The term "recommendations" was replaced with "written instructions" to mirror the terminology used throughout the Standards.

3.2.3 Performance Qualification

The facility shall **<u>demonstrate that equipment performs as expected for its intended use per facility developed predetermined criteria. Facility developed predetermined criteria shall meet or exceed the specifications established by the manufacturer</u>** ~~demonstrate that equipment performs as expected for its intended use~~.

~~**3.2.3.1** Appropriate staff shall be trained and deemed competent to demonstrate that equipment performs as indicated.~~

The committee elected to broaden the content of standard 3.2.3 for clarity. The committee feels that the standard now provides clarity for facility defined specifications for PQ. The committee also elected to delete standard 3.2.3.1 as it was deemed redundant to elements in chapter 2. The content will be moved to guidance.

3.4 Equipment Monitoring and Maintenance

The facility shall have a process for scheduled monitoring and maintenance of equipment that is in accordance with manufacturer's written instructions **<u>and in accordance with the FDA or relevant Competent Authority</u>**.

The committee added the clause to ensure that facilities mirror not only manufacturer's instructions but also those of their Competent Authority for completeness.

✎*F* **3.4.3 Monitoring, Maintenance, and Repair**

The facility shall:

6) Ensure that all critical equipment maintenance and repairs are performed by qualified individuals and in accordance with manufacturer's **written instructions** ~~recommendations~~.

Standard 3.2 applies.

The committee replaced "recommendations" with "written instructions" for parallel structure throughout the Standards. The crossreference to standard 3.2 ensures that facilities qualify all their equipment.

3.6.1 Alternative Systems

The facility shall have **validated** alternative systems to ensure access to critical information and continuous operation of critical activities in the event that electronic data and information system-assisted functions are not available.

The committee added the term "validated" for completeness.

✎*F* **3.6.1.1** The alternative systems shall be **verified at facility-defined intervals** ~~tested periodically~~.

The committee replaced "tested periodically" with "verified at facility defined intervals" for completeness and parallel construction. The term "verified" includes "testing" and more, which ensures that the standard is accurate, and the replacement of "periodically" with "facility defined intervals" was made for assessment purposes.

✎*C* **4.1 Agreement Review**

When the responsibilities for activities covered by these *CT Standards* involve more than one facility, there shall be agreements that define the following for the cellular therapy product from point of origin to administration including but not limited to:

The committee created new content for standard 4.1, which previously only appeared as a title. The content of this standard ensures that there are agreements containing certain requirements when responsibilities involve more than one facility responsible for activities covered in these Standards from the point of origin of the product until final administration.

4.1.1 Before acceptance of a **documented** verbal or written agreement, the agreement shall be reviewed by the facility or department to ensure that:

1) The customer's requirements are adequately defined **in compliance with these *CT Standards* and in accordance with applicable FDA or relevant Competent Authority requirements**.

2) Any differences between the agreement requirements and the cellular therapy products or services offered under the agreement are resolved.
3) The facility has the capability to meet the requirements **detailed in the** agreement.
4) Chain of Identity is from point of origin to point of administration or discard,
5) Chain of Custody is from point of origin to point administration or discard,
6) Quality is maintained from the point of origin to the point of administration or discard.
7) Conformance with accepted policies and procedures.
8) Conformance with safety requirements.

The committee edited the content of subnumber 1 for completeness. This edit matches similar additions placed throughout the Standards as it relates to compliance with this edition, but Competent Authority regulations as well.
Subnumber 3 was edited for clarity, the content of the standard has not changed.
Subnumbers 4 and 5 have been added to the proposed edition and in multiple locations throughout the proposed edition. The concept of chain of identity and custody has been a point of inclusion for this edition by the committee.
Subnumber 6 through 8 were included to ensure that a level of quality be maintained through conformance with policies, processes and procedures.

4.1.2.1 Roles and responsibilities of personnel. Standards 1.2.4, 5.14.1 and 5.17.1 apply.

The committee added new standard 4.1.2.1 to ensure that agreements define the roles and responsibilities of all personnel involved in the cellular therapy process.

4.1.2.2 Roles and responsibilities of each facility involved in the procurement, processing, labeling, storage, distribution, or administration of a cellular therapy product to maintain Chain of Identity and Chain of Custody.

The committee added new standard 4.1.2.2 to ensure that the responsibility of each facility involved in the agreement for all activities covered by these CT Standards to maintain both chain of identity and chain of custody.

4.1.2.3 Communication of critical information, including deviations, nonconformances and adverse events. Standard 5.7 applies.

The committee added new standard 4.1.2.3 to ensure that when a deviation, nonconformance or adverse event occur, that information is shared between the facilities that are a party to the agreement.

4.1.2.4 Reporting of adverse events and nonconformances to regulatory bodies, Competent Authorities, and registries, if applicable.

The committee added new standard 4.1.2.4 to ensure that facilities involved in agreement share any nonconformances to the relevant regulatory institutions where appropriate.

4.1.2.5 Specifications and requirements for donor and patient care, quality, safety, and other facility defined critical parameters.

The committee added new standard 4.1.2.5 to the proposed edition to ensure that agreements reflect requirements for donor and patient care as well as any other facility defined quality requirements.

***C*4.2 Changes to Agreements**

The facility shall define how changes to agreements are ~~made~~ **proposed, accepted** and communicated to affected parties.

The committee edited standard 4.2 for clarity, elucidating what the term "made" implied.

4.3 Agreements Relating to Cellular Therapy Products, Materials, and Services

When the responsibilities for activities covered by these *CT Standards* involve more than one facility or department, there shall be agreements **that define the following for the cellular therapy product from point of origin to administration** including but not limited to ~~the following~~:

The edit to this standard ensures parallel construction with standard 4.1 which ensures that there are agreements containing certain requirements when responsibilities involve more than one facility responsible for activities covered in these Standards from the point of origin of the product until final administration.

***F* 4.3.1 Medical Authorization for Procurement and Processing**

The~~re shall be policies, processes and procedures that define the following~~ **facility shall have medical authorization for procurement and processing of cellular therapy products except where the recipient is unknown and the procurement of the product is non invasive** ~~excluding HPC, Cord Blood products when the recipient is not know~~:

The committee edited this standard to revise the language without changing the intent to improve legibility.

4.3.2 Medical Authorization ~~Orders~~ for Distribution

The committee replaced the term "orders" with "authorization" for clarity.

✎*F* **4.3.3 Transfer of Products**

When products are transferred between departments or facilities, the following items shall be defined:

1) Responsibility for maintaining chain of **identity** ~~custody~~ during transfer.

2) Responsibility for maintaining chain of custody during transfer.

In an effort described above to ensure that both chain of identity and custody are maintained, the committee added new number 2 which focuses on chain of custody and replaced the word "custody" with "identity" in number 1 to ensure that proper flow is maintained.

✎*F* **4.3.4 ~~Providing~~ Instructions**

The title of standard 4.3.4 was updated for clarity, the new title better reflects the content of the standard below.

✎*C* **4.3.5 Records**

When products are transferred between departments or facilities, the following items shall be defined:

2) Responsibilities of each facility involved in the procurement, processing, labeling, storage, distribution, or administration of a cellular therapy product to provide ~~a copy of relevant~~ records **in a timely manner** upon request. Standard 5.7 applies.

The committee edited number 2 for clarity. The language in bold is similar to the content regarding retrieval of records in other sets of AABB Standards.

✎*C* **4.3.6 Supplier Qualification**

When cellular therapy product services involve more than one facility, each facility shall be qualified to perform the scope of activities defined in the agreement in accordance with these *CT Standards*.

This standard is new to the proposed edition and was modeled after similar standards in other sets of AABB Standards.

✎*C* **4.3.7 Conditions for Product Storage and Disposition**

When products are transferred between departments or facilities, the following conditions shall be defined:

1) Maintenance of Chain of Identity.

2) Maintenance of Chain of Custody.

To continue to ensure chain of identity and custody are included in this edition of CT Standards, numbers 1 and 2 have been included in this edition.

4.5.1 Donor informed consent templates shall be reviewed **at defined intervals** and **updated as needed and** approved by the **current** medical director of the facility responsible for obtaining informed consent.

The committee edited this standard for clarity. The language ensures that the informed consent documents are updated as needed and that the current medical director is aware of its contents.

4.5.2.2 There shall be a process to provide a qualified interpreter when required and/or when applicable.

The committee created new standard 4.5.5.2 for completeness. The committee feels that it is of paramount importance that those involved in the donor informed consent process have all the tools necessary to ensure that donors are fully aware of what will occur and what is expected of them.

4.6.1 Any authorization templates shall be reviewed **at defined intervals** and **updated as needed and** approved by the **current** medical director of the facility responsible for obtaining authorization.

The committee edited this standard for clarity and to match the edits made to standard 4.5.1.

4.7.1 Patient informed consent templates shall be reviewed **at defined intervals** and **updated as needed and** approved by the **current** medical director of the facility responsible for obtaining informed consent.

The committee edited this standard for clarity and to match the edits made to standards 4.5.1 and 4.6.1.

4.5A – Donor Informed Consent or Authorization

I. General Informed Consent ~~Requirements~~

The committee removed the term "requirements" as it was deemed unnecessary.

A. Description of participation, including:

4. **Specimen** ~~Sample~~ procurement and storage for possible future testing.

5. ~~Sample storage,~~ **Intended for use for manufacture or manipulation, including storage,** in-vitro manipulation, and analysis.

12. Financial or other incentives for donation of cellular therapy products.

In number 4, the committee replaced the term "sample" with "specimen" as this is a more accurate term. In number 5, the committee replaced the term "sample storage" with "intent for use for manufacture or intended manipulation including storage" for clarity. The clause better meets the intent of the standard and informed consent requirements.

Number 12 is new to the proposed edition and was included for completeness. There are times when donation of a product can be incentivized and this needs to be included as a part of the donor informed consent process.

B. The consenter(s) shall acknowledge in writing that they have received information concerning the risks, benefits, discomforts, and alternatives to human cellular therapy product donation; that they have had an opportunity to have access to donor advocacy **and translation** services; that they have been given the opportunity to ask questions and had those questions answered satisfactorily; and that they have been given a written copy of contact information for future questions related to cellular therapy product donation.

With the creation of new standard 4.5.5.2, the committee added the clause in bold to subletter B for completeness.

4.7A – Patient Informed Consent
I. General Informed Consent ~~Requirements~~

The committee removed the term "requirements" as it was deemed unnecessary.

B. The patient shall acknowledge in writing that they have received information concerning the risks, benefits, discomforts, and alternatives to the selected medical interventions; that they have had the opportunity to deny or withdraw consent to the treatment at any time without affecting their access to medical care; that they have had an opportunity to have access to patient and **translation** advocacy services; and that they have been given the opportunity to ask questions and had those questions answered satisfactorily.

With the creation of new standard 4.5.5.2, the committee added the clause in bold to subletter B for completeness.

C **5.1.2 Proficiency Testing**

The facility shall participate in an external proficiency testing program for each analyte measured by the laboratory. **Proficiency testing for each analyte shall be performed at least twice a year.**

This sentence in bold previously appeared as a stand alone standard, 5.1.2.2.1, the rationale was that this sentence fit better in the parent standard concerning proficiency testing.

5.1.2.1 ~~In the United States,~~ For each analyte requiring proficiency testing under Clinical Laboratory Improvement Amendments (CLIA)*, each laboratory shall participate in a Centers for Medicare and Medicaid Services (CMS) approved proficiency testing program.

*42 CFR 493.801

The committee removed this requirement as it was deemed redundant to the content of the standard which focused on CMS.

5.3.1 For the procurement and processing facilities, this shall include but is not limited to adverse events and complications attributed to procurement, processing, infusion, and/or engraftment, **as applicable**.

The committee added the clause "if applicable" as there are instances where this does not occur.

5.3.2 For the clinical facility, this shall include **the clinical outcomes as specified by the clinical protocols and as applicable** ~~but is not limited to~~:

1) Mortality and survival rates.
2) Disease status and/or relapse.
3) Adverse events and complications.
4) Disease modifying activity.
5) Engraftment.
6) **Immune effector cell endpoints.**
7) **Hematopoietic reconstitution.**
8) **Monitoring of patient safety**

The committee added the clause in bold to indicate that these elements would be determined by clinical protocols. The committee added elements 6 – 8 for completeness, understanding that clinical facilities would require that these elements be included as it pertains to outcomes data to be gathered.

5.3.2.1 The clinical facility shall determine the criteria for cellular therapy product safety, product efficacy, and/or clinical outcomes data and collect this data for analysis at defined intervals.

The committee added the new standard to the proposed edition for completeness. The intent being to ensure that the collection of outcomes data be done at facility defined intervals.

~~**5.3.3** For facilities that procure, process or administer products that will be used for hematopoietic reconstitution, there shall be a process for review of time to engraftment following cellular therapy product administration.~~

~~**5.3.4** For facilities that process or administer islet products, there shall be a process for recording and monitoring recipient safety and reviewing clinical outcomes.~~

Standards 5.3.3 and 5.3.4 have been deleted as they were deemed redundant to standards 5.3.1, 5.3.2 and

new standard 5.3.2.1.

5.3.4 For facilities that procure, process or administer investigational products, there shall be a process for recording and monitoring patient safety and reviewing clinical outcomes as specified by the independent ethics committee-approved protocol(s). ~~The facility shall submit clinical safety and outcomes data as required by national and local regulations.~~

The committee deleted the sentence in strikethrough as the concept is now fully covered by standards 5.3.2 and 5.3.2.1.

✎***C*** **5.4 Quality Control**

The facility shall establish a program of quality control that is sufficiently comprehensive to ensure that materials including **supplies**, reagents and equipment, **function** as specified.

The committee edited standard 5.4 for completeness.

5.5.3 Qualification of Critical Materials

Materials that come into contact with the patient or cellular therapy product shall be sterile and of appropriate grade for the intended use and ~~, whenever possible,~~ shall be approved for human use by the United States FDA or relevant Competent Authority.

The committee added the term "critical" to the title of the standard for completeness understanding that not all materials used in the facility would be deemed critical. The clause "whenever possible" was removed from the standard as it served as guidance and not necessary.

5.6.2 Aseptic Methods

Procurement, processing, and clinical facilities shall establish and maintain policies, processes, and procedures designed to minimize contamination of the product and infection of the ~~patient~~ **donor or recipient**. The following shall be addressed:

5) Workflow and movement of personnel through workspaces.

The committee replaced the term "patient" with "donor or recipient" as this is the accurate term to use in this instance. The committee has done a complete review of the standards to determine where patient vs recipient should be used and in this instance the term "recipient" was deemed most appropriate. Subnumber 5 is new to the standard and was added to ensure that the impact on product sterility as a result of personnel movement and instances where workflow is not followed are considered.

✎***C*** **5.6.2.1** The effectiveness of such measures shall be monitored and reviewed **at defined intervals** ~~on a regular basis~~.

The committee edited standard 5.6.2.1 to mirror the terminology used in the Standards.

5.6.3 Operational Controls

Operational controls shall prevent mix-ups and contamination. The following shall be defined:

1) Movement and storage of materials (including waste) and equipment ~~and workflow~~ within workspaces.

The committee removed the element from standard 5.6.3 in strikethrough as it was deemed to fit better in standard 5.6.2.

5.7 Product Identification and Traceability

The facility shall establish and maintain policies, processes, and procedures that ensure the **chain of identity and chain of custody for** identification and traceability of each cellular therapy product and all related samples from their initial source, through all processing and testing steps, to their final disposition. Policies, processes, and procedures shall also allow the identification and traceability of each cellular therapy product and all related samples from their final disposition, through all processing and/or testing steps, to their source.

The committee added the elements of "…chain of identity and chain of custody for…" for completeness and to continue the inclusion of these elements in the proposed edition.

✎***C*** **5.7.1 Traceability and Unique Identification**

A numeric or alphanumeric system shall be used that will make it possible to trace any cellular therapy product or sample from donor/source to recipient/final disposition and back to the donor/source and to review records applying to the specific cellular therapy product or sample, including those related to reported adverse events. ~~This~~ Unique **identifiers** ~~identification~~ shall not be obscured, altered, or removed.

Noting that the Standards require two unique identifiers, the committee adjusted the final sentence of the standard for completeness.

5.8.5 Cellular therapy products for investigational use or approved for use by the FDA or relevant Component Authority shall be labeled according to protocol and all elements required shall be included in the accompanying records or readily available. Reference standard 5.8.2A applies.

The committee added new proposed standard 5.8.5 to ensure that the Standards include a requirement for facilities that use investigational products are approved for use and labeled according to Competent Authority requirements.

✎***F*** **5.9 Transport and Shipping**

The facility shall establish and maintain policies, processes, and procedures that are intended to limit deterioration, prevent damage, ensure timely delivery, and protect the quality of the

materials and cellular therapy products during transport and shipping **while maintaining Chain of Custody and Chain of Identity**.

The committee added the elements of "chain of identity and chain of custody" for completeness and to continue the inclusion of these elements in the proposed edition.

✎C **5.9.2** **Shipping or transport** containers shall be qualified at defined intervals to ensure that they maintain temperatures within the acceptable range for the expected duration of transport or shipping.

The committee added the clause "shipping or transport" for completeness.

✎C **5.9.6** ~~The receiving~~ Facilities shall maintain records of product **origin, custody, transfer, identity, integrity** and acceptability.

The committee edited this standard for completeness, ensuring that the records to be maintained include everything now listed in the standard.

✎C **5.10.1 Receipt of Incoming Cells, Tissues, and Organs**

At the time of receipt, incoming cells, tissues, and organs shall be inspected, sampled, and/or tested, as appropriate, to determine their acceptability. Standards 5.8.1, 5.8.3 and 5.9.6 apply. Records of the following shall be maintained:

9) Results of inspection upon receipt, if applicable, including:
   d) Presence or absence of visible evidence of contamination **and tampering**.

The committee added the clause in bold for completeness understanding that tampering is a possible means of contamination of a received product.

5.10.1.1 Identification of Cells, Tissues, and Organs Upon Receipt

The facility shall establish and maintain policies, processes, and procedures to require verification of the **chain of identity** ~~identification~~ of cells, tissues, and organs.

The committee replaced the term "identification" with "chain of identity" for parallel construction throughout the document.

5.10.1.2 Cells, tissues, and organs shall be quarantined upon receipt and their disposition determined by a qualified **individual** ~~parallel~~ when any of the following occur:

The committee replaced the term "person" with "individual" as this term is more appropriate.

C **5.11.1.1** If cellular therapy products are stored in an open storage area, the ambient temperature **and humidity** shall be recorded at ~~least~~ **a minimum of** every 4 hours.

The committee added "humidity" to this standard for completeness, understanding that humidity has to be monitored for products maintained at room temperature. The committee also replaced "at least" with "at a minimum" for parallel construction with other standards.

5.12.2 Donor Eligibility
Donor eligibility, **when required** shall be determined before the initiation of any intervention that could potentially affect the health of a recipient.

The committee added the clause "when required" understanding there are instances where donor eligibility is not required to be determined.

F **5.12.2.2 Collection of Samples for Infectious Disease Testing**
Samples associated with the products listed below shall be collected within the following timeframes, unless FDA or relevant Competent Authority regulations are more stringent:

1) HPC, Cord Blood: **Obtain** ~~Collect~~ maternal sample within 7 days before **collection** ~~or after delivery~~.

The committee edited this standard to ensure that the language of subnumber 1 mirrored the language in the CFRs referenced with the standard. The intent of the standard has not changed.

5.12.2.1.2 The facility shall have a policy that addresses **and ensures** the privacy and confidentiality of the donor eligibility determination process.

The committee added the clause "and ensures" for completeness. As written previously the standard could be interpreted to not require that assurance of privacy.

5.12.6.2.2 For cadaveric donors, all infectious disease test results shall be reported to the procurement facility. The procurement facility shall report positive test results to appropriate authorities as **mandated** ~~requiring~~ by law or regulation, and test results shall be made available to the donor's legal next of kin **when** ~~if~~ the test result(s) could affect the health of others.

The committee edited the standard for clarity, however the intent of the standard has not changed.

5.12.10 Labeling for Autologous Products

Autologous units shall be labeled with the phrase "For autologous use only" and, if testing or screening is not completed **or performed** ~~in accordance with the requirement of the Competent Authority~~, it shall be labeled with the statement "Not evaluated for infectious substances." Reference Standard 5.9.5A, Labeling and Packaging Requirements Upon Shipping of Cellular Therapy Products, applies.

The committee added the clause "or performed" for completeness. The clause in strikethrough was removed as it was deemed not necessary.

C **5.14.2.3** **For marrow donors or donors of cells collected by apheresis, facilities shall:**

1) Define criteria to evaluate the results of a complete blood count before each procurement.

2) Define timeframes for obtaining a complete blood count prior to the initial procurement.

3) Obtain a complete blood count within 24 hours prior to each subsequent procurement after the initial procurement.

~~For donors of cells collected by apheresis, a complete blood count shall be obtained before mobilization and within 24 hours prior to each procurement procedure. For marrow donors, a complete blood count shall be obtained before procurement.~~

The committee edited this standard to ensure that the timeframes and determinations of when to perform a complete blood count is provided at several steps and is not conducted in a fashion that is harmful to the potential donor. This change also expands the standard to allow for all cells collected by apheresis to be procured, including CAR-T cells which do not require mobilization.

F **5.14.5 Procurement Records**

A procurement record shall include:

4) Unique donor **and/or patient** identifier, if available.

The committee added "and/or patient" for completeness. This change has been made to all standards that focus on records throughout chapter 5.

5.14.7 Procurement Record Availability

Each facility performing procurement shall provide a product procurement record to the facility receiving the product **while maintaining chain of custody**. Chapter 4, Agreements, applies.

The committee added the clause concerning the maintenance of chain of custody as a part of the overall inclusion into the standards of this concept.

5.14.7.1 Records shall include:
4) Unique donor **and/or patient** identifier, if available.

The committee added "and/or patient" for completeness. This change has been made to all standards that focus on records throughout chapter 5.

✎***F*** **5.17.2 Processing Record**
A complete processing record shall include:
4) Unique donor **and/or patient** identifier, if available.

The committee added "and/or patient" for completeness. This change has been made to all standards that focus on records throughout chapter 5.

5.17.5 Processing Records
Each facility(ies) performing processing, preservation, or storage shall provide a copy of the product processing record insofar as the processing records concern the safety, purity, and potency of the product involved or a summary of the product processing record to the facility(ies) receiving the product **while maintaining chain of custody**. Chapter 4, Agreements, applies.

The committee added the clause concerning the maintenance of chain of custody as a part of the overall inclusion into the standards of this concept.

✎***C*** **5.18 Storage of Noncryopreserved Products**
The facility shall establish for each type of product the storage specifications and defined storage conditions, including temperature range **and length of storage** to maintain viability and function.

The committee added the clause "and length of storage" to ensure that facilities determine the time that will ensure that products will maintain their viability.

✎***F*** **5.19.3 Records for Cryopreserved Products**
In addition to the items required by Standard 5.17.2, cryopreservation records shall include:
4) Unique donor **and/or patient** identifier, if available.

The committee added "and/or patient" for completeness. This change has been made to all standards that focus on records throughout chapter 5.

5.20.2.1 At a minimum, the stability program shall include product container integrity and viable cell recovery, **and a measure of potency** of the relevant cell population(s).

The committee added the clause concerning the need to be able to measure the levels of potency once products are recovered post thaw. This closes a gap in the standards that was identified by users of the previous edition.

5.22.2.2 Product Processing Review

Review of the final cellular therapy product processing record shall confirm that:

2) **Facility defined** specified requirements ~~as defined in applicable policies, processes and procedures~~ were achieved.

The committee edited the standard for clarity. By including "facility defined" the need to include the elements in strikethrough were deemed redundant. The edit does not change the intent of the standard.

5.24.2 At distribution and issue of allogeneic products, the following information shall accompany the product or be readily available wherever the product is located **to maintain chain of custody:**

The committee added the clause concerning the maintenance of chain of custody as a part of the overall inclusion into the standards of this concept.

5.25 Clinical Program

The facility shall have policies, processes, and procedures for patient care, including the administration of specific therapies and medical interventions **while maintaining chain of identity**.

The committee added the clause concerning the maintenance of chain of identity as a part of the overall inclusion into the standards of this concept.

5.25.1.1 Facilities administering investigational product(s) shall have policies, processes, and procedures to reevaluate the recipient before the administration of products.

The committee added new standard 5.25.1.1 for completeness understanding that recipients of investigational products need to be reevaluated prior to receipt of the product.

5.26.1 Medical Orders

Orders for clinical care of the **recipient** ~~patient~~ shall uniquely identify the **recipient** ~~patient~~ and medical treatment ordered. Specific instructions shall be provided in the order.

The committee performed a review of all uses of patient vs recipient and have updated the standards where necessary.

5.26.1.1 Medical therapy(ies) shall be ordered by a **qualified** physician or **an authorized** health-care professional.

The committee added the terms in bold for completeness and parallel construction with similar requirements throughout the edition.

***F*5.27Preparation of the Recipient for Administration of Cellular Therapy Products**

The facility shall have policies, processes, and procedures for the preparation of the **recipient** ~~patient~~ for administration of cellular therapy product(s) which shall address, at a minimum, the following:

The committee performed a review of all uses of patient vs recipient and have updated the standards where necessary.

5.28.1 Receipt of Cellular Therapy Products

The clinical facility shall have procedures for the receipt, and preparation, of products **while maintaining chain of identity and chain of custody**. Standards 5.7, 5.8, 5.10, and 5.22 apply.

The committee added the clause concerning the maintenance of chain of identity and chain of identity as a part of the overall inclusion into the standards of these concepts.

F **5.29.3** There shall be procedures for recording adverse events and processes for the communication of such events from the clinical facility to the issuing facility and/or registry **while maintaining chain of identity**. Chapter 7, Deviations, Nonconforming Products or Services, and Adverse Events, applies. Standards 4.3.4 and 4.3.5 apply.

The committee added the clause concerning the maintenance of chain of identity as a part of the overall inclusion into the standards of this concept.

F **5.29.4 Records of Administration**

Records of administration shall include:

1) **Patient's** ~~Recipient's~~ name and unique identifier(s).

The committee performed a review of all uses of patient vs recipient and have updated the standards where necessary.

F **5.29.5 Patient ~~Recipient~~ Records**

Patient ~~Recipient~~ records shall include the following:

1) **Patient's** ~~Recipient's~~ name and unique identifier(s).

11) Other relevant testing records.

The committee performed a review of all uses of patient vs recipient and have updated the standards where necessary.
The committee also added new #11 for completeness and parallel construction.

Reference Standard 5.8.2A – Requirements for Labeling of Cellular Therapy Products

Item No.	Element	Completion of Procurement[1]	In-Process Label[1]	Completion of Processing	Distribution and Issue[2]
11	**Patient**/Recipient name and/or identifier (if known)[9]	R	R	R	A[6]

[9] Ensure maintenance of chain of identity.

The committee performed a review of all uses of patient vs recipient and have updated the standards where necessary and in this case, included both.
The committee also included new footnote 9 in their effort to ensure chain of identity is maintained.

Reference Standard 5.8.2A – Requirements for Labeling of Cellular Therapy Products

Item No.	Element	Completion of Procurement[1]	In-Process Label[1]	Completion of Processing	Distribution and Issue[2]
14	**CMV status of the donor (if applicable)**	**N/A**	**N/A**	**N/A**	R

The committee added new entry 14 to ensure that products from donors who are CMV positive are identified as such on the accompanying label. This ensures that facilities test donors for CMV in accordance with other elements of this set of Standards.

Reference Standard 5.12A – General Requirements for Cellular Therapy Product Donors

I. Donor Advocacy and Translation Services

All allogeneic donors or their legally authorized representatives shall be provided with the opportunity to access donor advocacy **including translation** services.

With the creation of new standard 4.5.5.2, the committee added the clause in bold to subletter B for completeness.

B. Specific Donor Requirements

2) Autologous Donors

A ~~health~~ **medical suitability** assessment specific to the donation procedure shall be performed by a **qualified** health-care professional and approved by a physician before the scheduled procurement.

The committee added the terms in bold for completeness and parallel construction with similar requirements throughout the edition.

Reference Standard 5.17C – Processing Tests for Cellular Therapy Products Other than HPC, Apheresis, HPC, Marrow; and HPC, Cord Blood

4) **Characterization of cell identity** ~~Antigen expression~~ analysis specific to the cellular therapy product, if applicable.

The committee edited this entry in the reference standard for accuracy.

5) **Functional** ~~Potency~~ assay specific to the cellular therapy product, as applicable.

a) Relevant potency assay shall be defined by the facility.

The committee edited this entry in the reference standard in line with the change made to standard 5.20.2.1.

7) **Sterility** testing of cultured cells shall include endotoxin and mycoplasma **and other relevant assays**, unless not required under an Investigational New Drug (IND) or license application or as approved by the Competent Authority.

The committee updated this entry to mirror other changes made throughout the standards.

8) Characterization of cell product purity as required by an IND or license application or as approved by the Competent Authority.

The committee added this new entry to the reference standard to ensure that the standards are complete, recognizing the need to include the characterization of cell product purity and potency.

6.2.1.1 Record Traceability

The records system shall ensure the traceability **by maintaining chain of identity and chain of custody** of all of the following:

The committee added the clause concerning the maintenance of chain of identity and chain of custody as a part of the overall inclusion into the standards of these concepts.

6.2.4.1 Modifications or, any changes that can affect the safety of the recipient or quality of the cellular therapy product shall be approved by the authorized individual. Chain of identity shall be maintained.

The committee created new standard 6.2.4.1 for completeness. The new standard ensures that any changes to records that could affect the safety of the recipient be reviewed by an appropriate individual.

6.2.8 Confidentiality

The facility shall have policies that ensure the confidentiality **and privacy** of donor, employee, and patient records.

The committee added the clause requiring "privacy" be maintained as a part of the confidentiality perspective.

6.2.9 Retention

Records required by these *CT Standards* shall be retained for at least 10 years following either their creation (C) or the final disposition (F) of the cellular therapy product with which they are associated. Applicable **FDA or relevant Competent Authority**, ~~national, state,~~ or local law may exceed this period.

6.2.9.1 If the date of administration is unknown, records shall be retained for 10 years after the date of distribution, disposition, or expiration, whichever is latest. Applicable **FDA or relevant Competent Authority**, ~~national, state,~~ or local law may exceed this period.

In line with other changes throughout the document to remove US centric terms, "national and state" to allow the standards to be as internationally friendly as possible.

6.3.1.1 Individuals shall be identified and defined by job description that are authorized to create, modify, maintain or transmit records in a controlled and approved manner in conformance with the FDA or relevant Competent Authority requirements. ~~authorization to access and release data and information shall be defined, and individuals authorized to enter, change, and release results shall be identified.~~

The committee edited standard 6.3.1.1 to mirror what occurs and what is expected in terms of confidentiality of records and who has access to them. This standard was crafted with assistance from the IT committee liaison to the CT SC.

6.3.4.3 The ability to retrieve data from the backup system shall be tested at **defined intervals** ~~periodically~~

The committee edited standard 6.3.4.3 for clarity and to ensure parallel structure with other standards.

7.2.1 Product Review, Investigation and Lookback
The facility shall have policies, processes, and procedures to identify nonconforming products and the initiation of a lookback investigation as soon as possible.

The committee created new standard 7.2.1 to mirror the language contained in the Standards for Blood Banks and Transfusion Services, understanding the need for facilities to perform lookback procedures in the case of a nonconformance.

7.2.1.2 Products identified as nonconforming following distribution shall be reported to the FDA or relevant Competent Authority in accordance with written policies, processes, and procedures.

F **7.2.1.3 Customers shall be notified when the nonconforming products can impact the purity, potency, safety or efficacy of the product.**

In conjunction with the creation of new standard 7.2.1, standards 7.2.1.2 and 7.2.1.3 were created to accompany the creation of new standard 7.2.1.

C 8.4 Monitoring Clinical Activities
Facilities performing clinical activities shall have a program that addresses, **evaluates**, and monitors patient care practices for all cellular therapies. The following shall be monitored:

The committee expanded standard 8.4 for completeness.

10.0 Safety and Facilities
The facility shall establish and maintain policies, processes, and procedures designed to minimize risks to the health and safety of employees, donors, patients, volunteers, and other persons affected within the work environment. Suitable quarters, environment, and equipment shall be available to maintain safe operations. **FDA or relevant Competent Authority or** ~~National, state,~~ local regulations apply. Standard 2.1.4 applies.

In line with other changes throughout the document to remove US centric terms, "national and state" to allow the standards to be as internationally friendly as possible.

Glossary

Bioassay: A measurement of the concentration of potency or a substance by its effect on living cells or tissues.

Cellular Therapy Products: Cell based products **that may be minimally or more than minimally manipulated, including cellular immunotherapies, regenerative medicines, and other types of autologous and allogeneic tissues or cells.** ~~(ie, stem or differentiated cells) that are procured from a donor and intended for manipulation and/or administration.~~

Cellular Starting Materials (CSM): Cellular therapy products that may be further modified through various techniques such as processing, selection, expansion, gene-editing, and other combinations of engineering for therapeutic benefit.

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

Chain of Identity (COI): 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.

Characterization: A cell's identity by the expression, or activity, of certain genes in its DNA and the resulting production of particular proteins.
Lookback: The process of reviewing and, if necessary, removing from inventory any product that is potentially infectious or nonconforming.

Patient: An individual undergoing medical ~~treatment~~ care. ~~In these *CT Standards*, a patient is an individual who may receive a cellular therapy product and related care.~~ The individual may also be a research subject.

Recipient: The patient receiving a cellular therapy product.

Risk Assessment: A process that results in a report that analyzes the potential for deviations or nonconformances to occur and the corrective and preventive actions to be taken to prevent or minimize risk.

Storage Device: A piece of equipment used to keep a product in the physical state of storage.

Subject Matter Expert: A person who is qualified, competent and experienced in a particular task or functional area.

The committee either edited the terms above or added new terms to the Glossary based on additions to the standards themselves and the need for update.

1. ORGANIZATION

*C*1.0 Organization

The cellular therapy facility shall have a structure that clearly defines and documents the responsibility, authority, and relationship(s) of personnel who perform, verify, or manage work covered by these *CT Standards*, including, but not limited to, cellular therapy product procurement, processing, storage, testing, distribution, and administration; medical management of donors and patients; determination of donor eligibility; and key quality functions.

1.1 Executive Management

Each facility shall define executive management. Executive management shall have responsibility and authority for the facility's operations, appointing a quality representative, performing management reviews, and compliance with these *CT Standards* and all applicable laws and regulations. Executive management shall have the authority to establish or make changes to the facility's quality and operational policies, processes, and procedures.

1.1.1 The facility shall demonstrate institutional support for the cellular therapy program.

1.1.2 The facility shall register for all applicable products and activities with the Food and Drug Administration (FDA) or relevant Competent Authority. When applicable, the facility shall obtain regulatory approval for all products and activities.

1.1.3 Procurement Facilities

The procurement medical director shall be a member of executive management and responsible for performing the determination of donor eligibility (or review of records related to donor eligibility if performed by another facility) and procurement of the product.

1.1.3.1 Procurement Medical Director

The procurement medical director(s) shall be a licensed physician with relevant experience, and qualified by training. The procurement medical director shall participate in continuing education relevant to the activities performed by the facility as required by these *CT Standards*. The procurement medical director(s) shall have responsibility and authority for medical activities related to the procurement of cellular therapy products and related services. When the medical director delegates these responsibilities to another qualified medical professional (designee), the medical director shall retain ultimate responsibility.

C **1.1.3.1.1** The procurement medical director shall have managed or reviewed a minimum of 10 cell product procurement procedures throughout the preceding 2-year accreditation cycle and have at least 1 year of experience in the scope of procurement activities performed by that facility.

1.1.4 Processing Facilities

The laboratory medical director and the laboratory director shall be members of the executive management and responsible for the processing, storage, and/or provision of the product.

1.1.4.1 Laboratory Medical Director

The laboratory medical director(s) shall be a licensed physician with relevant experience, and qualified by training. The processing laboratory medical director shall participate in continuing education in activities performed by the facility as required by these *CT Standards*. The laboratory medical director(s) shall have responsibility and authority for medical activities related to the processing, and provision of cellular therapy products and related services. When the medical director delegates these responsibilities to another qualified medical professional (designee), the medical director shall retain ultimate responsibility.

C **1.1.4.1.1** The laboratory medical director shall have managed or reviewed a minimum of 10 cell product processing procedures throughout the preceding two year accreditation cycle and have at least one year of experience in the scope of processing activities performed by the facility.

1.1.4.2 Laboratory Director

The facility shall have a laboratory director(s), with a relevant doctoral degree, with relevant experience, and who is qualified by training. The laboratory director shall participate in continuing education for the specific cellular therapy products being produced. The laboratory director shall be responsible for all technical aspects of the facility that are related to the processing, and provision of cellular therapy products, related services, and consultative and support services. When the laboratory director delegates these responsibilities to a designee, the laboratory director shall retain ultimate responsibility.

C **1.1.4.2.1** The laboratory director shall have managed or reviewed a minimum of 10 cell product processing procedures throughout the preceding 2-year accreditation cycle and have at least 1 year of

experience in the scope of processing activities performed by the facility.

1.1.4.3 In order for the laboratory director to also serve as laboratory medical director, the individual shall meet the requirements stated in Standards 1.1.4.1 and 1.1.4.2.

1.1.5 Clinical Program

1.1.5.1 Clinical Facility

The clinical program director shall be a member of the executive management and responsible for patient care and product administration.

1.1.5.2 Clinical Program Director

The clinical program director shall be a board-certified physician licensed to practice medicine in at least one specialty or subspecialty, who is qualified by training with relevant experience. The clinical program director shall participate in continuing education for the clinical activities performed by the facility. This individual shall be responsible for all aspects of the clinical program, including quality management and the selection and care of patients and donors.

C **1.1.5.2.1** The clinical program director shall have at least 1 year of experience. Relevant continuing education shall be obtained throughout the accreditation cycle in the scope of clinical activities performed in the facility.

1.1.5.3 Clinical Team

The clinical facility shall define who is a member of the clinical team. The team shall consist of at least one physician who is board certified in the appropriate subspecialty. The team shall have access to and consult with the appropriate medical and surgical specialties as well as other health-care disciplines.

1.2 Quality

1.2.1 Quality Policy

The facility's executive management shall define and document the facility's policy for achieving and maintaining quality in all activities covered by these *CT Standards*. The quality policy shall describe the facility's objectives for quality and its commitment to quality. The facility's executive management shall ensure

that this quality policy is understood, implemented, and followed at all levels of the organization.

✎*C* **1.2.2 Quality System**
The facility shall establish and maintain a quality system to ensure that activities related to donor and patient care as well as the procurement, processing, storage, testing, distribution, administration, and post-administration monitoring of cellular therapies conform to specified requirements.

1.2.3 Policies, Processes, and Procedures
The facility shall develop and implement quality and operational policies, processes, and procedures to ensure the requirements of these *CT Standards* are met. Standard 6.1.5 applies.

✎*C* **1.2.3.1** All policies, processes, and procedures shall be in writing or captured electronically and shall be followed.

1.2.3.1.1 Signatures of the individual approving all policies, processes, and procedures shall comply with the requirements of the FDA or relevant Competent Authority.

✎*C* **1.2.3.2** The procurement medical director shall review and approve all procurement policies, processes, and procedures.

✎*C* **1.2.3.3** The laboratory medical director shall review and approve all medical laboratory policies, processes, and procedures.

✎*C* **1.2.3.4** The laboratory director shall review and approve all technical laboratory policies, processes, and procedures.

✎*C* **1.2.3.5** The clinical program director shall review and approve all clinical policies, processes, and procedures related to administration and patient care.

1.2.3.6 All exceptions to policies, processes, and procedures warranted shall require justification and preapproval by the procurement medical director, the laboratory medical director, the laboratory director, the clinical program director and/or the patient's physician, depending upon the circumstances.
Chapter 7, Deviations, Nonconforming Products or Services and Adverse Events, applies.

1.2.4 Quality Representative

The facility's executive management shall appoint a member of management who is qualified by training with relevant experience in quality management systems. The quality representative shall have defined independent authority for ensuring that the facility establishes, implements, and maintains a quality system that meets the requirements of these *CT Standards*. When the quality representative delegates these responsibilities to a designee, the quality representative shall retain ultimate responsibility.

✎*C* **1.2.4.1** This individual shall report to executive management at least quarterly on quality system activities and to other staff as appropriate.

✎*C* **1.2.4.2** These reports shall be used for management review and improvement of the quality system.

✎*C* **1.2.5 Executive Management Review**

The facility's executive management shall review the quality system on an annual scheduled basis to ensure that the system meets the requirements of these *CT Standards*.

✎*C***1.3 Emergency Operation Plans**

The facility's executive management shall ensure the facility has emergency operation plans to respond to the effects of internal and external disasters and other emergencies.

1.3.1 The emergency management plan shall be tested at defined intervals.

1.4 Operational Continuity

Executive management shall ensure that the facility has policies, processes and procedures that address continuity in the event that operations are at risk.

1.4.1 The facility shall have a policy to address critical supply shortages.

✎*C***1.5 Risk Assessment**

The facility's executive management shall ensure there is a process to identify, assess, and address the level of risk associated with activities performed in the facility that affect product quality and safety. Standards 5.2.1 and 6.1.5 apply.

1.5.1 Mitigation strategies shall identify, assess, and address the level of risk associated with activities performed in the facility.

1.6 Communication of Concerns

The facility's executive management shall ensure the facility has a process whereby individuals can anonymously communicate concerns about quality or safety. Contact information for executive management and AABB shall be readily available to staff.

1.7 Customer Focus

Executive management shall identify the facility's customers and their needs and expectations for products and services. Chapter 4, Agreements, applies.

1.8 Human Subjects Research

Executive management shall ensure that the applicable laws and regulations concerning research on human subjects, as well as any requirements stipulated by the facility's independent ethics committee are followed.

1.8.1 Executive management shall ensure that the design of research protocols prevents conflicts of interest that interfere with recipient care.

1.8.2 Executive management shall ensure that reviews or audits of the research design are performed at defined intervals.

2. RESOURCES

2.0 Resources

The facility shall identify and provide adequate staffing, materials, equipment, and facility infrastructure to perform, verify, and manage all activities covered by these *CT Standards*.

2.1 Human Resources

The facility shall have a process to ensure that there is an adequate number of qualified individuals.

C **2.1.1 Job Qualifications**

The facility shall identify qualifications for each job position on the basis of education, training, and experience.

C **2.1.2 Personnel Identification**

Records of names, signatures, initials or identification codes, and inclusive dates of employment shall be maintained.

C **2.1.3 Job Descriptions**

The facility shall establish and maintain job descriptions defining the roles and responsibilities for each job position related to the requirements of these *CT Standards*.

C **2.1.4 Training**

The facility shall establish and maintain policies, processes, and procedures for:

5) Orientation,
6) Initial job specific training,
7) Quality-systems-related training, and
8) Ongoing job-specific training.

2.1.4.1 The facility shall define the qualifications and approve subject matter experts who provide training.

F **2.1.5 Personnel Records**

Personnel records for each employee shall be maintained.

C **2.1.6 Competence**

Evaluations of competence shall be performed before independent performance of assigned activities.

2.1.6.1 Competence shall be evaluated annually for defined tasks and activities.*

*42 CFR 493.1413(b)(8), 42 CFR 493.1451(b)(8)

2.1.6.2 For individuals who perform moderate and high complexity testing, semi-annual reviews of competence shall be performed in their first year of employment. For facilities located in the United States, 42 CFR 493.1413(b)(9), and 42 CFR 493.1451(b)(9) apply.

2.1.6.3 Competence shall be assessed when new or novel processes or procedures are introduced. Standard 5.2.3 applies.

C **2.1.6.4** Corrective action shall be taken when competence has not been demonstrated.

C **2.1.7 Continuing Education**

Requirements for relevant continuing education in activities performed by the facility as required by these *CT Standards* shall be defined for and met by all employees who perform critical tasks.

2.1.7.1 The facility shall ensure that the medical, laboratory, procurement, and clinical program directors, and the quality representative, annually complete 10 hours of educational activities relevant to the role and the associated cellular therapy activity or activities performed in the facility*. Standards 1.1.3.1, 1.1.4.1, 1.1.4.2, and 1.1.5.2 apply.

*42 CFR 493.1413(b)(8) and 42 CFR 493.1451(b)(8).

2.2 Access to Ancillary Services and Direct Patient Care

The clinical facility shall have an agreement in place to ensure comprehensive care and relevant resources required for patient care in cellular therapies, including but not limited to:

8) Transfusion medicine
9) Services related to pharmacy.
10) Radiology.
11) Laboratory services.
12) Acute care or medical facilities.
13) Social and psychological support.
14) Long term follow-up based on protocol or treatment plan.

3. EQUIPMENT

3.0 Equipment

The facility shall establish and maintain policies, processes, and procedures to identify, control, operate, maintain, and monitor critical equipment.

3.1 Equipment Specifications and Selection

Equipment specifications shall be defined before selection and purchase.

F 3.2 Qualification of Equipment

All critical equipment shall be qualified for its intended use. Equipment repairs and upgrades shall be evaluated and equipment requalified, as appropriate, based on the facility's policies, equipment maintenance or repair reports and manufacturer's written instructions.

3.2.1 Installation Qualification

Equipment shall be installed per the manufacturer's specifications.

3.2.2 Operational Qualification

The functionality of each piece of equipment and each component of an information system shall be verified before actual use and shall meet the manufacturer's operational specifications.

3.2.3 Performance Qualification

The facility shall demonstrate that equipment performs as expected for its intended use per facility developed predetermined criteria. Facility developed predetermined criteria shall meet or exceed the specifications established by the manufacturer.

3.3 Use of Equipment

Equipment shall be used in accordance with the manufacturer's written instructions.

3.4 Equipment Monitoring and Maintenance

The facility shall have a process for scheduled monitoring and maintenance of equipment thatis in accordance with manufacturer's written instructions and in accordance with the FDA or relevant Competent Authority.

F 3.4.1 Calibration and Accuracy of Equipment

The facility shall:

1) Identify equipment that is to be maintained in a calibrated state.

2) Determine the measurements to be made and the accuracy and precision required.
3) Define the process for the calibration of equipment, including details of equipment type, unique identification, location, frequency of checks, check method, acceptance criteria, and limitations.
4) Calibrate equipment used for inspection, measuring, and testing before initial use, after repair, and at prescribed intervals, using equipment certified to meet nationally recognized measurement standards. Where no such measurement standards exist, the basis for calibration shall be described and recorded.
5) Safeguard equipment from adjustments that would invalidate the calibration setting.

F **3.4.2** There shall be a defined process when equipment is found to be out of calibration or specification. When equipment is found to be out of calibration or specification, the validity of previous inspection and test results and the conformance of provided cellular therapy products and services to the required specifications shall be assessed. Chapter 7, Deviations, Nonconforming Products or Services and Adverse Events, applies.

F **3.4.3 Monitoring, Maintenance, and Repair**

The facility shall:

1) Define cleaning and sanitization methods and intervals for each piece of equipment.
2) Ensure that environmental conditions are suitable for the calibrations, inspections, measurements, and tests carried out.
3) Define a process to inform personnel when equipment is malfunctioning/out of service.
4) Monitor equipment to ensure that defined parameters are maintained.
5) Ensure that the handling, maintenance, and storage of equipment are such that the equipment remains fit for use.
6) Ensure that all critical equipment maintenance and repairs are performed by qualified individuals and in accordance with manufacturer's written instructions.

Standard 3.2 applies.

F **3.5 Equipment Traceability**

The facility shall maintain records of equipment use in a manner that permits:

1) Equipment to be uniquely identified and traceable.
2) Tracing of any given cellular therapy product to all equipment associated with the procurement, processing, storage, distribution, and administration of the cellular therapy product.

3) Identification and recall of all cellular therapy products associated with a specific piece of equipment.

F 3.6 Information Systems

Implementation and modification of information system software, hardware, and databases shall be planned and controlled. Elements of planning and ongoing control shall include:

1) Designation of system versions with inclusive dates of use.
2) Validation/verification of system software, hardware, databases, and user-defined tables prior to implementation.
3) Fulfillment of life-cycle requirements for internally developed software.
4) Defined processes for system operation and maintenance.
5) Defined process for authorizing and documenting modifications to the system.
6) System security to prevent unauthorized access.
7) Policies, processes, and procedures and other instructional documents developed using terminology that is understandable to the user.
8) Functionality that allows for display and verification of data before final acceptance of the additions or alterations.
9) Defined process for monitoring of data integrity for critical data elements.
10) System design that establishes and maintains unique identity of donor, product, and recipient (as applicable).
11) Training and competency of personnel who use information systems.
12) Procedures to ensure confidentiality of protected health information.

3.6.1 Alternative Systems

The facility shall have validated alternative systems to ensure access to critical information and continuous operation of critical activities in the event that electronic data and information system-assisted functions are not available.

F **3.6.1.1** The alternative systems shall be verified at facility-defined intervals.

3.6.2 A process shall be in place to ensure that the facility has measures to minimize the risk of internal and external data breach.

4. AGREEMENTS

4.0 Agreements

The facility shall establish, implement, and maintain policies, processes, and procedures for developing, approving, and reviewing agreements.

✎C4.1 Agreement Review

When the responsibilities for activities covered by these *CT Standards* involve more than one facility, there shall be agreements that define the following for the cellular therapy product from point of origin to administration including but not limited to:

4.1.1 Before acceptance of a documented verbal or written agreement, the agreement shall be reviewed by the facility or department to ensure that:

1) The customer's requirements are adequately defined in compliance with these *CT Standards* and in accordance with applicable FDA or relevant Competent Authority requirements.
2) Any differences between the agreement requirements and the cellular therapy products or services offered under the agreement are resolved.
3) The facility has the capability to meet the requirements detailed in the agreement.
4) Chain of Identity is from point of origin to point of administration or discard,
5) Chain of Custody is from point of origin to point of administration or discard,
6) Quality is maintained from the point of origin to the point of administration or discard.
7) Conformance with accepted policies and procedures.
8) Conformance with safety requirements.

4.1.2 Agreements shall define and describe the following:

4.1.2.1 Roles and responsibilities of personnel. Standards 1.2.4, 5.14.1 and 5.17.1 apply.

4.1.2.2 Roles and responsibilities of each facility involved in the procurement, processing, labeling, storage, distribution, or administration of a cellular therapy product to maintain Chain of Identity and Chain of Custody.

4.1.2.3 Communication of critical information, including deviations, nonconformances and adverse events. Standard 5.7 applies.

4.1.2.4 Reporting of adverse events and nonconformances to regulatory bodies, Competent Authorities, and registries, if applicable.

4.1.2.5 Specifications and requirements for donor and patient care, quality, safety, and other facility defined critical parameters.

4.1.3 Agreements shall be reviewed at defined intervals to ensure that the terms of the agreement continue to meet requirements.

***C*4.2 Changes to Agreements**

The facility shall define how changes to agreements are proposed, accepted and communicated to affected parties.

4.3 Agreements Relating to Cellular Therapy Products, Materials, and Services

When the responsibilities for activities covered by these *CT Standards* involve more than one facility or department, there shall be agreements that define the following for the cellular therapy product from point of origin to administration including but not limited to:

F **4.3.1 Medical Authorization for Procurement and Processing**

The facility shall have medical authorization for procurement and processing of cellular therapy products except where the recipient is unknown and the procurement of the product is non invasive:

1) Responsibility of the procuring facility to obtain a medical order before the procurement procedure.
2) Responsibility of the processing facility to obtain a medical order before the processing procedure, if applicable.
3) Responsibility for the clinical facility to provide the medical order for procurement or processing.

Standards 5.14.1 and 5.17.1 apply.

4.3.2 Medical Authorization for Distribution

The facility shall ensure that agreements define the following:

1) Responsibility for the distributing facility to obtain a medical order before distribution.
2) Responsibility for the receiving facility to provide a medical order for distribution.

F **4.3.3 Transfer of Products**

When products are transferred between departments or facilities, the following items shall be defined:

1) Responsibility for maintaining chain of identity during transfer.

2) Responsibility for maintaining chain of custody during transfer.
3) Timing of product delivery and administration.
4) Agreement by all parties to provide the necessary documentation including timing of:
a. mobilization,
b. procurement, and
c. recipient conditioning, as applicable.

✎*F* **4.3.4 Instructions**

When products are transferred between departments or facilities, the following items shall be provided:

1) Instructions for collection, transport, receipt, handling, and administration of the cellular therapy product(s).
2) Instructions for reporting adverse events to the issuing facility and other parties.
3) Instructions for obtaining recipient postinfusion outcome data.

✎*C* **4.3.5 Records**

When products are transferred between departments or facilities, the following items shall be defined:

1) Responsibility of the administering facility or registry for the creation and retention of records listed in Standards 5.3 through 5.3.4.1.
2) Responsibilities of each facility involved in the procurement, processing, labeling, storage, distribution, or administration of a cellular therapy product to provide records in a timely manner upon request. Standard 5.7 applies.

✎*C* **4.3.6 Supplier Qualification**

When cellular therapy product services involve more than one facility, each facility shall be qualified to perform the scope of activities defined in the agreement in accordance with these *CT Standards*.

✎*C* **4.3.7 Conditions for Product Storage and Disposition**

When products are transferred between departments or facilities, the following conditions shall be defined:

1) Maintenance of Chain of Identity.
2) Maintenance of Chain of Custody.
3) Terms and lengths of storage.
4) Possible transfer to another facility.
5) Disposition of the cellular therapy product, including discard.

4.3.8 Information about Product Administration

When products are transferred between departments or facilities, the following items shall be obtained:

1) Summary record of cellular therapy product administration.
2) Summary of adverse events suspected to be linked to the cellular therapy product. Standard 7.3 applies.

✎*F* **4.3.9 International Requests for Cellular Therapy Products**

When products are shipped or transported, the following shall be obtained:

1) Before shipment or transport, verification by the shipping facility that its local and FDA or relevant Competent Authority requirements for cellular therapy product manufacture and export have been met.
2) Before shipment or transport, verification by the receiving facility or registry that its local and FDA or relevant Competent Authority requirements for intended use of the cellular therapy products are met.
3) Agreement by all parties to exchange/provide the necessary documentation to meet export/import requirements.

✎*F* **4.4 Educational and Promotional Materials**

The facility shall maintain records justifying claims made in its educational and promotional materials.

4.4.1 Therapeutic and scientific claims in educational and promotional materials shall comply with applicable regulations and be approved by the medical director.

4.4.2 Therapeutic and scientific claims shall not promote or advertise experimental cellular therapies for administration outside the context of an independent ethics committee-approved protocol.

✎*F* **4.5 Donor Informed Consent**

Informed consent of donors shall be obtained in conformance with Reference Standard 4.5A, Donor Informed Consent or Authorization.*

*21 CFR Part 11

4.5.1 Donor informed consent templates shall be reviewed at defined intervals and updated as needed and approved by the current medical director of the facility responsible for obtaining informed consent.

4.5.2 Informed consent from the donor or a legally authorized representative shall be obtained (or initiated, for cord blood or gestational materials) before the procurement of cells, tissues, or organs from the donor.

4.5.2.1 There shall be a process to identify vulnerable donor populations that require a donor advocate to address informed consent issues.

4.5.2.2 There shall be a process to provide a qualified interpreter when required and/or when applicable.

4.5.3 The terms and length of storage, the possible transfer to another facility, and the disposition, including discard of the cellular therapy product, shall be addressed with:

1) The donor (or other consenters, including the donor's legally authorized representative, or, in the case of cord blood or gestational materials, the birth mother, biologic mother, and, where applicable, surrogate mother).
2) If known, the intended recipient and the recipient's physician.

✎*F*4.6 Authorization for Cadaveric Donors

Authorization of donors shall be obtained in conformance with Reference Standard 4.5A, Donor Informed Consent or Authorization.

4.6.1 Any authorization templates shall be reviewed at defined intervals and updated as needed and approved by the current medical director of the facility responsible for obtaining authorization.

4.6.2 The legal record of authorization shall be obtained before the procurement of cells, tissues, or organs from the donor.

4.6.3 The terms and length of storage, the possible transfer to another facility, and the disposition, including discard, of the cellular therapy product shall be addressed with:

1) The donor's legally authorized representative.
2) If known, the intended recipient and the recipient's physician.

✎*F*4.7 Patient Informed Consent

Informed consent for patients receiving cellular therapy treatment and administration of products shall be obtained in conformance with Reference Standard 4.7A, Patient Informed Consent.

4.7.1 Patient informed consent templates shall be reviewed at defined intervals and updated as needed and approved by the current medical director of the facility responsible for obtaining informed consent.

4.7.2 The informed consent process for administration of products under research protocols shall be approved by an independent ethics committee.

4.7.3 Informed consent from the patient shall be obtained before the start of any preparative therapy.

4.8 Obtaining Materials, Services, and Cellular Therapy Products

The facility shall establish and maintain policies, processes, and procedures to ensure that purchased, donated, or otherwise acquired materials, services, or cellular therapy products conform to specified requirements.

F **4.8.1 Evaluation and Qualification of Suppliers of Materials and Services**

The facility shall ensure that suppliers of critical materials or services are qualified and selected based on the supplier's ability to meet specified requirements, including the following:

1) Ensure that training and qualifications of personnel who perform activities related to the provision of materials and/or services are addressed.
2) Ensure that facilities providing tests or manufacturing services required by these *CT Standards* shall be accredited by AABB or another accrediting body.

4.8.1.1 The facility shall review package inserts for all infectious disease test reagents, sample requirements and kits to verify they are approved for their intended use in testing of cellular therapy products. Standards 5.12.2.6 and 5.12.2.10 apply.

F **4.8.2 Evaluation and Qualification of Suppliers of Cellular Therapy Products**

The facility shall ensure that suppliers of cellular therapy products are qualified and selected based on the facility's ability to meet the following requirements:

1) Ensure that the source facility is authorized, designated, licensed, registered, and/or accredited.
2) Ensure that specified product procurement requirements are met when these activities are performed by a supplier.
3) Ensure that training and qualifications of personnel who perform activities related to the supply of cellular therapy products are addressed.
4) Ensure that facilities providing cellular therapy products are accredited by AABB or other accrediting body.

F **4.8.3 Monitoring of Suppliers of Materials, Services, and Cellular Therapy Products**

The facility shall:

1) Monitor the performance of critical suppliers as needed based on the nature of the material, service, or product and the impact on the quality of the cellular therapy product.
2) Take corrective action and report to management when a supplier fails to meet specified requirements. Standard 9.1 applies.

C **4.8.4 Notification**

The agreement between the receiving facility and the supplier shall include a process to notify the shipping facility and the manufacturer (if applicable) when materials are received in an unacceptable condition. Chapter 7, Deviations, Nonconforming Products or Services, and Adverse Events, applies.

Reference Standard 4.5A—Donor Informed Consent or Authorization

The informed consent process for donors or their legally authorized representative shall include an explanation, in understandable terms, to the consenter(s), of any applicable risks, discomforts, benefits, and alternatives. Elements of informed consent shall include the following:

I. General Informed Consent

A. Description of participation, including:
   1. The consenter's rights as a donor and, where applicable, as a research subject.
   2. Cellular procurement procedure, including, but not limited to, risks associated with procurement and side effects of growth factors and/or other pharmacologic agents, if applicable.
   3. General explanation of the indications for and expected outcome of cellular procurement, including the possibility of future product procurement, if applicable.
   4. Specimen procurement and storage for possible future testing.
   5. Intended use for manufacture or manipulation, including storage, in-vitro manipulation, and analysis.
   6. Testing for infectious diseases and genetic disorders or other conditions, as indicated.
   7. Notification of abnormal test results.
   8. Review of medical history.
   9. Review of medical records.
   10. Description of confidentiality, including the need for disclosure to other entities of personal and family health information that might affect the intended recipient.
   11. Ownership, transfer, and/or disposition of the cellular therapy product.
   12. Financial or other incentives for donation of cellular therapy products.

B. The consenter(s) shall acknowledge in writing that they have received information concerning the risks, benefits, discomforts, and alternatives to human cellular therapy product donation; that they have had an opportunity to have access to donor advocacy and translation services; that they have been given the opportunity to ask questions and had those questions answered satisfactorily; and that they have been given a written copy of contact information for future questions related to cellular therapy product donation.

C. The informed consent process shall conform to all applicable law(s).

D. Informed consent requirements and regulations that apply to donors who are noncompetent persons or persons who may temporarily lack decisional capacity shall be met.

E. The consenter(s) shall have the opportunity to deny or withdraw consent to the procurement procedures at any time without affecting their access to medical care. Information regarding consequences to the recipient if the donor chooses to withdraw consent, particularly after the initiation of preparative regimen, shall be discussed.

F. The person presenting information and/or answering questions during informed consent shall be a health-care professional who is knowledgeable about the cellular therapy procedure.

G. The facility shall have a policy to identify and disclose potential conflicts of interest in the donor informed consent process.

II. Additional Informed Consent for Cord Blood and Gestational Material Consenters (Allogeneic and Autologous)

A. Informed consent for procurement shall be obtained from the mother or a legally authorized representative before the mother is in active labor.

B. Consent for banking shall be obtained before or within 48 hours after procurement.

C. The consenter(s) shall agree to provide information related to the biologic family's medical and genetic history.

D. The consenter(s) shall agree to provide information to the cord blood bank if the neonatal donor later develops a disease that may pose a risk to a recipient.

III. Authorization for Cadaveric Donors

A. Authorization to procure tissues and make them available for transplantation, therapy, research, or education shall occur in accordance with applicable laws or regulations.

B. Authorization shall be expressed in either of two ways:
1) Document of gift made prior to death such as in a donation registry or other legally acceptable method that produces a record; or
2) Document of authorization from the person, other than the donor, who is authorized by law to make an anatomical gift.

C. The original document or a copy shall be maintained in the donor's record at the organization responsible for procurement, as well as in the donor record at the organization responsible for determination of medical suitability and eligibility.

Reference Standard 4.7A—Patient Informed Consent

The informed consent process for patients shall include an explanation, in understandable terms, to the patient or legally authorized representative, of any applicable risks, discomforts, benefits, and alternatives to cellular therapy. Elements of informed consent shall include the following:

I. General Informed Consent

A. Description of participation, including:
   1. The individual's rights as a patient and, where applicable, as a research subject.
   2. Risks associated with the selected medical interventions, including the administration of cellular therapy products and side effects of drugs and other treatment that is part of the preparative regimen.
   3. General explanation of the indications for, and expected outcome of, cellular therapy.
   4. Discussion of confidentiality, including the need for disclosure to other entities of personal and family health information.

B. The patient shall acknowledge in writing that they have received information concerning the risks, benefits, discomforts, and alternatives to the selected medical interventions; that they have had the opportunity to deny or withdraw consent to the treatment at any time without affecting their access to medical care; that they have had an opportunity to have access to patient and translation advocacy services; and that they have been given the opportunity to ask questions and had those questions answered satisfactorily.

C. The informed consent process shall conform to all applicable law(s).

D. Informed consent requirements and regulations that apply to patients who are noncompetent persons or persons who may temporarily lack decisional capacity shall be met.

E. The person presenting information and/or answering patient questions during informed consent shall be a health-care professional who is knowledgeable about the cellular therapy procedure.

F. The facility shall have a policy to identify and disclose of potential conflicts of interest in the patient informed consent process.

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5. PROCESS CONTROL

5.0 Process Control

The facility shall identify, design, modify, and validate the policies, processes, and procedures that affect the quality of cellular therapy products, services, and patient care.

5.1 General Elements

The facility shall ensure that these policies, processes, and procedures are carried out under controlled conditions that are designed to optimize donor, product, and recipient safety. Controlled conditions shall include:

1) Use of approved policies, processes, and procedures for donor and recipient care activities, products, and services.
2) Compliance with policies, processes, and procedures and external standards. Chapter 7, Deviations, Nonconforming Products or Services, and Adverse Events, applies.
3) Performance by qualified, trained, and competent staff.
4) Use and control of suitable equipment, materials, and working environments.

5.1.1 Processing facilities shall have policies, processes, and procedures designed to prevent contamination of cellular therapy products; maintain the cellular therapy product's identity, function, safety, purity and potency, and integrity; and prevent the transmission of infectious disease. These shall include:

1) Defining criteria for acceptable results of in-process tests and final cellular therapy product characteristics.
2) Monitoring and control of suitable process parameters and cellular therapy product characteristics.
3) Use of statistical techniques required for establishing, controlling, and verifying process requirements and product characteristics.

C **5.1.2 Proficiency Testing**

The facility shall participate in an external proficiency testing program for each analyte measured by the laboratory. Proficiency testing for each analyte shall be performed at least twice a year.

5.1.2.1 For each analyte requiring proficiency testing under Clinical Laboratory Improvement Amendments (CLIA)*, each laboratory shall participate in a Centers for Medicare and Medicaid Services (CMS) approved proficiency testing program.

*42 CFR 493.801

5.1.2.2 In the absence of an approved external proficiency testing program, proficiency testing shall include comparison of test results from an outside laboratory.

✎*C* **5.1.2.3** Proficiency testing results shall be reviewed by the medical or laboratory director or designee.*

*42 CFR 493.1236

5.1.2.3.1 Proficiency testing shall be successful. Failures shall be investigated and corrective actions taken.*

*42 CFR 493.803 and 42 CFR 493.1236(b)

✎*C***5.2 Process and Procedure Development and Change**

The development of new or changed processes and procedures shall be controlled.

5.2.1 Change Control

The facility shall identify the reasons for a change and obtain the appropriate approval(s) before implementation. Any changes that may affect the safety of the recipient or the identity, purity, potency, integrity, safety or efficacy of the cellular therapy product shall be validated before the change is implemented.

5.2.2 Process Planning

Quality requirements shall be incorporated into the development of new or changed processes, products, services, and novel methods. Standard 4.0 applies. Planning and implementation activities at a minimum shall include the following:

1) Evaluation of accreditation, regulatory, and legal requirements related to the new or changed process, product, or service.
2) Review of current available knowledge (eg, review of medical practice and literature).
3) Evaluation of risk vs benefit.
4) Identification of affected internal and external parties and mechanism to communicate relevant information.
5) Identification of performance measures as applicable to the new or changed process, product, or service.
6) Evaluation of resource requirements.
7) Evaluation of the impact of the new or changed process, product, or service on other facility (or program) processes. Standard 2.1.4 and 10.0 apply.

8) Evaluation of the need to create or revise documents for the new or changed process, product, or service.
9) Review and approval of the output of process development and design activities (eg, pilot or scale-up study results, process flow charts, procedures, data forms).
10) Evaluation of the extent and scope of process validation or revalidation depending on the level of risk and impact of the new or changed products or services.

5.2.3 Process Validation

Before implementation, the new or changed processes and procedures (including novel methods and those affecting equipment and information system use) shall be validated.

5.2.3.1 Validation activities at a minimum shall include the following:
1) Identification of goals, individual(s) responsible, expected outcomes, and/or performance measures.
2) Criteria for review of outcomes.
3) Approval of validation plan.
4) Review and approval of actual results.
5) Actions to be taken if goals are not met.

Standards 2.1.4 and 2.1.6 apply.

5.2.4 Process Implementation

The implementation of new or changed processes and procedures shall be planned and controlled.

5.2.4.1 Postimplementation evaluations of new or changed processes and procedures shall be performed.

***F*5.3 Outcomes Data**

The facilities shall have a program to obtain, audit, and monitor clinical outcomes of cellular therapy products at defined intervals. Standard 5.30 applies.

5.3.1 For the procurement and processing facilities, this shall include but is not limited to adverse events and complications attributed to procurement, processing, infusion, and/or engraftment, as applicable.

5.3.2 For the clinical facility, this shall include the clinical outcomes as specified by the clinical protocols and as applicable:
1) Mortality and survival rates.
2) Disease status and/or relapse.

3) Adverse events and complications.
4) Disease modifying activity.
5) Engraftment.
6) Immune effector cell endpoints.
7) Hematopoietic reconstitution.
8) Monitoring of patient safety

5.3.2.1 The clinical facility shall determine the criteria for cellular therapy product safety, product efficacy, and/or clinical outcomes data and collect this data for analysis at defined intervals.

5.3.3 For facilities that procure, process or administer investigational products, there shall be a process for recording and monitoring patient safety and reviewing clinical outcomes as specified by the independent ethics committee-approved protocol(s).

5.3.4 The sharing and review of data shall be defined. Chapter 7, Deviations, Nonconforming Products or Services, and Adverse Events, applies. Standard 4.3 applies.

✎***F*** **5.3.4.1** There shall be defined processes and procedures for the issuing facility and/or product manufacturer to obtain information on adverse events and patient outcomes appropriate for each cell type.

✎***C*****5.4Quality Control**

The facility shall establish a program of quality control that is sufficiently comprehensive to ensure that materials including supplies, reagents and equipmentfunction as specified.

5.4.1 Quality control results shall be reviewed and evaluated against acceptance criteria. Quality control failures shall be investigated before release of test results, products, or services.

5.4.2 The validity of test results and methods and the acceptability of products or services provided shall be evaluated when quality control failures occur.

✎***C*****5.5Materials Management**

There shall be policies, processes, and procedures for the qualification, receipt, handling, storage, and utilization of all materials used in the procurement, processing, and administration of cellular therapy products. Critical materials shall be identified and traceable.

5.5.1 All critical materials, including containers and solutions used for collection, processing, preservation, and storage of cellular therapy products, and all reagents used for tests, shall be stored and used in accordance with the manufacturer's written instructions and shall meet specified requirements.

5.5.2 Receipt of Materials

The facility shall ensure that incoming materials that come into contact with the patient or cellular therapy product or that directly affect the quality of a cellular therapy product are not used until they have been inspected or otherwise verified as conforming to requirements. Standard 4.8 applies.

C **5.5.2.1** Records of the following shall be maintained:

1) Identification of the material.
2) Name of the manufacturer.
3) Lot number.
4) Date of receipt.
5) Date of manufacture and/or expiration date.
6) Results of visual inspection upon receipt, if applicable.
7) Identity of the person receiving the material, if applicable.
8) Indication of acceptance or rejection.
9) Identity of the person determining acceptance or rejection of the material.
10) Certificate of Analysis, manufacturer's insert, or equivalent, if applicable.
11) Quantity.

C **5.5.2.2 Emergency Use of Material**

When a material is used on an emergency basis (before final acceptance), the material shall be identified to permit recall and quarantine of associated products. Standard 7.1 applies.

5.5.3 Qualification of Critical Materials

Materials that come into contact with the patient or cellular therapy product shall be sterile and of appropriate grade for the intended use and shall be approved for human use by the United States FDA or relevant Competent Authority.

5.5.3.1 Materials that are not approved for human use by the FDA or relevant Competent Authority shall be qualified on the basis of one or more of the following criteria:

1) Medical literature supporting the use of the material for the specified purpose.
2) Approval by the facility's independent ethics committee.
3) Investigational new drug (IND) or device approval for the specific

material and indication, as permitted by the FDA or relevant Competent Authority.

5.5.3.1.1 The facility shall perform testing to ensure suitability of the material for its intended use.

✎*C* **5.5.4** Reagents prepared in-house shall be produced using a validated method. Such reagents shall be inspected before release. Standards 5.5.2.1, 5.5.5, and 5.5.6 apply.

✎*C* **5.5.5 Utilization**
Non-single-use materials that come into contact with the patient or cellular therapy products during procurement, processing, or administration shall be cleaned and sterilized. Sterilization methods shall be validated and monitored.

✎*F* **5.5.6** Use of critical materials shall be recorded in a manner that ensures complete and accurate traceability of any given cellular therapy product to all critical materials that come into contact with the patient or cellular therapy product. Chapter 7, Deviations, Nonconforming Products or Services, and Adverse Events, applies.

✎*C* **5.5.6.1** For all critical materials used, records of the following shall be retained:

1) The manufacturer's package insert, if applicable.
2) Certificates of Analysis or equivalent, as defined by the facility's qualification program.
3) Any manufacturer's documentation, including recall or defect notices, advisories, and other communications related to material usage.

5.6 Methods and Operational Controls

5.6.1 Cellular Therapy Product Manipulation

Policies, processes, and procedures used during cellular therapy product manipulation shall address the following:

1) Staff attire, gowning, and use of personal protective equipment.
2) Use of biologic safety cabinets or other environmentally controlled spaces, if applicable.
3) Materials and equipment for each specific process.
4) Manipulation of materials.
5) Critical calculations.
6) Transfer of source material, cellular therapy products, media, or reagents between containers.
7) Sampling of source material, cellular therapy products, media, reagents, or other materials used in product manipulation.

8) Acceptable control limits for temperature, humidity, and gases such as oxygen and CO_2, if applicable.
9) Disposition of cellular therapy by-products and waste.

5.6.2 Aseptic Methods

Procurement, processing, and clinical facilities shall establish and maintain policies, processes, and procedures designed to minimize contamination of the product and infection of the donor or recipient. The following shall be addressed:

1) Environmental controls and monitoring commensurate with the risk of product contamination.
2) Process controls.
3) Staff training in aseptic technique.
4) Attire, gowning, and use of personal protective equipment.
5) Workflow and movement of personnel through workspaces.

C **5.6.2.1** The effectiveness of such measures shall be monitored and reviewed at defined intervals.

5.6.3 Operational Controls

Operational controls shall prevent mix-ups and contamination. The following shall be defined:

1) Movement and storage of materials (including waste) and equipment within workspaces.
2) Physical and/or temporal segregation of equipment or materials.
3) Physical and/or temporal segregation for processing different cellular therapy products or cellular therapy product lots.
4) Use and storage of materials that may adversely affect the quality of the cellular therapy product.
5) Cleaning and setup of spaces and equipment between production runs.
6) Labeling processes.
7) Clerical identification checks at critical steps.

Chapter 7, Deviations, Nonconforming Products or Services, and Adverse Events, applies.

5.6.4 Irradiation and Leukocyte Reduction

Policies, processes, and procedures shall be in place regarding irradiation or leukocyte reduction of cellular therapy products.

5.6.4.1 Methods shall be in place to prevent unintentional irradiation or leukocyte reduction (eg, filtration) of cellular therapy products. Reference Standard 5.8.2A, Requirements for Labeling of Cellular Therapy Products, applies.

5.7 Product Identification and Traceability

The facility shall establish and maintain policies, processes, and procedures that ensure the chain of identity and chain of custody for identification and traceability of each cellular therapy product and all related samples from their initial source, through all processing and testing steps, to their final disposition. Policies, processes, and procedures shall also allow the identification and traceability of each cellular therapy product and all related samples from their final disposition, through all processing and/or testing steps, to their source.

✎C 5.7.1 Traceability and Unique Identification

A numeric or alphanumeric system shall be used that will make it possible to trace any cellular therapy product or sample from donor/source to recipient/final disposition and back to the donor/source and to review records applying to the specific cellular therapy product or sample, including those related to reported adverse events. Unique identifiers shall not be obscured, altered, or removed.

5.7.1.1 Unique Identification of Intermediate Facility

If an intermediate facility assigns a local, unique, numeric, or alphanumeric identification to the cellular therapy product, the label shall be affixed to the cellular therapy product and shall identify the facility assigning the identification and shall be traceable to the original cellular therapy product.

5.7.1.2 Special Requirements for Pooled Cellular Therapy Products or Combined Products

Where pooling or combining of cellular therapy products is permissible, there shall be a procedure to ensure traceability of all cellular therapy products in a pool, and the (quantitative) contribution of each product to the final cellular therapy product.

5.7.1.3 Sample Traceability

Samples from donors, products, and recipients shall be labeled in a manner to ensure traceability of the sample to its source.

5.8 Labels, Labeling, and Labeling Controls

The facility shall have policies, processes, and procedures for labels and labeling of products and samples^. At a minimum, they shall address:

1) The acquisition and creation of cellular therapy product label templates.
✎C 2) Verification that the label stock meets facility-defined specifications.
✎C 3) The qualification, review, and approval of labels before use. Standard 6.1.2 applies.
4) The controls in place to ensure proper cellular therapy product identification.
✎C 5) The control of label inventory and templates, including discard. Chapter 6,

Documents and Records, applies.

Standard 1.1.2 applies.

^21 CFR 1271.10(a)(2)

FDA Guidance, July 21, 2020, "Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use."

✎*C* **5.8.1** Cellular therapy products shall be labeled in conformance with the current versions of ISBT 128 or Eurocode labeling.* Standard 5.7 applies.

*http://www.isbt128.org

5.8.1.1 Apheresis and marrow products shall be labeled with ISBT 128 or Eurocode labels at the time of procurement.

5.8.1.1.1 Other cellular therapy products shall be labeled with the proper product name and a unique alpha or numeric identifier at the time of procurement.

5.8.1.2 Cellular therapy products shall be labeled with ISBT 128 or Eurocode labels at the completion of processing.

5.8.1.3 The receiving facility shall have a process in place for the traceability of products labeled in a different system or version.

5.8.2 All containers of source materials, in-process cellular therapy products, and final products shall be labeled in accordance with Reference Standards 5.8.2A, Requirements for Labeling of Cellular Therapy Products, and 5.8.2B, Requirements for Labeling Shipping Containers.

5.8.2.1 Regulated investigational products shall be labeled according to local and/or FDA and relevant Competent Authority regulations.

5.8.2.2 Products approved or licensed by applicable local and/or FDA and relevant Competent Authority shall be labeled according to the terms of licensure or approval.

✎*C* **5.8.3 Packaging and Labeling**
Labeling information shall be verified for accuracy and completeness.

5.8.3.1 The procurement facility shall verify labeling immediately after procurement.

5.8.3.2 The processing and/or storage facility shall verify labeling at the following times, at a minimum:

1) Upon receipt at the processing and/or storage facility.
2) At facility-defined in-process steps, including transfer to a different storage location and removal/retrieval of attached segments and/or samples, if applicable.
3) At completion of processing and/or before storage.
4) Before distribution or issue.

5.8.3.3 The administering facility shall verify labeling before administration of the cellular therapy product.

5.8.4 Label Terminology

Product names, attributes, and descriptions on product labels shall use the terms and definitions found in the Standard Terminology for Medical Products of Human Origin* or terminology consistent with Eurocode labeling terminology.

*http://www.isbt128.org

5.8.5 Cellular therapy products for investigational use or approved for use by the FDA or relevant Component Authority shall be labeled according to protocol and all elements required shall be included in the accompanying records or readily available. Reference standard 5.8.2A applies.

✎***F*** **5.9 Transport and Shipping**

The facility shall establish and maintain policies, processes, and procedures that are intended to limit deterioration, prevent damage, ensure timely delivery, and protect the quality of the materials and cellular therapy products during transport and shipping while maintaining Chain of Custody and Chain of Identity.

5.9.1 The facility shall control packaging to ensure conformance with specified requirements. Local, FDA or relevant Competent Authority, and/or international transport/shipping regulations apply.

✎***C*** **5.9.2** Shipping or transport containers shall be qualified at defined intervals to ensure that they maintain temperatures within the acceptable range for the expected duration of transport or shipping.

✎***F*** **5.9.3** When products are transported or shipped, the extent of temperature monitoring shall be defined and shall be appropriate to the duration of transport or shipping.

✎***F*** **5.9.3.1** When cryopreserved products are shipped, the temperature of the shipping

container shall be continuously monitored.

5.9.4 The facility shall label shipping containers and cellular therapy products in a manner designed to allow positive identification and to inform the carrier of the appropriate handling. Reference Standards 5.8.2A, Requirements for Labeling of Cellular Therapy Products and 5.8.2B, Requirements for Labeling Shipping Containers, apply.

5.9.5 Product or package inserts and records shall accompany products being shipped or transported between facilities. When the product is transported within a facility, product or package inserts and records shall be readily available. Reference Standard 5.9.5A, Labeling and Packaging Requirements Upon Shipping of Cellular Therapy Products, and Standard 4.3.8 apply.

✎*C* **5.9.6** Facilities shall maintain records of product origin, custody, transfer, identity, integrity and acceptability.

✎*C* **5.10 Inspection and Testing of Products**

The facility shall establish and maintain policies, processes, and procedures for inspection and testing activities to verify that the specified requirements for products are met.

✎*C* **5.10.1 Receipt of Incoming Cells, Tissues, and Organs**

At the time of receipt, incoming cells, tissues, and organs shall be inspected, sampled, and/or tested, as appropriate, to determine their acceptability. Standards 5.8.1, 5.8.3 and 5.9.6 apply. Records of the following shall be maintained:

1) Name of the supplier(s)/procurement facility.
2) Donation identification number.
3) Product description code, type of collection and division code.
4) Product name and attributes.
5) Unique donor identifier, if required.
6) Date and time of receipt.
7) Date and time of procurement and/or manufacture
8) Date of expiration, if applicable.
9) Results of inspection upon receipt, if applicable, including:
    a) Product appearance.
    b) Appropriate labeling.
    c) Integrity of the container(s).
    d) Presence or absence of visible evidence of contamination and tampering.
    e) Temperature acceptability.
10) Identity of the person receiving and/or inspecting the product.
11) Indication of acceptance, quarantine, or rejection.

12) Disposition.
13) Certificate of Analysis or manufacturer's insert or equivalent, if applicable.
14) Identification of the intended recipient, if applicable.

5.10.1.1 Identification of Cells, Tissues, and Organs Upon Receipt
The facility shall establish and maintain policies, processes, and procedures to require verification of the chain of identity of cells, tissues, and organs.

5.10.1.2 Cells, tissues, and organs shall be quarantined upon receipt and their disposition determined by a qualified individual when any of the following occur:
1) There is a delay in inspection, labeling, sampling, or testing procedures for determination of acceptability.
2) The cells, tissues, or organs are judged as not meeting acceptance criteria.
3) The cells, tissues, or organs require further sampling, labeling, processing, or testing before disposition.

✎*C* **5.10.2 In-Process and Final Product Inspection and Testing**
In-process testing and monitoring shall be defined. The facility shall:
1) Inspect and test the cellular therapy product during processing as defined by policies, processes, and procedures.
2) Quarantine the product until any required inspection, tests, processing, and eligibility determination have been completed or necessary reports received and verified, except when the product is released pursuant to Standard 5.22.3.
3) Report to the customer(s) identified in the disposition agreement any patient-specific cellular therapy products that are lost, damaged, or otherwise unsuitable for use. Standard 7.0 applies.

5.11 Storage and Preservation
The facility shall establish and maintain policies, processes, and procedures for storage of materials and cellular therapy products in order to prevent mix-ups and limit deterioration, contamination, and improper distribution of cellular therapy products. This shall include the use of designated, secure storage areas with controlled access. Chapter 7, Deviations, Nonconforming Products or Services and Adverse Events applies.

✎*C* **5.11.1** Storage areas shall have the capacity and design to ensure that proper temperature and humidity are maintained.

✎*C* **5.11.1.1** If cellular therapy products are stored in an open storage area, the ambient temperature and humidity shall be recorded at a minimum of every 4 hours.

5.11.2 Storage devices shall have the capacity and design to ensure that proper temperature and/or liquid nitrogen level is maintained.

✎*C* **5.11.3** Storage devices containing cellular therapy products and critical materials shall have a system to continuously monitor and also record at defined intervals the temperature and/or liquid nitrogen levels. Standard 5.9 applies.

5.11.3.1 The temperature and/or liquid nitrogen levels of freezers where cellular therapy products are immersed in liquid nitrogen shall be recorded every 24 hours at a minimum.

5.11.3.2 The temperature of refrigerators and freezers where cellular therapy products are not immersed in liquid nitrogen shall be recorded every 4 hours at a minimum.

✎*C* **5.11.4** Storage devices containing cellular therapy products and/or critical materials shall have an alarm system that is set to activate under conditions that will allow proper action to be taken before products or reagents reach unacceptable conditions. Alarm activation shall require personnel to investigate and document the condition activating the alarm and to take immediate corrective action as necessary.

Procurement Activities

✎***F*5.12 Donor Evaluation**

Donor evaluation shall be performed and informed consent obtained, in accordance with Reference Standards 4.5A, Donor Informed Consent or Authorization; 5.12A, General Requirements for Cellular Therapy Product Donors; 5.12B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.12C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.12D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Materials Donors; and 5.12E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors.

5.12.1 Medical Suitability

The facility shall define medical suitability criteria to protect the safety of the donor and the intended recipient. Medical suitability shall be determined before

the initiation of any intervention that could potentially affect the health of a donor or recipient. The facility shall identify donor medical conditions that may adversely affect the potential therapeutic value of the cellular therapy product. This evaluation shall be conducted by a health-care professional and shall include, based on examination, clinical history, and relevant medical record(s):

5.12.1.1 The ability to tolerate the collection procedure.

5.12.1.2 Risk of any acquired condition, such as malignancy or any inherited condition that could be transferred to the recipient by transplant.

5.12.1.3 If applicable, risk for hemoglobinopathy.

5.12.1.3.1 For HPC, Apheresis, and HPC, Marrow, the donor evaluation criteria shall include risk for hemoglobinopathy.

5.12.1.4 If applicable, pregnancy evaluation.

5.12.1.5 If applicable, the administering facility shall ensure that HLA typing is performed on the donor and verify that the HLA type meets specified HLA requirements. Reference Standards 5.12B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors and Reference Standards 5.17B, Processing Tests for HPC, Cord Blood or Gestational Materials Products, 5.17C Processing Tests for Cellular Therapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood apply.

5.12.1.5.1 HLA typing shall be performed by a facility accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), College of American Pathologists (CAP), European Federation for Immunogenetics (EFI), or other equivalent accrediting body.

5.12.1.5.2 For HPC, Apheresis, and HPC, Marrow, intended for allogeneic transplantation, the donor evaluation criteria shall include HLA matching.

5.12.1.6 The facility shall have a policy that addresses the privacy and confidentiality of the medical suitability determination process.

5.12.1.7 The facility shall define criteria for evaluating pediatric donors.

5.12.2 Donor Eligibility

Donor eligibility, when required shall be determined before the initiation of any intervention that could potentially affect the health of a recipient.

5.12.2.1 The facility shall define donor eligibility criteria to protect the safety of the intended recipient.

5.12.2.1.1 Donor eligibility criteria shall include:
1) Donor screening including a physical exam, review of relevant medical records and a current medical history interview to identify risk for relevant communicable disease.
2) Testing.

5.12.2.1.2 The facility shall have a policy that addresses and ensures the privacy and confidentiality of the donor eligibility determination process.

F **5.12.2.2 Collection of Samples for Infectious Disease Testing**

Samples associated with the products listed below shall be collected within the following timeframes, unless FDA or relevant Competent Authority regulations are more stringent:

1) HPC, Cord Blood: Obtain maternal sample within 7 days before collection.
2) HPC, Marrow; HPC, Apheresis: Collect from the donor within 30 days before procurement.
3) All other cellular therapy products: Collect from the donor within 7 days before or after procurement.

F **5.12.2.3 Cadaveric Donor Eligibility**

The evaluation of the donor's eligibility required by Reference Standard 5.12A, General Requirements for Cellular Therapy Product Donors, shall be performed by interviewing a family member or other knowledgeable person.

F **5.12.2.4** Donor testing shall be performed in conformance with Reference Standards 5.12B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.12C Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.12D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or

Gestational Materials Donors; and 5.12E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors.

5.12.2.5 There shall be a process to evaluate samples when the level of plasma dilution may affect test results.*

*FDA Guidance, August 8, 2007, "Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)."

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5.12.2.5.1 If plasma dilution is potentially sufficient to affect infectious disease testing results, the donor shall be considered ineligible unless one of the following conditions is met:

1) A suitable new sample is collected and used for testing.
2) A suitable sample before transfusion and/or infusion is used for testing.
3) An appropriate algorithm is applied to determine that plasma dilution has not affected the acceptability of the blood sample.

5.12.2.6 All donor infectious disease testing shall be performed using assays in accordance with the manufacturer's written instructions that have been approved for donor screening by the FDA or relevant Competent Authority, if such assays are available. Standard 4.3.8 applies.

5.12.2.7 Infectious disease testing shall be performed on all donors of products with the potential for allogeneic use.

5.12.2.8 The following tests shall be performed:

- Hepatitis B virus (HbsAg; anti-HBc; HBV DNA).
- Hepatitis C virus (anti-HCV; HCV RNA).
- Human immunodeficiency virus (anti-HIV -1/2; HIV-1 RNA).
- Human T-cell lymphotropic virus, type I and II (anti-HTLV-I/II) for viable leukocyte-rich products only.
- Antibody to cytomegalovirus for viable leukocyte-rich products only.
- A serologic test for syphilis.*
- West Nile virus (WNV RNA)

Reference Standards 5.12B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.12C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.12D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Materials Donors; and 5.12E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors, apply.

* FDA Guidance for Industry, September 2015, "Use of Donor Screening Tests to Test Donors of Human Cells, Tissues and Cellular and Tissue-Based Products for Infection with *Treponema pallidum* (Syphilis)".

5.12.2.8.1 For facilities not subject to United States laws and regulations, hepatitis B virus (HBV) DNA testing is acceptable in place of anti-HBc testing.

5.12.2.9 Testing shall be performed by a laboratory qualified by FDA or relevant Competent Authority (eg, CMS) and shall meet testing requirements for donors of cellular therapy products in that country.

5.12.2.10 The facility shall have policies, processes, and procedures to ensure relevant infectious diseases, and emerging infectious diseases are addressed and action taken in regard to the donor screening and testing process.

5.12.3 Samples for Testing Donations after Brain or Cardiac Death

5.12.3.1 Blood samples for testing shall be collected before the cessation of the donor's circulation, if possible.

5.12.3.1.1 If blood is collected after cessation of circulation, infectious disease testing of samples shall be performed using assays that have been approved for donor screening by the FDA or relevant Competent Authority and specifically labeled for cadaveric specimens, when available.

F **5.12.4 Evaluation of Cellular Therapy Products**

Before shipment or transport of cellular therapy products, the receiving facility shall review the donor screening and infectious disease testing records for

compliance with applicable local and FDA or relevant Competent Authority regulations of the receiving facility and to ensure the product meets specified requirements.

✎ *F* **5.12.5** A final determination of donor eligibility for allogeneic donors shall be made and shall include the following information:

1) A statement that the donor has been determined to be eligible or ineligible, noting the name and address of the facility that made the donor eligibility determination. Standards 5.12.1.5.1 and 5.12.8 apply.
2) A statement that the infectious disease testing was performed by a laboratory that has been certified to perform such testing on human samples under the CLIA or that has met equivalent requirements as determined by the CMS. For facilities located outside of the United States, the use of a laboratory authorized as a testing center by the FDA or relevant Competent Authority is permissible.
3) For a product from an ineligible donor, a statement noting the reason(s) for the determination of ineligibility.

5.12.6 Abnormal Results on Donor Screening and Testing

5.12.6.1 The facility shall establish policies, processes, and procedures for notification of abnormal or reactive infectious disease test results. Standard 7.2 applies.

✎ *F* **5.12.6.2** Abnormal findings on donor screening, examination and review of relevant clinical history or testing that may affect the donor's health shall be communicated to the donor or donor's physician. Reference Standards 4.5A, Donor Informed Consent or Authorization, and 4.7A, Patient Informed Consent, apply.

5.12.6.2.1 For cord blood or gestational materials, the donor's mother or appropriate physician shall be notified.

5.12.6.2.2 For cadaveric donors, all infectious disease test results shall be reported to the procurement facility. The procurement facility shall report positive test results to appropriate authorities as mandated by law or regulation, and test results shall be made available to the donor's legal next of kin when the test result(s) could affect the health of others.

✎ *F* **5.12.6.3** Abnormal findings on donor screening, examination or review of relevant clinical history or testing that may affect the recipient's

health or the therapeutic value of the cellular therapy product shall be communicated to the recipient's physician and to the recipient before distribution of the cellular therapy product for clinical use. Reference Standards 4.5A, Donor Informed Consent or Authorization, and 4.7A, Patient Informed Consent, apply.

✎C **5.12.6.4** Records of donors determined ineligible after procurement of the product shall be maintained.

5.12.6.4.1 Records of cord blood or gestational materials donors shall include the birth mother and, if applicable, the biologic mother.

✎ F **5.12.7 Products from Ineligible Donors**

The biohazard label shall be attached to any allogeneic product for which there are abnormal donor screening or testing results. All allogeneic products from ineligible donors shall be provided only under urgent medical need and shall be labeled with the phrase "WARNING: Advise patient of communicable disease risks." Reference Standard 5.8.2A, Requirements for Labeling of Cellular Therapy Products, applies.

5.12.7.1 Any product with abnormal donor testing results shall also be labeled with the phrase "WARNING: Reactive test results for [name of disease agent or disease]."

✎ F **5.12.8 Donors with Incomplete Eligibility Determinations**

Allogeneic donors who were not screened or tested in conformance with requirements of the FDA or relevant Competent Authority shall have an incomplete donor eligibility determination for that donation.

5.12.8.1 If testing is not performed in conformance with Standard 5.12.2.8 or if testing does not meet the requirements of the manufacturer of the test kit, the donor eligibility determination shall be incomplete.

5.12.8.1.1 If testing is not complete, a listing of all pending infectious disease test results and an interpretation of those performed shall be retained and accompany the product.

✎C **5.12.8.2** When the donor eligibility determination is incomplete, the facility shall complete the eligibility determination during or after use of the product, if possible, or indicate in the associated records the reason that the eligibility determination could not be completed.

The results of the determination of donor eligibility shall be communicated to the recipient's physician.

5.12.9 Products from Donors with Incomplete Donor Eligibility

Products from allogeneic donors with incomplete donor eligibility determination (donor screening and/or testing not completed in accordance with the requirements of the FDA or relevant Competent Authority) shall be provided only under urgent medical need, and shall be labeled with the statements "Not evaluated for infectious substances" and "WARNING: Advise patient of communicable disease risks." Standard 5.24.2 applies.

5.12.9.1 If infectious disease testing is performed on a sample that does not meet the requirements of the manufacturer of the test kit, the product shall be determined to have an incomplete donor eligibility determination and shall be labeled with the phrase "Not evaluated for infectious substances," even if all donor screening and testing were completed and if there were no abnormal results.

5.12.9.2 Allogeneic units from donors with incomplete donor eligibility determinations or from ineligible donors shall be released only under urgent medical need.

5.12.10 Labeling for Autologous Products

Autologous units shall be labeled with the phrase "For autologous use only" and, if testing or screening is not completed or performed, it shall be labeled with the statement "Not evaluated for infectious substances." Reference Standard 5.9.5A, Labeling and Packaging Requirements Upon Shipping of Cellular Therapy Products, applies.

5.12.10.1 The biohazard label shall be attached to autologous products for which there are abnormal donor testing or donor screening results . Any product with abnormal donor testing results shall also be labeled with the statement "WARNING: Reactive test results for [name of disease agent or disease]."

5.13 Medical Management and Emergency Care of Donors

5.13.1 The availability of medical care shall be based on the risks and clinical situation associated with each category of donation. Facilities procuring cells, tissues, or organs from living donors shall have provisions for emergency care and medical management of adverse events in those donors.

✎***C*** **5.13.2** When a central venous access device is used for a procurement procedure, the

following requirements shall apply:

1) The device shall be placed by a qualified person (under the supervision of a licensed physician if the individual is not a physician).
2) Before procurement, the correct anatomic location of the access device shall be confirmed by methods appropriate for the placement site.

5.13.3 Administration of a pharmacologic or biologic agent(s) to the donor shall be performed under the supervision of a licensed physician experienced in the use of said agent(s) and management of complications.

✎***C*** **5.13.3.1** Allogeneic and autologous donors shall be evaluated for the risk of hemoglobinopathy before the administration of a mobilizing agent.

5.13.4 Administration of local anesthesia to the donor shall be performed under the supervision of a credentialed physician. Sedation (monitored anesthesia care), regional anesthesia, or general anesthesia shall be administered under the supervision of a licensed anesthesiologist. Pain management for postprocedure care shall be available, if necessary.

5.13.5 The procurement facility shall have policies, processes, and procedures that are designed to protect the health and safety of the donor. Criteria for discontinuation of procurement due to medical complications shall be specified.

5.13.5.1 Cord blood or gestational materials procurement procedures shall ensure the safety of the birth mother and the neonate.

5.14 Procurement

There shall be policies, processes, and procedures for each procurement method performed in the facility.

✎***F*** **5.14.1 Medical Order for Procurement**

The procuring facility shall obtain a medical order before the procurement procedure for all cellular therapy products other than for cord blood or gestational materials . The medical order shall include procurement goals. Standard 5.15 applies.

5.14.2 Verification of Medical Suitability

5.14.2.1 Before procurement, the procurement facility shall verify that the determination of medical suitability has been completed. Standard 5.12.1 and Reference Standards 5.12B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.12C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.12D, I, Clinical Evaluation

and Laboratory Testing of Mothers of Cord Blood or Gestational Materials Donors; and 5.12E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors, apply.

F **5.14.2.2** Before any procurement procedure, the procuring facility shall obtain final approval and documentation by the donor's physician, or by another physician who is not directly involved with the care of the recipient, that the donor is suitable to proceed with donation, in conformance with Reference Standards 5.12A, General Requirements for Cellular Therapy Product Donors; 5.12B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; and 5.12C Clinical Evaluation and Laboratory Testing of Autologous Donors.

C **5.14.2.3** For marrow donors or donors of cells collected by apheresis, facilities shall:

1) Define criteria to evaluate the results of a complete blood count before each procurement.

2) Define timeframes for obtaining a complete blood count prior to the initial procurement.

3) Obtain a complete blood count within 24 hours prior to each subsequent procurement after the initial procurement.

F **5.14.2.4** On each day of procurement, a health-care professional at the procurement site shall confirm that the donor's medical status permits procurement and document that the donor's health status is acceptable for donation. Reference Standard 5.12A, General Requirements for Cellular Therapy Product Donors, applies.

5.14.3 Verification of Donor Eligibility

On each day of procurement, the procurement facility shall verify that the determination of donor eligibility has been completed and confirm that the donor's health history has not changed, other than for cord blood or gestational materials. Standard 5.12.8 applies.

F ### 5.14.4 Donor Identity

At the time of procurement, the donor's identity shall be confirmed by at least two independent identifiers.

5.14.4.1 For cord blood or gestational materials, the identity of the birth mother shall be confirmed by at least two independent identifiers.

F ### 5.14.5 Procurement Records

A procurement record shall include:

1) Donation identification number.
2) Product description code, type of collection and division code.
3) Product name and attributes.
4) Unique donor and/or patient identifier, if available.
5) Date and time of procurement.
6) Name and address of the procurement facility.
7) Details of the procured product/ procurement process.
8) Identification of persons responsible for each step of procurement.
9) Names, manufacturers, lot numbers, and expiration dates of critical materials and reagents and quantities used in procurement.
10) Identification of equipment used for procurement.

Standards 5.8.1, 7.2.1 and 7.3 apply.

F **5.14.6 Review of Procurement Records**

The facility shall ensure that the procurement record for each cellular therapy product is accurate and complete in a specified time frame.

5.14.7 Procurement Record Availability

Each facility performing procurement shall provide a product procurement record to the facility receiving the product while maintaining chain of custody. Chapter 4, Agreements, applies.

5.14.7.1 Records shall include:

1) Donation identification number.
2) Product description code, type of collection and division code.
3) Product name and attributes.
4) Unique donor and/or patient identifier, if available.
5) Date and time of procurement, including time zone if applicable.
6) Name and address of the procurement facility.

F **5.15 Procurement Goals**

Procurement goals shall be defined.

5.15.1 Unrealized Goals

If expected goals are not met, Chapter 7, Deviations, Nonconforming Products or Services, and Adverse Events, applies as applicable.

5.15.1.1 If expected goals are not met the intended recipient's physician, the processing facility, and other relevant parties shall be notified.

Standard 7.1.3.1 applies.

5.16 Packaging

As soon as possible after procurement, each organ, tissue component, or cellular therapy product shall be packaged in an individually labeled container suitable for the specific product. Reference Standard 5.8.2A, Requirements for Labeling of Cellular Therapy Products, applies.

5.16.1 The facility shall verify the accuracy of the procurement container label and donor identification in the proximity of the donor.

5.16.1.1 For in-utero cord blood or gestational materials collections, the procurement facility shall verify the accuracy of the collection container label and donor identification in the proximity of the donor.

5.16.1.2 For ex-utero cord blood or gestational materials collections, the procurement facility shall have policies, processes, and procedures to verify the label on the collection container against the donor identification.

Processing Activities

5.17 Processing

Cellular therapy products shall be tested during processing in conformance with Reference Standards 5.17A, Processing Tests for HPC, Apheresis, and HPC, Marrow; 5.17B, Processing Tests for HPC, Cord Blood Products or Gestational Materials; and 5.17C, Processing Tests for Cellular Therapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood or Gestational Materials. Specifications for the following stages shall be defined for each type of cellular therapy product:

1) Incoming cells, tissues, and organs.
2) Intermediate products, if applicable.
3) Final products.

F **5.17.1 Medical Order for Processing, Preservation, or Storage**

The facility (except for cord blood or gestational materials manufacturing facilities) performing processing, preservation, or storage shall obtain an order from a health-care provider. The order shall contain information that uniquely identifies the donor and the recipient. Specific instruction for cell processing and preservation shall be provided in the order as appropriate.

F **5.17.2 Processing Record**

A complete processing record shall include:

1) Donation identification number.
2) Product description code, type of collection and division code.
3) Product name and attributes.
4) Unique donor and/or patient identifier, if available.
5) Date and time of procurement.
6) Name and address of processing facility.
7) All details of critical processing, preservation, and storage steps. For cryopreservation records, Standard 5.19.3 applies.
8) Date and time (if applicable) of critical steps.
9) Names of persons responsible for each step.
10) Names, manufacturers, lot numbers, and expiration dates of all critical materials used in processing, preservation, and storage.
11) Quantities of reagents used.
12) Identifiers of equipment used.
13) Documentation of product distribution or final disposition.
14) Final review as defined by the facility's policies, processes, and procedures.

✎*C* **5.17.3 Determination of Acceptable Values or Ranges**

The facility shall define test methods and the acceptable values or ranges for defined critical characteristics of each product [eg, recovery of specific cell populations, cell viability, cell identification and potency assays, function(s), purity, as appropriate, and sterility]. Reference Standards 5.17A, Processing Tests for HPC, Apheresis, and HPC, Marrow; 5.17B, Processing Tests for HPC, Cord Blood Products or Gestational Materials; and 5.17C, Processing Tests for Cellular Therapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood or Gestational Materials apply.

✎*F* **5.17.4 Managing Red Cell Antigen Incompatibility**

The processing facility shall have policies, processes, and procedures for managing red cell antigen incompatibility, as applicable, between the donor and the recipient.

5.17.5 Processing Records

Each facility(ies) performing processing, preservation, or storage shall provide a copy of the product processing record insofar as the processing records concern the safety, purity, and potency of the product involved or a summary of the product processing record to the facility(ies) receiving the product while maintaining chain of custody. Chapter 4, Agreements, applies.

✎*C***5.18Storage of Noncryopreserved Products**

The facility shall establish for each type of product the storage specifications and defined storage conditions, including temperature range and length of storage to maintain viability and function.

5.18.1 Management of Stored Noncryopreserved Inventory

5.18.1.1 Cellular therapy products shall be maintained under defined conditions, including temperature range, between donation and final disposition.

5.18.1.2 Aliquot(s) of cellular therapy products shall be maintained under defined conditions, including temperature range.

5.18.1.3 The use and disposition of cellular therapy products (and aliquots if applicable) shall be defined in the facility's policies, processes, and procedures.

5.18.1.4 The facility shall have processes to ensure traceability for any given product (and aliquots if applicable) from donation to final disposition.

5.19 Cryopreservation

Cellular therapy products shall be cryopreserved using a controlled-rate freezing procedure or equivalent procedure validated to maintain viability. The temperature of the product(s) and/or freezing process shall be monitored according to the facility's policies, processes, and procedures.

5.19.1 Management of Cryopreserved Stored Inventory

5.19.1.1 An aliquot of cryopreserved cellular therapy products shall be retained and stored under conditions equivalent to those of the cellular therapy product. The use and disposition of aliquot(s) shall be defined in the facility's policies, processes, and procedures.

5.19.1.2 An inventory control system shall be defined and validated to ensure that any given cellular therapy product, aliquots, and reference samples can be located while in storage.

5.19.2 Special Requirements for Cord Blood

5.19.2.1 Cord blood products shall have at least two integrally attached segments cryopreserved with the product. Standard 5.7.1.3 and Reference Standard 5.17B, Processing Tests for HPC, Cord Blood

Products (#5), apply.

✎*C* **5.19.2.1.1** The identity of the cord blood product and segment(s) shall be confirmed by two individuals or one individual and an electronic device that has been validated to fulfill the labeling identification function(s) when integrally attached segments are removed.

5.19.2.2 Cryopreserved cord blood products shall be stored at temperatures at or below –150 C in liquid or vapor phase of liquid nitrogen.

✎*F* **5.19.3 Records for Cryopreserved Products**

In addition to the items required by Standard 5.17.2, cryopreservation records shall include:

1) Donation identification number.
2) Product description code, type of collection and division code.
3) Product name and attributes.
4) Unique donor and/or patient identifier, if available.
5) Date and time of procurement.
6) Concentration or quantitation of the relevant cell type(s).
7) Cell viability.
8) Name and volume or concentration of the cryoprotective agent(s).
9) Date and time of cryopreservation.
10) Temperature record during cryopreservation, if applicable.
11) Endpoint temperature after cryopreservation.
12) Storage location of the cryopreserved product and any related test aliquots.

✎C **5.20 Expiration Dates and Stability of Products**

5.20.1 The facility shall have policies, processes, and procedures to define and validate expiration dates. Reference Standard 5.8.2A, Requirements for Labeling of Cellular Therapy Products (#13), applies.

5.20.2 Cryopreserved products shall be monitored through a stability program. Sampling and evaluation shall be performed, at a minimum, on an annual basis. The facility's sampling plan shall be included in the facility's policies, processes, and procedures.

5.20.2.1 At a minimum, the stability program shall include product container integrity and viable cell recovery, and a measure of potency of the relevant cell population(s).

5.20.3 If cryopreserved products are to be distributed past their assigned expiration date, the facility shall have processes for review and approval of product release.

5.20.3.1 If facilities re-assign product expiration dates based on documented stability program data, the facility shall have policies, processes, and procedures to re-label products with new expiration dates. Reference Standard 5.8.2A, Requirements for Labeling of Cellular Therapy Products, applies.

F **5.21 Discard and Disposal**

The facility shall have policies, processes, and procedures regarding discard and disposal of products and aliquots that are consistent with requirements outlined in the facility's informed consent process and applicable laws and regulations. Standard 4.3.6 applies.

5.22 Evaluation to Make a Product Available for Distribution

The facility shall define requirements for inspections and test results necessary to make a product available for distribution. The facility shall ensure that these requirements are met before distribution. Standards 5.24.1, 5.28.2, 7.1.3, and 7.2.2.2 apply.

5.22.1 Products shall not be made available for distribution or listed on a registry until the medical director or designee and the quality representative or designee have approved the release of the product.

F **5.22.2** Before a product is made available for distribution, the records relevant to Standards 5.22.2.1 and 5.22.2.2 shall be reviewed. The responsibility for completion and review of these records shall be defined in an agreement between the applicable parties.

5.22.2.1 Donation Criteria

Review of donation criteria shall confirm that:

1) Donor informed consent was obtained.
2) Donor eligibility determination was performed, when applicable. Standards 5.12 and 7.2 apply.
3) The donor met other applicable selection criteria.
4) The procurement order was obtained.

5.22.2.2 Product Processing Review

Review of the final cellular therapy product processing record shall confirm that:

1) Processing order was obtained, if applicable.
2) Facility defined specified requirements were achieved.
3) Records of processing, cryopreservation, and storage are

complete and contain appropriate initials and/or signatures, and critical calculations have been verified.

4) Appropriate, in-date, critical reagents and materials were used and lot numbers recorded in a manner that ensures traceability.
5) Appropriate equipment was used and identification numbers recorded in a manner that ensures traceability.
6) The accuracy and completeness of the product labeling was verified.
7) All pending infectious disease testing, if applicable, was completed.

✎*C* **5.22.2.3 Product Record Review**

Before final distribution, the following items shall be reviewed:

1) List of the specified requirements.
2) Acceptable values or range for each test.
3) Actual product value for each test.
4) Indication of whether each given value falls within the acceptable range.
5) Documentation that the product review was acceptable and the identity of the person making that determination.
6) Comments or annotations if the product does not meet specified requirements.

5.22.3 Failure to Meet Specified Requirements

Products that do not meet specified requirements are considered nonconforming and shall not be used except as defined in Standard 7.2.2.2.

✎*C***5.23 Distribution**

Upon request for distribution, the following items shall be reviewed:

1) Documentation that the product was requested.
2) The accuracy and completeness of the product labeling and identification verified by two individuals or one individual and an electronic device that has been validated to fulfill the labeling identification function(s).
3) Product condition by visual inspection.
4) Recipient identification, if applicable.
5) Documentation of compatibility for the intended recipient.
   a) ABO and other blood group and type antigen compatibility, if applicable.

b) HLA compatibility, if applicable.

5.23.1 Instructions shall be made available for the handling, storage, and preparation of products for administration.

***F*5.24 Product Issue**

Before issue, the following items shall be reviewed:

1) Medical order for issuing the product.
2) The accuracy and completeness of the product labeling and identification verified by two individuals or electronic equivalent.
3) Product condition by visual inspection.
4) Recipient identification.
5) Documentation of compatibility for the intended recipient.
   a) ABO and other blood group and type antigen compatibility, if applicable.
   b) HLA compatibility, if applicable.

F **5.24.1** The issuing facility shall review and verify the following items at the time of final cellular therapy product distribution/issue:

1) Recipient's name and unique identifier(s).
2) Donation identification number.
3) Product description code, type of collection and division code.
4) Product name and attributes.
5) Unique donor identifier, if available.
6) Product condition by visual inspection.
7) Names and/or identifiers of persons verifying that the product is the product intended for the recipient.
8) Identification of the person issuing the product.
9) Identification of the person to whom the product was issued.
10) Date and time of issue.

5.24.2 At distribution and issue of allogeneic products, the following information shall accompany the product or be readily available wherever the product is located to maintain chain of custody:

1) A statement that the donor has been determined to be eligible or ineligible, or donor eligibility determination is incomplete, noting the name and address of the facility that made the donor eligibility determination. Standard 5.12.5 applies.
2) A statement that the infectious disease testing was performed by a laboratory that has been certified to perform such testing on human samples under current CLIA regulations or that has met equivalent requirements as determined by CMS. For testing facilities located outside of the United States, the use of a non-US laboratory as a testing center is

permissible if authorized by the FDA or relevant Competent Authority as an approved laboratory in that country for infectious disease testing.

3) A listing and interpretation of the results of all donor screening and infectious disease tests performed or pending.
4) For a product from an ineligible donor, a statement noting the reason(s) for the determination of ineligibility.
5) Instructions for the storage and handling of the products before administration.

5.24.3 Records provided at the time of distribution for donors with incomplete eligibility determination shall indicate the testing and screening that was completed and the testing and screening that has not yet been completed.

Clinical Activities

5.25 Clinical Program

The facility shall have policies, processes, and procedures for patient care, including the administration of specific therapies and medical interventions while maintaining chain of identity.

5.25.1 Patient (Recipient) Evaluation

The facility shall have policies, processes, and procedures to define the clinical indications and evaluation criteria for treatment. This evaluation shall be conducted by a health-care professional and approved by a physician.

5.25.1.1 Facilities administering investigational product(s) shall have policies, processes, and procedures to reevaluate the recipient before the administration of products.

5.25.2 The facility shall ensure that orders and responsibility for the provision of patient care are defined and communicated whenever responsibility changes.

*F*5.26 Clinical Care of the Recipient

The facility shall have policies, processes, and procedures addressing the clinical care of the recipient, including the following, if applicable:

1) Blood products.
2) Chemotherapy.
3) Radiation therapy.
4) Conditioning regimens.
5) Infectious disease management.
6) Graft-versus-host disease, cytokine release syndrome and other cellular therapy-associated complications.

5.26.1 Medical Orders

Orders for clinical care of the recipient shall uniquely identify the recipient and medical treatment ordered. Specific instructions shall be provided in the order.

5.26.1.1 Medical therapy(ies) shall be ordered by a qualified physician or an authorized health-care professional.

✎*F* **5.26.1.2** Orders for cellular therapy product administration shall uniquely identify the recipient, type of cellular therapy product ordered, and the dose. The order shall be obtained before the product is released for administration. Specific instructions for administration shall be provided.

✎*F*5.27 Preparation of the Recipient for Administration of Cellular Therapy Products

The facility shall have policies, processes, and procedures for the preparation of the recipient for administration of cellular therapy product(s) which shall address, at a minimum, the following:

1) Administration of the preparative regimen, if applicable.
2) Prevention of cellular therapy product-associated toxicities.
3) Management of cellular therapy product-associated toxicities.

Standard 5.28.1 applies.

5.28 Receipt and Storage of the Product

5.28.1 Receipt of Cellular Therapy Products

The clinical facility shall have procedures for the receipt, and preparation, of products while maintaining chain of identity and chain of custody. Standards 5.7, 5.8, 5.10, and 5.22 apply.

✎*F* **5.28.2** The clinical facility shall review and verify the following items at the time of final cellular therapy product receipt:

1) Recipient's name and unique identifier(s).
2) Donation identification number.
3) Product description code, type of collection and division code.
4) Product name and attributes.
5) Product condition by visual inspection. Standard 4.3.6 applies.
6) Summary of donor eligibility determination. Standards 5.24.2 and 5.24.3 apply.

5.28.3 Storage at Administering Facility

The administering facility shall maintain the product according to specifications provided by the processing facility. Standard 4.3.6 applies.

✎***F*5.29 Administration**

Immediately before the administration of the final cellular therapy product, two individuals [or one individual and an electronic device that has been validated to fulfill the labeling identification function(s)] at the clinical facility shall confirm the identity of the product and the intended recipient. Intended recipients shall be identified using at least two identifiers.

5.29.1 The facility shall have policies, processes, and procedures for the administration of cellular therapy products. These shall be consistent with information contained in the current *Circular of Information for the Use of Cellular Therapy Products*, investigator's brochure for investigational products, and/or package insert for licensed cellular therapy products.

5.29.2 The clinical facility shall have policies, processes, and procedures for monitoring and observation of the recipient commensurate with the nature of the procedure and product type. These shall include:

1) Infusional toxicities and adverse reactions resulting from cellular therapy product administration.
2) Prevention of regimen-related toxicities.
3) Management of regimen-related toxicities.
4) Identification and management of red cell antigen incompatibility.
5) Recipient immunosuppression for allogeneic cellular products.
6) Treatment of or prophylaxis for infectious disease.
7) Use of blood products.
8) Management of graft-versus-host-disease for allogeneic products.
9) Complications of immune effector cellular therapy.

✎*F* **5.29.3** There shall be procedures for recording adverse events and processes for the communication of such events from the clinical facility to the issuing facility and/or registry while maintaining chain of identity. Chapter 7, Deviations, Nonconforming Products or Services, and Adverse Events, applies. Standards 4.3.4 and 4.3.5 apply.

5.29.3.1 Responsibility for treating recipient adverse events shall be defined. Standard 7.3.2 applies.

✎***F*** **5.29.4 Records of Administration**

Records of administration shall include:

2) Patient's name and unique identifier(s).
3) Donation identification number.
4) Product description code, type of collection and division code.
5) Product name and attributes.
5) Medical order for administration.
6) Confirmation of recipient and product identity before administration.
7) Names and/or identifiers of persons who administered the product.
8) Dates and times of product administration initiation and completion.
9) All administration information, including the patient's vital signs and the time of all recorded events.
10) Whether any adverse events occurred, including a reference to the appropriate documentation of adverse event forms.
11) Records of notification if an adverse event occurred.
12) Critical steps related to product administration shall be entered into the permanent medical record by the ordering or administering qualified health-care professional according to facility-defined protocol. An anesthesiology record (if anesthesia is required) shall become part of the permanent medical record.

F **5.29.5 Patient Records**

Patient records shall include the following:

1) Patient's name and unique identifier(s).
2) Donation identification number.
3) Product description code, type of collection and division code.
4) Product name and attributes.
5) Medical and surgical history and physical examination.
6) If applicable, interpretation of tests for infectious disease markers.
7) Signed informed consent for administration of the cellular therapy product.
8) Unique cellular therapy product identifier(s).
9) If applicable, interpretation of ABO and other red cell antigen and Rh typings and, for allogeneic recipients, documentation of:
   a) The detection and identification of unexpected red cell antibodies.
   b) Assessment of blood grouping compatibility between the intended donor and recipient.
10) Documentation of HLA typing results, if indicated.
11) Other relevant testing records.

5.29.6 The facility shall have policies, processes, and procedures regarding the discharge and follow-up of patients after the administration procedure.

5.30 Postadministration Monitoring

The facility shall have policies, processes, and procedures for recipient follow-up, including the collection of outcome data following the administration of cellular therapy products and to communicate this information with the procurement and/or processing facility. This shall include any immediate or late adverse event suspected to be linked to the cellular therapy product. Standard 7.3 applies.

5.30.1 When data are reported to a registry, the outcomes data shall be entered into the facility's database in a manner to ensure that data can be queried, extracted, analyzed and reported to stakeholders in a consistent manner.

Reference Standard 5.8.2A—Requirements for Labeling of Cellular Therapy Products

(For labeling of regulated investigational products or licensed products, Standards 5.8.2.1 and 5.8.2.2 apply.)

Item No.	Element	Completion of Procurement[1]	In-Process Label[1]	Completion of Processing	Distribution and Issue[2]
1	Donation Identification Number (Unique alpha and/or numeric identifier of the product)[3]	P	P	P	P
2	Name of the product	P	P	P	P
3	Product attributes[4]	A[6]	R	A[6]	P[7]
4	Product Code[3] • Product Description Code • Collection Type Code • Division Code	P	N/A	P	P
5	Donor identifier or name[5]	A	N/A	A[6]	A[6]
6	Date of procurement	R	N/A	R	R
7	Time of completion of procurement (time zone, if applicable) [8]	R	N/A	R	R
8	Name of procurement facility/donor registry	R	N/A	R	R
9	Approximate product volume or weight (if applicable)	R	N/A	R	R
10	Names/volumes of anticoagulants and other additives (if applicable)	R	N/A	A[6]	A[6]
11	Patient/Recipient name and/or identifier (if known)[9]	R	R	R	A[6]
12	Expiration date and time (if applicable)	N/A	N/A	A[10]	A

13	ABO and Rh of the donor (if applicable)	N/A	N/A	R	R
14	CMV status of the donor (if applicable)	N/A	N/A	N/A	R
15	Red cell compatibility (if applicable)	N/A	N/A	N/A	R
16	Recommended storage temperature (in degrees Celsius)	R	N/A	A	A
17	Name and address of the facility that determines the product has met release criteria and makes the product available for distribution	N/A	N/A	N/A	R
18	Biohazard label (if applicable; see Reference Standard 5.8.2B, Requirements for Labeling Shipping Containers)	A	A[6]	A[6]	A[6]
19	Phrase: "Do Not Irradiate" (if applicable)	N/A	R	A[6]	A[6]
20	Phrase: "Do Not Use Leukoreduction Filters" (if applicable)	N/A	N/A	A[6]	A[6]
21	Phrase: "NOT EVALUATED FOR INFECTIOUS SUBSTANCES" and the statement "WARNING: Advise Patient of Communicable Disease Risks" (if applicable)	A	A[6]	A[6]	A[6]
22	Phrases: "Warning: Reactive Test Results for [name of disease agent or disease]" and "WARNING: Advise Patient of Communicable Disease Risks" (if applicable)	A	A[6]	A[6]	A[6]
23	Phrase: "For Autologous Use Only" (if applicable)	A	A[6]	A[6]	A[6]
24	Phrase: "For Use by Intended Recipient Only" (if applicable)	N/A	A[6]	A[6]	A[6]

25	Phrase: "Properly Identify Intended Recipient and Product"	N/A	A[6]	A[6]	A[6]
26	Phrase: "Caution: New Drug – Limited by Federal (or United States) Law to Investigational Use" (if applicable)	N/A	N/A	N/A	A[6]
27	Phrase: "For Nonclinical Use Only" (if applicable)	N/A	R	A[6]	A[6]

[1]The in-process label may be used during processing and prior to distribution and issue.
[2]The final labeling information for distribution shall be on or included with the container before the product is issued or transported.
[3] Standard 5.8.1 applies
[4] Additional characteristics that uniquely define a cellular therapy product. A group of attributes, called Core Conditions, are required; these conditions include anticoagulant and/or additive, nominal collection volume, and storage temperature. Labeling terminology shall conform to current ICCBBA or Eurcode labeling requirements, as applicable.
[5]In cases where donor anonymity must be preserved, such as with products from unrelated donor registries, this information is not required.
[6]If affixing or attaching the applicable warnings and statements to the container is physically impossible, then the labeling must accompany the human cells, tissues, and cellular- and tissue-based products.
[7] If label size precludes displaying all product attributes, the label shall refer to accompanying documentation for details.
[8] Time zone, only applicable if the procurement Facility is different from the processing facility.
[9] Ensure maintenance of chain of identity.
[10]If expiration date is not affixed to cryopreserved products at the end of processing, then records of stability studies shall be available to demonstrate expiration date at release of the cryopreserved product.

P = permanently affixed; A = attached (may be permanently affixed); R = accompanying records; N/A = not applicable.

Reference Standard 5.8.2B—Requirements for Labeling Shipping Containers

Item No.	Element	Shipping Document*	Outer Shipping Container
1	Biohazard label (if applicable)	R	N/A
2	Phrase: "Do Not Irradiate" (if applicable)	R	A
3	Phrase: "Do Not X-Ray" (if applicable)	R	A
4	Phrases: "Medical Specimen" or "Human Cells for Transplantation" or equivalent	N/A	A
5	Date of distribution	R	R
6	Name and street address of receiving facility	R	A
7	Name and phone number of contact person at receiving facility	R	A

*Shipping document shall be placed within the shipping container.
R = accompanying records; N/A = not applicable; A = affixed or attached using a tie-tag.

Reference Standard 5.9.5A—Labeling and Packaging Requirements Upon Shipping of Cellular Therapy Products

1) Summary of processing records; statement of donor eligibility determination; infectious disease testing results; and testing records, including name, address, and emergency contact information for shipping/issuing facility.[1]

2) Warning label(s) for potentially toxic or volatile packing materials, including dry ice or liquid nitrogen.

3) Instructions for receiving and opening the container.

4) Current *Circular of Information for the Use of Cellular Therapy Products*, certificate of analysis, manufacturer's insert, investigator's brochure, or equivalent .[2]

5) Notification of biohazardous materials (see Standard 5.10.1).

[1]21 CFR 1271.55(a), 21 CFR 1271.55(b), 21 CFR 1271.60(d)(2), 21 CFR 1271.65(b)(2), 21 CFR 1271.90(c) and 21 CFR 1271.370(c).
[2]Includes, but is not limited to, a written description of product.

Reference Standard 5.12A—General Requirements for Cellular Therapy Product Donors[1]

I. Donor Advocacy and Translation Services

All allogeneic donors or their legally authorized representatives shall be provided with the opportunity to access donor advocacy including translation services.

II. Donor Education

A. The prospective donor [or legally authorized representative(s), if applicable] shall be provided with educational materials that describe the donation process and its potential risks and complications. Prospective donors [or legally authorized representative(s), if applicable] shall acknowledge in writing that they have read the educational material, have been given the opportunity to ask questions, and have had those questions answered satisfactorily.

B. Educational materials shall include the following elements:
   1) General explanation of the indications for and results of cellular therapy.
   2) General description of the donation process, donation alternatives, and the risks of donation.
   3) For marrow donors:
      a) Information about the bone marrow donation procedure.
      b) Risks and discomforts of marrow donation.
      c) General risks and discomforts of anesthesia.
   4) For apheresis donors:
      a) Information about the apheresis procedure.
      b) Risks and discomforts of the apheresis procurement procedure.
      c) Possibility of access device placement, along with its risks and discomforts, if peripheral venous access is unsuitable.
      d) Risks and discomforts of growth factor and/or other pharmacologic agent(s), where applicable.

III. Determination of Donor Eligibility and Medical Suitability

A. All Donors
   1) The facility shall define donor eligibility and medical suitability criteria to protect the safety of the donor and intended recipient and, when applicable, to identify conditions that may adversely affect the potential therapeutic value of the cellular therapy product.
      a) For cord blood or gestational materials donors, in addition to evaluating the mother's medical history and infectious disease

risk, the facility shall have policies, processes, and procedures to assess the health status of the neonatal donor that may potentially affect the safety of the recipient or the therapeutic value of the cellular therapy product. Reference Standard 5.12A III B 3 c applies.

2) Medical suitability shall be determined by a physician who, in the case of allogeneic donors, cannot be directly involved with the care of the recipient.
   a) For cord blood or gestational materials donors, the medical suitability shall be determined by a health-care professional.
   b) Standard 5.12.6.2 applies.
3) The facility shall evaluate donor eligibility and medical suitability according to defined risk-based clinical and laboratory testing criteria.
4) Eligibility and medical suitability determination shall be performed and approved in a manner and timeframe that provides current relevant information and protects the safety of the intended recipient and donor.
5) Donor eligibility and medical suitability records shall be reviewed before administration of a conditioning regimen to the recipient and the beginning of mobilization.
6) Use of products from allogeneic donors who do not meet eligibility criteria (determined to be incomplete or ineligible) shall require written approval and documentation of urgent medical need by the recipient's physician. Product shall be labeled appropriately.
7) For donors with incomplete screening or testing results, to complete eligibility determination, the facility shall:
   a) Complete eligibility determination if possible, or document in the records the reason that the eligibility could not be completed.
   b) Communicate results of the determination of donor eligibility to recipient's physician.
   c) Provide a list of screening and testing that has been completed and a list of screening and testing that has not been completed.
8) For donors who are determined to be ineligible, the applicable facility(ies) shall keep records of:
   a) Reason that the donor did not meet eligibility criteria.
   b) Donor notification of clinically significant findings.
   c) Identification and disposition of collected products.

B. Specific Donor Requirements
   1) Living Allogeneic Donors
      a) Evaluation and approval of medical suitability and eligibility shall be performed before the recipient receives myeloablative

marrow conditioning therapy or is otherwise prepared for donation.

b) Interim health assessments, including psychosocial evaluation as appropriate, shall be performed by a health-care professional during the procurement-associated interventions (if applicable) and through procurement.

c) Donor eligibility determination shall be reviewed before procurement-associated interventions.

d) For any procurement procedure, a health-care professional at the procurement site shall confirm that the donor's medical status permits procurement and document that the donor's health status is acceptable for donation.

2) Autologous Donors

A medical suitability assessment specific to the donation procedure shall be performed by a qualified health-care professional and approved by a physician before the scheduled procurement.

3) Mothers of Cord Blood or Gestational Materials Donors

a) Personal, family medical, and genetic histories of the family of the prospective cord blood or gestational materials donor shall be obtained before procurement but no later than 7 days after procurement.

b) If the medical history is obtained more than 7 days before procurement, the health history shall be reviewed for changes in infectious disease exposures in the birth mother.

c) In the case of a surrogate mother, her medical history shall be obtained and documented in addition to that of the biologic parents. A genetic history of the surrogate mother need not be obtained.

4) Cadaveric Donors

a) The evaluation of the donor's eligibility shall be performed by interviewing a family member or other knowledgeable person.

b) When organs or tissues are procured from cadaveric donors, the facility shall specify the type of donor (donation after brain death or donation after cardiac death) by the protocol in use.

[1]FDA Guidance, August 8, 2007, "Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)."

21 CFR 1271

Reference Standard 5.12B—Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors

I. Clinical Evaluation to Protect the Safety of the Donor	**Required (Yes/No)**
Physical examination and health history	Yes
Hemoglobinopathy risk[1]	Yes
Anesthesia risk, if applicable	Yes
Vascular access	Yes
Pregnancy in female donors	Yes

II. Clinical Evaluation to Protect the Safety of the Recipient[2]	
Donor screening for clinical and physical evidence of risk for, or symptoms of, relevant communicable disease[3]	Yes
Hemoglobinopathy risk[1]	Yes
Risk of any condition, such as malignancy or any inherited condition that could be transferred to the recipient by transplant	Yes
Evaluate for recent immunization and vaccination history.	Yes

History and behavioral risk for exposure to the following infectious agents or diseases[2]:	
HIV	Yes
HBV	Yes
HCV	Yes
HTLV (viable, leukocyte-rich products only)	Yes
Syphilis	Yes
WNV[4]	Yes
Vaccinia (smallpox vaccine)	Yes
Human TSEs	Yes
Malaria (travel or residence in malaria-endemic areas)[5]	Yes

Trypanosoma cruzi (Chagas disease)[5]	Yes
Sepsis	Yes
Zika [6]	Yes

III. Laboratory Testing for Allogeneic Donors[2,7]

HIV-1/2	Yes
HBV	Yes
HCV	Yes
Syphilis	Yes
HTLV-I/II (viable, leukocyte-rich products only)	Yes
CMV (viable, leukocyte-rich products only)	Yes
HLA Type, if applicable[8,9]	Yes
ABO/Rh, if applicable[8]	Yes
CBC, if applicable	Yes
WNV[4]	Yes
Trypanosoma cruzi (Chagas disease)[5]	No
Zika[6]	No

[1]Applies only to donors whose hemoglobinopathy will put the donor or recipient at risk.
[2]Relevant medical records as described in 21 CFR 1271.3(s).
[3]The relevant communicable disease agents or diseases are described in 21 CFR 1271.3(r)(1)(i)(ii) and 1271.3(r)(2).
[4]In the United States, West Nile virus is considered a relevant communicable disease agent or disease as defined under 21 CFR 1271.3(r)(2) by the FDA Guidance for Industry, "Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)", August 2007. Testing is per Guidance for Industry, "Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Living Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)", September 2016, corrected May 2017.
[5]As of this date, in the United States, the FDA does not consider these risk factors to render donors ineligible; facility policies must define how health history risks identified and the test results for these diseases affect eligibility determination.

[6] In the United States, Zika virus is considered a relevant communicable disease agent or disease as defined under 21 CFR 1271.3(r)(2) by the FDA. Guidance for Industry "Donor Screening Recommendations to Reduce the Risk of Transmission of Zika virus by Human Cells, Tissues, and Cellular and Tissue-Based Products", March 2016, updated May 2018.
[7] In the United States, perform tests for relevant communicable disease agents or diseases as required by the FDA and interpret positive/reactive test results as described in 21 CFR 1271.80(d)(1).
[8]Testing shall be performed whenever this information is necessary for the selection and/or clinical use of a cellular therapy product.
[9]*HLA-A*, *HLA-B*, and *HLA-DRB1* loci shall be determined. All typing used for the final selection of the donor shall use DNA-based technologies.

HIV = human immunodeficiency virus; HBV = hepatitis B virus; HCV = hepatitis C virus; HTLV = human T-cell lymphotropic virus; WNV = West Nile virus; TSEs = transmissible spongiform encephalopathies; CMV = cytomegalovirus (anti-CMV, IgG and IgM); CBC = complete blood count.

These *CT Standards* are minimum requirements and are not meant to preempt any local or FDA or relevant Competent Authority regulations that may be more stringent. Standard 5.12.2.6 applies.

Reference Standard 5.12C—Clinical Evaluation and Laboratory Testing of Autologous Donors

I. Clinical Evaluation to Protect the Safety of the Donor/Recipient	(Required Yes/No)
Physical examination and health history	Yes
Hemoglobinopathy risk[1]	Yes
Anesthesia risk, if applicable	Yes
Vascular access	Yes
Pregnancy in female donors	Yes
Sepsis	Yes

II. Laboratory Testing	
ABO/Rh, if applicable[2]	Yes
CBC, if applicable	Yes

[1]Applies only to donors whose hemoglobinopathy will put the donor or recipient at risk.
[2]Testing shall be performed whenever this information is necessary for the selection and/or clinical use of a cellular therapy product.

CBC = complete blood count.

These *CT Standards* are minimum requirements and are not meant to preempt any local or FDA or relevant Competent Authority regulations that may be more stringent. Standard 5.12.2.6 applies.

Reference Standard 5.12D—Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Material Donors

I. Clinical Evaluation to Protect the Safety of the Donor	**(Required Yes/No)**
Physical examination and health history	Yes

II. Clinical Evaluation to Protect the Safety of the Recipient[1,2]	
Donor screening for clinical and physical evidence of risk for, or symptoms of, relevant communicable disease[3]	Yes
Risk of any condition, such as malignancy or any inherited condition, that could be transferred to the recipient by transplant	Yes
Evaluate for recent immunization and vaccination history	Yes

History and Behavioral Risk for Exposure to the Following Infectious Agents or Diseases[1,2]:	
HIV	Yes
HBV	Yes
HCV	Yes
HTLV (viable, leukocyte-rich products only)	Yes
Syphilis	Yes
WNV[4]	Yes
Vaccinia (smallpox vaccine)	Yes
Human TSEs	Yes
Malaria (travel or residence in malaria-endemic areas)[5]	Yes
Trypanosoma cruzi (Chagas disease)[5]	Yes
Sepsis	Yes
Zika[6]	Yes

III. Laboratory Testing [2, 7]

HIV-1/2	Yes
HBV	Yes
HCV	Yes
Syphilis	Yes
HTLV-I/II (viable, leukocyte-rich products only)	Yes
CMV (viable, leukocyte-rich products only)	Yes
WNV[4]	Yes
Trypanosoma cruzi (Chagas disease)[5]	No
Zika[6]	No

[1]Relevant medical records as described in 21 CFR 1271.3(s).
[2] Required for cord blood or gestational materials with the potential for allogeneic use
[3] The relevant communicable disease agents or diseases are described in 21 CFR 1271.3(r)(1)(i)(ii) and 1271.3(r)(2)
[4] In the United States, West Nile virus is considered a relevant communicable disease agent or disease as defined under 21 CFR 1271.3(r)(2) by the FDA Guidance for Industry **"**Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)", August 2007. Testing is per Guidance for Industry, "Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Living Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)", September 2016, corrected May 2017.
[5]As of this date, in the United States, the FDA does not consider these risk factors to render donors ineligible; facility policies must define how health history risks identified and the test results for these diseases affect eligibility determination.
[6] In the United States Zika virus is considered a relevant communicable disease agent or disease as defined under 21 CFR 1271.3(r)(2) by the FDA. Guidance for Industry "Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products, March 2016, updated May 2018
[7] In the United States, perform tests for relevant communicable disease agents or diseases as required by the FDA and interpret positive/reactive test results as described in 21 CFR 1271.80(d)(1).

HIV = human immunodeficiency virus; HBV = hepatitis B virus; HCV = hepatitis C virus; HTLV = human T-cell lymphotropic virus; WNV = West Nile virus; TSEs = transmissible spongiform encephalopathies; CMV = cytomegalovirus (anti-CMV, IgG, and IgM); CBC = complete blood count.

These *CT Standards* are minimum requirements and are not meant to preempt any local or FDA or relevant Competent Authority regulations that may be more stringent. Standard 5.12.2.6 applies.

Reference Standard 5.12E—Clinical Evaluation and Laboratory Testing of Cadaveric Donors

I. Clinical Evaluation to Protect the Safety of the Recipient[1]	**Required (Yes/No)**
Donor screening for clinical and physical evidence of risk for, or symptoms of, relevant communicable disease.[2]	Yes
Risk of any condition, such as malignancy or any inherited condition that could be transferred to the recipient by transplant.	Yes
Evaluate for recent immunization and vaccination history	Yes
Coroner and/or autopsy report (if available)	Yes

History and Behavioral Risk for Exposure to the Following Infectious Agents or Diseases[1]:	
HIV	Yes
HBV	Yes
HCV	Yes
HTLV (viable, leukocyte-rich products only)	Yes
Syphilis	Yes
WNV[3]	Yes
Vaccinia (smallpox vaccine)	Yes
Human TSEs	Yes
Malaria (travel or residence in malaria-endemic areas)[4]	Yes
Trypanosoma cruzi (Chagas disease)[4]	Yes
Sepsis	Yes
Zika[5]	Yes

II. Laboratory Testing[6]	
HIV-1/2	Yes
HBV	Yes

HCV	Yes
Syphilis	Yes
HTLV-I/II (viable, leukocyte-rich products only)	Yes
CMV (viable, leukocyte-rich products only)	Yes
HLA Type, if applicable[7]	Yes
ABO/Rh, if applicable[7]	Yes
WNV [3]	No
Trypanosoma cruzi (Chagas disease)[4]	No
Zika[5]	No

[1]Relevant medical records as described in 21 CFR 1271.3(s).
[2]The relevant communicable disease agents or diseases are described in 21 CFR 1271.3(r)(1)(i)(ii) and 1271.3(r)(2)and physical assessment is described at 1271.3(o). Standard 5.12.2.5 applies.
[3] In the United States, West Nile virus is considered a relevant communicable disease agent or disease as defined under 21 CFR 1271.3(r)(2) by the FDA Guidance for Industry "Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps), August 2007**.**
[4]As of this date, the FDA does not consider these risk factors to render donors ineligible; facility policies must define how health history risks identified and the test results for these diseases affect eligibility determination.
[5] In the United States Zika virus is considered a relevant communicable disease agent or disease as defined under 21 CFR 1271.3(r)(2) by the FDA. Guidance for Industry "Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products, March 2016, updated May 2018
[6]In the United States, perform tests for relevant communicable disease agents or diseases as required by the FDA and interpret positive/reactive test results as described in 21 CFR 1271.80(d)(1).
[7]Testing shall be performed whenever this information is necessary for the selection and/or clinical use of a cellular therapy or tissue product.

HIV = human immunodeficiency virus; HBV = hepatitis B virus; HCV = hepatitis C virus; HTLV = human T-cell lymphotropic virus; WNV = West Nile virus; TSEs = transmissible spongiform encephalopathies; CMV = cytomegalovirus (anti-CMV, IgG and IgM); CBC = complete blood count.

These *CT Standards* are minimum requirements and are not meant to preempt any local or FDA or relevant Competent Authority regulations that may be more stringent. Standard 5.12.2.6 applies.

Reference Standard 5.17A—Processing Tests for HPC, Apheresis, and HPC, Marrow

The following processing tests shall be performed on each cellular therapy product at defined steps during processing:

1) Cell count and viability specific to the cellular therapy product. This includes:
   a) Total nucleated cell count.
   b) CD34+ cell count.

2) Microbial contamination (culture for aerobic and anaerobic bacterial and fungal elements) at the completion of processing.
   a) Notify the recipient's physician of positive culture results.
   b) If results affect the donor's health, as determined by the appropriate medical director, notify the donor's physician.
   c) If the results affect the therapeutic value of the product or the recipient's health, as determined by the appropriate medical director, notify the recipient's physician of positive culture results.

3) ABO grouping and Rh typing shall be performed on a cellular therapy product or donor sample obtained at the time of procurement and compared to previous records.

Reference Standard 5.17B—Processing Tests for HPC, Cord Blood

1) Testing for ABO group and Rh type shall be performed on the cord blood obtained before cryopreservation.

2) HLA testing shall be performed on all products designated for possible allogeneic use. The test shall be performed on a sample obtained from the product or from the donor. At a minimum, *HLA-A*, *HLA-B*, and *HLA-DRB1* loci shall be determined using DNA-based technologies.

3) The following processing tests shall be performed on a sample obtained after processing but before the addition of cryoprotectant:
   a) Total nucleated cell count.
   b) Total nucleated cell and/or CD45 viability
   c) CD34 cell enumeration.
   d) Nucleated red cell count or corrected total nucleated cell count)

4) Tests for microbial contamination (culture for aerobic and anaerobic bacterial and fungal elements) shall be performed on a sample obtained after processing and before the addition of cryoprotectant solution if the cryoprotectant is cultured separately or purchased as sterile and connected as closed system.

   Otherwise, microbial testing shall be performed after the addition of the cryoprotectant. For products cryopreserved for possible future use, speciation and antibiotic drug sensitivities shall be performed.

   If results affect the donor's health as determined by the appropriate medical director, notification of the positive culture results shall be given to:

   a) the mother's physician or; if a physician is not identified, notify the mother
   b) the recipient's physician.

   If the results affect the therapeutic value of the product or the recipient's health, as determined by the appropriate medical director, notify the recipient's physician of positive culture results.

5) The following tests shall be performed before issue:
   a) Confirmatory HLA testing on a sample obtained from an integrally attached segment for autologous and allogeneic cord blood products.
   b) If used for hematopoietic reconstitution, hemoglobinopathy testing of allogeneic cord blood units on a sample obtained from the product or from the donor.

c) Viable CD34 assay (direct measurement) after cryopreservation from an integrally attached segment on products that will be used for hematopoietic reconstitution.

d) Other tests as required by the applicable registry.

6) Testing of cultured cells shall include endotoxin and mycoplasma testing, unless not required under an Investigational New Drug (IND) or license application or as approved by the FDA or relevant Competent Authority.

Reference Standard 5.17C—Processing Tests for Cellular Therapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood

The following processing tests shall be performed on each cellular therapy product at defined steps during processing:

1) If the final product contains red cells, testing for ABO group and Rh type shall be performed before cryopreservation.

2) Testing specific to the cellular therapy product shall include:

   a) For T cells, CD3+ cell count.
   b) For islets, islet equivalents (IEQ).
   c) For other cellular therapy products the relevant cell count shall be defined by the facility, when applicable.
   d) Cell viability, when applicable.

3) Microbial contamination (culture for aerobic and anaerobic bacterial and fungal elements) at the completion of processing.
   a) If results affect the donor's health, as determined by the appropriate medical director, notify the donor's physician.
   b) If the results affect the therapeutic value of the product or the recipient's health, as determined by the appropriate medical director, notify the recipient's physician of positive culture results.

4) Characterization of cell identity analysis specific to the cellular therapy product, if applicable.

5) Functional assay specific to the cellular therapy product, as applicable.
   a) Relevant potency assay shall be defined by the facility

6) If the final product contains red cells, after receipt or before administration, ABO grouping and Rh typing shall be performed on a cellular therapy product or donor sample obtained at the time of procurement and compared to previous records.

7) Sterility testing of cultured cells shall include endotoxin and mycoplasma and other relevant assays, unless not required under an Investigational New Drug (IND) or license application or as approved by the FDA or relevant Competent Authority).

8) Characterization of cell product purity as required by an IND or license application or as approved by the FDA or relevant Competent Authority.

6. DOCUMENTS AND RECORDS

6.0 Documents and Records

The facility shall have policies, processes, and procedures to ensure that documents are identified, reviewed, approved, and retained and that records are created, stored, and archived in accordance with record retention policies.

6.1 Document Control

The facility shall establish, implement, and maintain policies, processes, and procedures to control all documents that relate to the requirements of these *CT Standards*. Documents shall be protected from unauthorized access and accidental or unauthorized modification, deletion, or destruction.

6.1.1 Format

Policies, processes, and procedures established by the facility shall be in standardized formats. Additional policies, processes, and procedures (such as those in an operator's manual) may be incorporated by reference.

✎C 6.1.2 Document Review, Approval, and Distribution

The facility shall review and approve all controlled documents before use. The document control process shall ensure that policies, processes, and procedures:

1) Are reviewed by personnel trained and/or qualified in the subject area.
2) Are approved by an authorized individual.
3) Are identified with the current version and effective date.
4) Are available at all locations where operations covered by these *CT Standards* are performed.
5) Prevent the use of invalid or obsolete documents.
6) Suitably identify any archived or obsolete documents as such.

✎C 6.1.3 Document Changes

6.1.3.1 Changes to documents shall be reviewed and approved by an authorized individual before new and/or revised procedures become effective.

6.1.3.2 The facility shall have processes to track changes to documents.

✎C 6.1.4 List of Documents

The facility shall maintain complete lists of all active policies, processes, procedures, labels, forms, and other documents that relate to the requirements of these *CT Standards*.

C **6.1.5 Review of Policies, Processes, and Procedures**

Review of each policy, process, and procedure shall be performed by an authorized individual at a minimum every 2 years.

C **6.1.6 Document Retention**

The facility shall determine which documents shall be archived, destroyed, or made obsolete.

6.1.6.1 Documents shall be stored in a manner that preserves integrity and legibility; protects from accidental or unauthorized access, loss, destruction, or modification; and is accessible and retrievable.

6.1.7 Document Retrieval

The facility shall ensure that documents are retrievable in a timely manner, as defined by the facility.

6.2 Record Control

6.2.1 Original Records

The facility shall establish and maintain policies, processes, and procedures for identification, collection, indexing, accessing, filing, storage, maintenance, and disposition of original records. All records identified in Reference Standard 6.2.1A, Retention of Records, shall be retained.

6.2.1.1 Record Traceability

The records system shall ensure the traceability by maintaining chain of identity and chain of custody of all of the following:

1) Critical activities performed.
2) The individual who performed the activity.
3) Date the activity was performed.
4) Time the activity was performed, if applicable.
5) Results obtained.
6) Method(s) used.
7) Equipment used.
8) Critical materials used.
9) The facility where the activity was performed.

6.2.2 Information to Be Retained

Records shall be maintained that demonstrate that a material, product, or service conforms to specified requirements and that the quality system is operating effectively. Records from suppliers shall be an element of this information.

6.2.3 Legibility
All records shall be legible and indelible.

✎*C* **6.2.4 Record Change**
Facilities shall establish and maintain processes for changing records. The date and identity of the person making the change shall be recorded. Record changes shall not obscure previously recorded information.

6.2.4.1 Modifications or changes that can affect the safety of the recipient or quality of the cellular therapy product shall be approved by the authorized individual. Chain of identity shall be maintained.

✎*C* **6.2.5** The actual result of each action performed shall be recorded immediately, and the final interpretation shall be recorded upon completion of testing.

6.2.6 Records shall be created concurrently with the performance of each critical activity. The record shall identify the work performed, the individual performing the activity, and when it was performed.

✎*C* **6.2.7 Copies**
Before the destruction of the original records, copies of records shall be verified as containing the original content and shall be legible, complete, and accessible.

6.2.8 Confidentiality
The facility shall have policies that ensure the confidentiality and privacy of donor, employee, and patient records.

6.2.9 Retention
Records required by these *CT Standards* shall be retained for at least 10 years following either their creati©(C) or the final disposition (F) of the cellular therapy product with which they are associated. Applicable FDA or relevant Competent Authority, or local law may exceed this period.

6.2.9.1 If the date of administration is unknown, records shall be retained for 10 years after the date of distribution, disposition, or expiration, whichever is latest. Applicable FDA or relevant Competent Authority, or local law may exceed this period.

✎*C* **6.2.10 Record Review**
Records shall be reviewed for accuracy, completeness, and compliance with applicable standards, laws, and regulations.

6.2.11 Storage of Records
Records shall be stored to:

1) Preserve record legibility and integrity for the entire retention period.
2) Protect from accidental or unauthorized access, loss, deterioration, damage, destruction, mix-up, or modification.
3) Permit ready identification
4) Allow retrieval in a defined timeframe.

6.2.12 Destruction of Records
Destruction of records shall be conducted in a manner that protects the confidential content of the records.

***C*6.3Electronic Records**

6.3.1 Access to Data and Information
Access to data shall be controlled. Unauthorized access to and release of data and information shall be prevented.

6.3.1.1 Individuals shall be identified and defined by job description that are authorized to create, modify, maintain or transmit records in a controlled and approved manner in conformance with the FDA or relevant Competent Authority requirements.

C **6.3.1.1.1** Electronic records shall include the date and identity of the person making a change.

6.3.2 Data Integrity
Data integrity shall be maintained to ensure that data are retrievable and usable.

6.3.2.1 Data shall be accurately and reliably sent from the point of entry to final destination in a timely manner.

6.3.2.2 Data shall be retrievable for the entire retention period.

6.3.2.2.1 The facility shall have a process to access archived records on media and platforms no longer in use.

6.3.3 Storage Media
Data storage media shall be protected from damage or unintended destruction.

6.3.4 Backup Data
The facility shall define and routinely back up all critical data.

6.3.4.1 Backup data shall be stored in a secure off-site location.

6.3.4.2 Backup data shall be protected from unauthorized access, loss, or modification.

6.3.4.3 The ability to retrieve data from the backup system shall be tested at defined intervals.

Reference Standard 6.2.1A—Retention of Records

Item No.	Relevant Standard	Record to Be Retained	Retention After Creation or Final Disposition of Related Product
General Quality System Records			
1	1.0	Responsibility, authority, and relationship of personnel who perform, verify, or manage work covered by the *CT Standards*	C
2	1.1.3.1	Procurement medical director management or review of 10 cell procurement procedures	C
3	1.1.4.1.1	Laboratory medical director management or review of 10 cell product processing procedures	C
4	1.1.4.2.1	Laboratory director management or review of 10 cell product processing procedures	C
5	1.1.5.2.1	Relevant continuing education of the clinical program director	C
6	1.2.2	Established quality system	C
7	1.2.3.1	Policies, processes, and procedures (current and obsolete archived versions) and other documentation related to the quality system	C
8	1.2.3.2	Procurement medical director review and approval of all medical policies, processes, and procedures	C
9	1.2.3.3	Laboratory medical director review and approval of all medical policies, processes, and procedures	C
10	1.2.3.4	Laboratory director review and approval of all technical policies, processes, and procedures	C
11	1.2.3.5	Clinical program director review and approval of all clinical policies, processes, and procedures	C
12	1.2.4.1, 1.2.4.2	Quarterly reports by quality representative to executive management	C
13	1.2.5	Executive management review of the quality system and related reports	C
14	1.3	Emergency operation plans to respond to the effects of disasters and other emergencies	C
15	1.5	Level of risk associated with facility activities	C
16	2.1.1	Job qualifications for each position	C

17	2.1.2	Records of names, signatures, initials or identification codes, and inclusive dates of employment	C
18	2.1.3	Job descriptions for each position	C
19	2.1.4,	Identification of training needs and provisions of training for all personnel who perform activities that affect product or service quality; identification of qualifications required for trainers	C
20	2.1.5	Personnel records of each employee	C
21	2.1.6	Evaluations of competence	C
22	2.1.7, 2.1.7.1	Continuing education (definition of requirements and verification of fulfillment) of all employees	C
23	3.2	Qualification and requalification of equipment for intended use	C
24	3.4.1	Equipment calibration activities	F
25	3.4.2	Equipment found to be out of calibration	F
26	3.4.3	Equipment monitoring, maintenance, and repair	F
27	3.5	Equipment traceability	F
28	3.6	Implementation and modification of software, hardware, or databases	F
29	3.6.1.1	Testing of alternative systems	F
30	4.1	Review of agreements before acceptance and at facility-defined intervals	F
31	4.2	Agreement changes communicated to affected parties	F
32	4.3.1	Agreements for the timing and responsibility of medical orders	F
33	4.3.3	Agreements between departments or facilities regarding the transfer of products	F
34	4.3.4	Agreements for the collection, transport, receipt, handling, and administration of the cellular therapy product, reporting adverse events, and obtaining outcome data	F
35	4.3.5	Agreement between processing/issuing facility and the administering facility or registry for creation and retention of records; agreements for each facility to access relevant records	C
36	4.3.6	Agreements between more than one facility is involved.	C
37	4.3.7	Conditions for product storage and disposition	C
38	4.4	Claims in educational and promotional materials	F
39	4.5	Donor informed consent	F
40	4.6	Authorization for cadaveric donors	F
41	4.7	Patient informed consent	F

42	4.8.1, 4.8.2	Evaluation, qualification, and selection of suppliers of materials, services, and products	F
43	4.8.3	Monitoring of suppliers (including reporting to management of a supplier's failures to meet specified requirements)	F
44	4.8.4	Notification of shipping facility and manufacturer (if applicable) when materials are received in an unacceptable condition	C
45	5.1.2	Participation in an external proficiency testing program	C
46	5.1.2.3	Proficiency testing results reviewed by the medical or laboratory director.	C
47	5.2, 5.2.1, 5.2.2, 5.2.3, 5.2.4	Process change control, development/validation, and implementation of novel methods	C
48	5.3	Outcomes data	F
49	5.4	Quality control	C
50	5.5	Qualification of all materials used in the procurement, processing, and/or administration of cellular therapy products	C
51	5.5.5	Validation and monitoring of equipment, materials, and methods used in cleaning and sterilization of non-single-use materials	C
52	5.5.6	Use of and identification of critical materials that come into contact with the patient or cellular therapy product	F
53	5.5.6.1	Package inserts, certificates of analysis, or any manufacturer's documentation, including recall or defect notices, advisories, etc, for all critical materials used	C
54	5.9.2	Qualification of shipping containers and periodic requalification	C
55	5.10	Inspection and testing activities	C
56	5.11.1	Storage area temperature and humidity	C
57	5.11.1.1	If cellular therapy products are stored in an open storage area, the ambient temperature shall be recorded at least every 4 hours.	C
58	5.11.3, 5.11.4	Monitoring of temperature and/or liquid nitrogen levels in storage devices and documentation of alarm activation	C
59	5.14.1	Medical orders for procurement	F
60	5.17.1	Medical orders for processing, preservation, or storage	F

61	5.20	Stability program for each type of cellular therapy product and expiration dates	F
62	5.21	Disposition of products consistent with informed consent and laws and regulations	F
63	5.26.1.2	Medical orders for administration	F
64	6.1.2	Document control, including review and approval of all documents before use	C
65	6.1.3	Review and approval of changes to documents	C
66	6.1.4	List of all active policies, processes, procedures, labels, and forms	C
67	6.1.5	Biennial review of each policy, process, or procedure	C
68	6.1.6	Documents that are archived, destroyed, or made obsolete	C
69	6.2.4	Record change	C
70	6.2.5	Result of each action performed and the final interpretation	C
71	6.2.7	Verification that copies of records contain the original content and are legible, complete, and accessible before the original records are destroyed	C
72	6.2.10	Review of records for accuracy, completeness, and compliance with applicable standards, laws, and regulations	C
73	6.3	Electronic records	C
74	6.3.1.1.1	Electronic records include date and identity of person making the change	C
75	7.0	Capture, investigation, assessment, and reporting of failures to meet internal or external requirements	F
76	7.2	Identification, documentation, evaluation, segregation, and disposition of nonconforming materials and products	F
77	7.2.1.3	Impact of noconforming products on purity, potency, safety or efficacy of the product.	F
78	7.2.2.2	Authorized release of nonconforming products	F
79	7.3.	Detection, reporting, and evaluation of procurement-related donor adverse events	F
80	7.3.2	Evaluation reported adverse events.	F
81	7.3.3	Detection, reporting, evaluation, and treatment of administration-related recipient adverse events	F
82	8.1	Results of internal assessments	F
83	8.2	Participation in external assessment program	C

84	8.3	Reporting of assessment results to executive management; corrective and preventive actions (or other actions) taken in response to results of assessments	C
85	8.4	Monitoring of clinical activities	C
86	9.1, 9.2	Corrective and preventive actions	C
87	10.1.3.1.1	Alarm investigation	F
88	10.2.1.1	Environmental monitoring	C
Records Pertaining to Donor Eligibility/Management Issues			
89	5.12,5.12.2.2	Determination of donor eligibility and verification that procurement criteria (eg, informed consent) have been met, in conformance with Reference Standards 4.5A, 5.12A, 5.12B, 5.12C, 5.12D, and 5.12E	F
90	5.12.2.2	Infectious disease testing of donors	F
91	5.12.2.3	Cadaveric donor eligibility	F
92	5.12.2.4	Donor testing shall be performed in conformance with Reference Standards 5.12B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.12C Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.12D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Materials Donors; and 5.12E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors.	F
93	5.12.4	Review of donor screening and infectious disease testing record before international shipment or transport	F
94	5.12.5	Final determination of donor eligibility	F
95	5.12.6.2	Communication of abnormal results on medical history screening or testing that may affect the donor's health	F
96	5.12.6.3	Communication of abnormal results on medical history screening or testing that may affect the recipient's health or the therapeutic value of the cellular therapy product	F
97	5.12.6.4	Ineligible donors	C
98	5.12.7	Products from ineligible donors	F
99	5.12.8	Incomplete donor eligibility determination for donors not screened or tested	F
100	5.12.8.2	Physician notification of incomplete donor eligibility	C
101	5.13.2	Central venous access device placement by qualified individual or physician	C
102	5.13.3.1	Evaluation of allogeneic and autologous donors for the risk of hemoglobinopathy before the administration of a mobilizing agent	C

103	5.14.2.2, 5.14.2.4	Final approval and documentation by the donor's physician (or by a health-care professional, if appropriate) that the donor is able to proceed with donation in conformance with Reference Standard 5.12A, General Requirements for Cellular Therapy Product Donors	F
104	5.14.2.3	For donors of mobilized cells (apheresis), a complete blood count obtained within 24 hours before each procurement procedure; for marrow donors, a complete blood count obtained before procurement	C
105	5.14.4	Confirmation of donor identity, at the time of procurement, by two identifiers	F
106	5.14.5	Identification numbers and expiration dates of lot numbers of all disposables and additives used in procurement	F
107	5.14.5.1, 5.14.6	Complete procurement record; review of procurement record	F
Records Pertaining to the Unit/Recipient			
108	4.3.9	Shipment of cellular therapy products	F
109	5.3.6.1	Notification by patient-care service to issuing or processing facility of adverse events	F
110	5.5.2.1	Complete records of the inspection of incoming materials that come into contact with the cellular therapy product or that directly affect the quality of the product	C
111	5.5.2.2	Identification of materials used on an emergency basis	C
112	5.5.4	Inspection of in-house reagents	C
113	5.6.2.1	Monitoring and review of the effectiveness of aseptic methods	C
114	5.7.1	Unique identification and traceability of cellular therapy products and samples from source to final disposition	C
115	5.8 #2, 3, 5	Labeling controls;	C
116	5.8.1	ISBT 128 implementation	C
117	5.8.3	Verification of product packaging and labeling	C
118	5.9	Transport of products	F
119	5.9.3	Monitoring of temperature for noncryopreserved products	F
120	5.9.3.1	Continuous monitoring of temperature for cryopreserved products	F
121	5.9.6	Product acceptance and shipper temperature upon receipt	C
122	5.10.1	Inspection of incoming cells, tissues, and organs	C

123	5.10.2	Inspection and testing of products during processing	C
124	5.11.4	Investigation and resolution when alarms on storage devices are activated	C
125	5.15	Definition of procurement endpoints	F
126	5.17.2, 5.17.3	Complete processing record; verification that acceptable values or ranges for defined critical characteristics for each product were obtained	F
127	5.17.4	Procedures used to manage red cell antigen incompatibility	F
128	5.18	Product-specific specifications and acceptable storage conditions of noncryopreserved products	C
129	5.19.2.1.1	Segment identification by two individuals	C
130	5.19.3	Complete cryopreservation records	F
131	5.22.2, 5.22.2.3	Review of donation criteria, final processing criteria, and final product-specified requirements	F
132	5.23	Request for distribution	C
133	5.24	Product issue	F
134	5.24.1, 5.28.2	Review of criteria for issue	F
135	5.26	Clinical care of the recipient	F
136	5.27	Preparation of the recipient for administration of the cellular therapy product	F
137	5.29	Confirmation of identity of the product and the intended recipient, using at least two identifiers	F
138	5.29.4	Identification of adverse events occurring during the infusion of final cellular therapy products and communication to the issuing facility	F
139	5.29.5, 5.29.6	Complete administration record and recipient records	F

7. DEVIATIONS, NONCONFORMING PRODUCTS OR SERVICES, AND ADVERSE EVENTS

***F*7.0 Deviations, Nonconforming Products or Services, and Adverse Events**
The facility shall have policies, processes, and procedures to capture, monitor, investigate, assess, and report deviations, nonconforming products or services, and adverse events.

7.1 Deviations

7.1.1 Deviations shall be reported as soon as possible after detection.

7.1.2 Deviations shall be evaluated to determine the need for corrective and preventive action. Standards 9.1 and 9.2 apply.

7.1.3 For deviations having the potential to adversely affect the safety, purity, or potency of a product; donor safety; employee safety; or the safety of a patient, approval of an individual qualified to evaluate the deviation shall be obtained before final release of the product.

7.1.3.1 The release approval shall be made by the procurement medical director, the laboratory medical director, the laboratory director, clinical program director, and/or the patient's physician, depending upon the circumstances.

***F*7.2 Control of Nonconforming Products or Services**
The facility shall establish and maintain policies, processes, and procedures to prevent the unintended use or release of nonconforming materials, products, or services. This control shall provide for identification, documentation, evaluation, segregation (when appropriate), and disposition of nonconforming materials and products.

7.2.1 Product Review, Investigation and Lookback
The facility shall have policies, processes, and procedures to identify nonconforming products and the initiation of a lookback investigation as soon as possible.

7.2.1.1 Customer Notification
The facility shall report to the customer:
1) Any cellular therapy products lost, damaged, or otherwise unsuitable for use.
2) Released products or delivered services that are determined to be nonconforming, as soon as possible.

7.2.1.2 Products identified as nonconforming following distribution shall be reported to the FDA or relevant Competent Authority in accordance with written policies, processes, and procedures.

F **7.2.1.3** Customers shall be notified when the nonconforming products can impact the purity, potency, safety or efficacy of the product.

7.2.2 Review and Disposition of Nonconforming Products and Services
Authority for determining disposition of nonconforming products and review of nonconforming services shall be defined.

7.2.2.1 A nonconforming material or product shall be handled in one of the following ways:
1) Reworked to meet the specified requirements.
2) Accepted by the customer, after disclosure of the nonconformance.
3) Relabeled, in conformance with applicable requirements.
4) Destroyed.

F **7.2.2.2 Authorized Release of Nonconforming Products**
A nonconforming product shall be released by exception only when there is a documented clinical need for the product and when approved by the medical director.

7.2.2.2.1 The following are required:
1) Notification to the recipient's physician of the out-of-specification or nonconforming values or results.
2) Documentation of the recipient's physician's approval for use of the product. Standard 5.25.1 applies.

7.2.3 Microbially Contaminated Products
The facility shall have policies, processes, and procedures addressing the management of cellular therapy products with positive microbial culture results, including:
1) Product labeling.
2) Investigation of cause.
3) Notification of other facilities and/or departments involved in procurement, processing, and distribution of the product.
4) Notification of the donor's physician, if it affects the donor's health.
5) Notification of recipient's physician.
6) Recipient follow-up and outcome analysis.
7) Reporting to regulatory agencies, if appropriate.

7.3 Adverse Events

✎*F* **7.3.1** The procurement facility shall have a process to detect, monitor, evaluate, manage, and report donor adverse events.

✎*F* **7.3.2** The clinical facility shall have a process to detect, monitor, evaluate, manage, and report recipient adverse events related to the cellular therapy. Standard 5.30 applies

✎*F* **7.3.3** The processing facility shall have a process to evaluate reported adverse events.

7.3.4 Records of adverse events and the related investigations, evaluations, and notifications shall be maintained.

7.3.5 Investigation results and analysis shall be communicated among all facilities involved in the procurement, processing, and administration, as appropriate.

7.4 Reporting

Reporting of deviations, nonconforming products, and adverse events shall be in accordance with the facility's policies, these *CT Standards*, and applicable laws and regulations.

8. INTERNAL AND EXTERNAL ASSESSMENTS

8.0 Internal and External Assessments

The facility shall perform assessments that verify that the quality system and operational activities comply with specified requirements.

✎C 8.1 Internal Assessments

The facility shall establish, implement, and maintain policies, processes, and procedures for scheduling, conducting, documenting, and reviewing internal assessments. Internal assessments shall be performed by personnel independent of those having direct responsibility for the activity being assessed.

✎C 8.2 External Assessments

The facility shall participate in an external assessment program applicable to the activities performed in the facility. Standard 1.0 applies.

✎C 8.3 Management of Assessment Results

The results of assessments shall be:

1) Reviewed by the personnel having responsibility for the area assessed.
2) Evaluated to determine the need for corrective and preventive action (Chapter 9, Process Improvement, applies).
3) Communicated to the appropriate staff.
4) Reported to executive management.

✎C 8.4 Monitoring Clinical Activities

Facilities performing clinical activities shall have a program that addresses, evaluates, and monitors patient care practices for all cellular therapies. The following shall be monitored:

1) Ordering practices.
2) Patient identification.
3) Sample collection and labeling.
4) Medication errors.
5) Near-miss events.
6) Adverse events.
7) Ability of services to meet patient needs.
8) Compliance with peer-reviewed recommendations.
9) Adherence to research protocols or investigator's brochures, if applicable.
10) Critical process points (eg, hand-offs, confirmation of patient identification before medical intervention) for conformance with policies, processes, procedures, and protocols.

8.5 Quality Monitoring

The facility shall have a process to collect and evaluate quality indicator data on a scheduled basis, including adverse events. Standard 1.2.4 applies.

9. PROCESS IMPROVEMENT

9.0 Process Improvement

The facility shall establish, implement, and maintain policies, processes, and procedures for corrective and preventive action plans to address the root cause of deviations and nonconformances. Management shall review relevant information on corrective or preventive actions taken. Any corrective or preventive actions taken to eliminate the causes of actual or potential nonconformances shall be proportional to the magnitude of problems and the risks encountered.

✎*F*9.1 Corrective Action

The process for corrective action shall include:

1) Investigation of the root cause of nonconformances relating to the product, the process, and the quality system.
2) Investigation of complaints.
3) Determination of the corrective action needed to eliminate the cause of nonconformances.
4) Ensuring that corrective action is reviewed and found to be effective.

✎*F*9.2 Preventive Action

The process for preventive action shall include:

1) The analysis of appropriate sources of information (such as policies, processes, and procedures that affect product or service quality, assessment results, proficiency testing results, quality control records, customer complaints, and other aggregate data) to detect, analyze, and eliminate potential causes of nonconformances.
2) Determination of steps needed to address any problems requiring preventive action.
3) Initiation of preventive action and application of controls to ensure that it is effective.

9.3 Performance Improvement

The facility shall track and identify trends in information related to its operational and quality system performance to identify opportunities for improvement. Standard 5.3 applies.

10. SAFETY AND FACILITIES

10.0 Safety and Facilities

The facility shall establish and maintain policies, processes, and procedures designed to minimize risks to the health and safety of employees, donors, patients, volunteers, and other persons affected within the work environment. Suitable quarters, environment, and equipment shall be available to maintain safe operations. FDA or relevant Competent Authority or local regulations apply. Standard 2.1.4 applies.

10.1 Safety

10.1.1 Policies, processes, and procedures shall identify and address the hazards present in the facility—including biological, chemical, and, where applicable, radiation safety—and appropriate intervention to limit exposure and shall include a system for monitoring training and compliance.

10.1.2 Biohazardous materials shall be handled and discarded in a manner that minimizes the potential for human exposure to infectious agents.

10.1.3 Where liquid nitrogen is present, specific hazards shall be addressed.

10.1.3.1 The facility shall have a system in place to monitor oxygen levels and an alarm system set to activate under conditions that will allow action to be taken.

✎***C*** **10.1.3.1.1** Alarm activation shall require personnel to investigate and document the condition activating the alarm and to take immediate corrective action as necessary.

10.2 Facilities

The facility shall be designed to ensure donor, patient, employee, and product safety and shall be suitable for the activities performed. Standard 5.6 applies.

10.2.1 Environmental Controls

The facility shall design, approve, and implement an environmental control system that monitors the following conditions:

1) Optimizes donor, patient, and employee safety.
2) Ensures product integrity and safety.
3) Minimizes contamination or accidental exposure to infectious disease agents.

C **10.2.1.1** The degree of environmental monitoring shall be specific to the cellular therapy product manipulation performed.

10.2.2 The clinical facility shall have either onsite or ready access to services to manage anticipated adverse events and provide emergency medical care.

10.3 General Operational Controls

Access to facilities used for procurement, processing, preservation, and storage shall be limited to authorized individuals.

GLOSSARY

Active Labor: A period characterized by regular painful uterine contractions, a substantial degree of cervical effacement and more rapid cervical dilatation from 5 cm until full dilatation for first and subsequent labors.

Administration: With respect to cellular therapy products, the act of delivering the product into a recipient, including, but not limited to, infusion, transplantation, implantation, or injection.

Adverse Event: A suspected or proven unfavorable response to the procurement or administration of cellular therapy products, manifested by signs or symptoms.

Advocacy: A service whereby an impartial individual or a team who has/have working knowledge of cellular therapy and whose interest is centered on the well-being of the subject and speaks on the subject's behalf. The subject could be a donor or recipient. The service helps the subject understand the process, procedures, and the potential risks or benefits.

Agreement: A contract, order, or understanding between two or more parties, such as between a facility and one of its customers. Agreements can be written or verbal, with verbal agreements documented (eg, a written summary of the agreement should be available).

Agreement Review: Systematic activities carried out by two or more parties before finalizing the agreement to ensure that requirements are adequately defined, free from ambiguity, documented, and achievable by the supplier.

Allogeneic Donor: An individual from whom cellular therapy products intended for another person are procured. This individual may or may not be genetically related to the recipient.

Analyte: Substance or chemical constituent that is assayed.

Aseptic Methods: Methods designed to eliminate the risk of microbial contamination to a product, reagent, sample, or person in a laboratory or clinical-care setting.

Assessment: A systematic and independent examination to determine whether activities comply with planned activities and whether these activities are implemented effectively and are suitable to achieve objectives. Assessments also include comparison of results to expected results. Types of assessments include external assessments, internal assessments, peer reviews, and self-assessments.

Attributes: Additional characteristics that uniquely define a cellular therapy product.

Authorization (in relation to procurement from cadaveric donors): A legal record providing permission for postmortem recovery of cells/tissues and subsequent use.

Autologous Donor: A person who acts as his or her own cellular therapy product donor.

Available for Distribution: The determination that a product has met all relevant requirements (eg, donor eligibility, product processing, etc) and can be issued for clinical use.

Bacteremia: Systemic inflammatory response due to an infectious agent and accompanied by characteristic clinical and laboratory findings.

Bioassay: A measurement of the concentration or potency of a substance by its effect on living cells or tissues.

Biologic Agent: A biologic agent is a protein-based substance that is made from a living organism or its products and is used in the prevention, diagnosis, or treatment of cancer and other diseases. Biologic agents include antibodies, interleukins, and vaccines.

Biologic Mother: The female who is the source of the ovum.

Birth Mother: The female carrying the fetus to term.

By-Products: Portions of the original cellular therapy product retained for nonclinical use. Examples include cell fractions and removed plasma.

Cadaveric Donor: A deceased donor from whom cellular therapy products or organs are procured. If donation occurs following cardiac death, infectious disease testing must be performed using test kits that are specifically cleared or approved for use in cadaveric donors.

Calibrate: To set or align measurement equipment against a known standard.

Cellular Starting Materials (CSM): Cellular therapy products that may be further modified through various techniques such as processing, selection, expansion, gene-editing, and other combinations of engineering for therapeutic benefit.

Cellular Therapy Product: Cell-based products that may be minimally or more than minimally manipulated, including cellular immunotherapies, regenerative medicines, and other types of autologous and allogeneic tissues or cells.

Certified by Centers for Medicare and Medicaid Services (CMS): Having met the requirements of the Clinical Laboratory Improvement Amendments of 1988 through inspection by the CMS, a deemed organization, or an exempt state agency.

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

Chain of Identity (COI): 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.

Characterization: A cell's identity by the expression, or activity, of certain genes in its DNA and the resulting production of particular proteins.

Clinical Activities: The tasks performed by integrated patient care teams linked by a uniform quality management system and reflected in the organizational structure.

Clinical Facility: The facility(ies) responsible for the administration of the product and related patient care activities.

Clinical Program Director: A qualified physician who is board certified and licensed to practice medicine in at least one specialty or subspecialty and who is responsible for all aspects of the clinical program.

Combined Cellular Products: Products that come from two or more different cell sources.

Competence: Ability of an individual to perform a specific task according to procedures shall be evaluated on an ongoing basis.

Competent Authority: The agency responsible under its national law for regulations applicable to cellular therapy.

Completion of Processing: The point in processing at which no further actions are required to be taken in connection with a cellular therapy product before it is placed into storage.

Compliance: See Conformance.

Conformance: Fulfillment of requirements.

Consenter(s): Individual(s) whose consent is obtained for the procurement of cellular therapy products. For cord blood or gestational materials procurement, this may include, but is not limited to, the neonatal donor's birth mother, biologic mother, surrogate mother, and any legal custodians (when applicable). For cadaveric donors, this may include the donor, the donor's next of kin, or a legally authorized representative.

Contamination: Introduction of unwanted chemical or biologic matter from the environment or from another cellular therapy product.

Continuous Monitoring: A mechanism that allows for surveillance of a process or system intended to ensure proper operation and the detection of control exceptions.

Controlled-Rate Freezing: A procedure using a device to control the temperature of a product during the freezing process.

Cord Blood: The portion of the blood of a fetus or neonate that remains in the placenta or umbilical cord following delivery of the neonate and clamping of the umbilical cord. Umbilical cord blood is typically rich in hematopoietic progenitor cells.

Cord Blood Donor: The neonate who is the source of a cellular therapy product.

Corrective Action: An activity performed to eliminate the cause of an existing nonconformance or other undesirable situation(s) in order to prevent recurrence.

Critical: Elements (such as materials, equipment, steps, or tasks) that canaffect the safety of the donor or recipient and the identity, purity, potency, integrity, safety or efficacy of the cellular therapy product or service.

Cryopreservation: The process of low-temperature freezing and storage of cellular therapy products in order to preserve cells that, after thawing, retain a significant measure of their prefreeze viability and function.

Cryoprotectant: A solution or additive that, when combined with living cells, provides protection from damage otherwise induced by the freezing and/or thawing process.

Cultured Cells: Cells that are expanded and/or differentiated in vitro in media requiring monitoring of gas levels, temperature, humidity, and sterility.

Customer: The receiver of a product or service provided by the supplier. A customer may be internal (ie, another department or person within the same organization) or external (ie, a person or organization that receives a product, a service, or information but is not part of the organization supplying it).

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

Deviation: Failure to follow the appropriate policies, processes, or procedures or meet the acceptable criteria of the facility, these *CT Standards,* or applicable laws and regulations. Deviations can be planned or unplanned. Not all deviations result in an unacceptable product or result.

Disposition: For cellular therapy products, the status or control of a cellular therapy product in a given facility. For records, disposition occurs at the end of their retention period.

Distribution: The act of releasing a cellular therapy product or an authorized nonconforming product meet applicable requirements.

Document (noun): Written or electronically generated information (ie, quality manuals, policies, processes, procedures, agreements/contracts, labels, or forms).

Donation Identification Number: A 13 character code that identifies products from a single donation event that allows each event to be uniquely identified. The DIN contains three elements: the five character alphanumeric Facility Identification Number (FIN), the two character numeric DIN year code, and the six character numeric DIN sequence number.

Donor: A living or deceased person who is the source of a cellular therapy product.

Donor Screening: The process of identifying risk factors for relevant communicable disease through review of a current donor medical history interview (to include high-risk behaviors), physical examination results, and other relevant medical records.

Educational and Promotional Materials: Information made available by the cellular therapy facility to potential donors, patients, and others, including, but not limited to, therapeutic benefit claims on the facility's website, facility information, in advertisements, in marketing materials, and in enrollment documents, and information provided by the facility to the media that explains the procurement, processing, use, benefits, and alternatives to the donation.

Eligibility: With respect to donors, the evaluation of cellular therapy donors for risk factors and clinical evidence of relevant infectious disease agents or diseases for the purpose of preventing the introduction, transmission, and spread of infectious disease. A donor may be found to be eligible or ineligible (see "ineligible donors"). Alternatively, the determination may be incomplete (eg, screening is incomplete or donor testing is not performed in a timeframe specified by the test kit manufacturer's instructions).

Engraftment: The reconstitution of recipient hematopoiesis with white cells, red cells, and platelets from the donor. Engraftment of other types of cells generally will be shown by evidence of graft function specific to the organ of engraftment.

Environmental Monitoring: Policies, processes, and procedures used for monitoring any or all of the following: temperature, humidity, particulates, and microbial contamination in a specific area. Where appropriate, the program shall include sampling sites, frequency of sampling, and investigative and corrective actions that should be followed when specified limits are exceeded.

Equipment: A durable item, instrument, or device used in a process or procedure. Examples of equipment include production equipment (eg, cell separator, freezer, selection device, centrifuge) or inspection, measurement, or test equipment (eg, thermometer, cell counter, scales).

Establish: Define, document, and implement, then follow, review, and, as needed, revise on an ongoing basis.

Exception: An action or condition that is not part of normal operations.

Executive Management: The highest level of personnel within an organization, including employees and independent contractors, who have responsibility and authority for the facility's operation and the authority to establish or change the facility's quality policy and quality system. Executive management may be an individual or a group of individuals (eg, medical director, laboratory director, chief executive officer, quality assurance committee).

Facility: A location where any activities covered by these *CT Standards* are performed. These activities include determination of donor eligibility, procurement, processing, storage, distribution, issue, administration, and related patient care activities. AABB accreditation is granted to specified facilities for specific activities.

Final Cellular Therapy Product: A cellular therapy product that is ready for issue or final distribution.

Final Disposition: The terminal status of the product after which no further action can be taken, eg, discarded or infused.

Final Inspection and Testing: An activity (such as measuring, examining, or testing one or more characteristics of a product or service) that compares the results with specified requirements in order to establish whether conformance is achieved for each characteristic.

Function: The special, normal, or proper physiologic activity of a cellular therapy product that can be qualitatively or quantitatively evaluated (eg, by in vitro, in vivo, or ex vivo assays).

Gestational Materials: Any tissue procured at or near the time of birth; e.g., umbilical cord tissue, placental tissue, amniotic fluid.

Growth Factors: Recombinant cytokines that promote proliferation and/or differentiation of specific cell types or lineages. Certain growth factors can be used in vivo (eg, mobilization of hematopoietic progenitor cells) or ex vivo (eg, cell expansion, vaccine development, and adoptive cellular therapy).

Health-Care Professional: An individual employed by a facility qualified by education, training, and experience to perform the duties assigned.

Hematopoietic Progenitor Cells (HPCs): Primitive pluripotent hematopoietic cells capable of self-renewal and/or differentiation as well as maturation into any of the hematopoietic lineages (granulocytes, monocytes, erythrocytes, and platelets), including committed and lineage-restricted progenitor cells, unless otherwise specified, regardless of source (eg, marrow, mobilized peripheral blood, or umbilical cord blood).

Identity: A set of factors that distinguishes one product from another. For cellular therapy products, identity is often stated in terms of specific positive and negative markers expressed by the cells.

In-House Reagents: See Reagents.

In Process Label: A label used to identify a cellular therapy product at any intermediate processing step when a full label cannot be used due to space or size limitations.

In Vitro: Observable in an artificial environment.

In Vivo: Within the living body.

Incoming Materials: Materials at the time of receipt into a facility.

Independent Ethics Committee: An independent body (for example, a review board or committee that is either institutional, regional, national, or supranational), consisting of medical professionals and nonmedical members. The group is responsible for ensuring the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection by reviewing and approving and/or providing professional opinion on a trial protocol, including the suitability of investigator(s), facilities, and the methods and materials used in recruiting participants and obtaining and documenting informed consent of the trial subjects. The legal status, composition, function, operations, and regulatory requirements pertaining to independent ethics committees may differ between countries, but the independent ethics committee should promote good clinical practice.

Ineligible Donor: A designation applied to a donor whose product may be at risk of transmitting an infectious disease as detected by testing and/or by donor screening history.

Inner Shipping Container: A box, container, or bag that holds a labeled product during shipping inside an outer shipping container.

Inspect (inspection): To measure, examine, or test one or more characteristics of a product or service and compare results with specific requirements.

Intermediate Facility: Any facility other than the procurement facility and administering facility that manipulates or performs any activity covered by these *CT Standards*.

Investigator's Brochure: A compilation of clinical and nonclinical data about the investigational cellular therapy product(s) used in research of human subjects. It describes the product's formulation and effects, including information related to the safety, effectiveness, risk of adverse events, and monitoring relevant to the investigational product.

Investigational New Drug (IND): An investigational drug or biological product administered to humans under a protocol or research program authorized by the Competent Authority.

Islets: A cellular therapy product consisting of partially purified pancreatic islets of Langerhans. Insulin-producing beta cells within such islets make up the functional component of the product.

Issue: To release a final cellular therapy product for clinical use (eg, physical transfer of the cellular therapy product to the medical service responsible for administering the product to the patient by infusion, injection, or other method).

Issuing Facility: The facility that issues the cellular therapy product for clinical use.

Label: An inscription affixed or attached to a product for identification.

Label (Accompanying): Product information is available with the product, or is available electronically.

Label (Affixed): A label that is in physical contact with the container.

Label (Attached): A label that is securely fastened to the product container by means of a tie-tag or alternative method.

Labeling: Information that is required or selected to accompany a cellular therapy product, which may include content, identification, description of processes, storage requirements, expiration date, cautionary statements, and/or indications for use.

Laboratory Attire: Attire worn in the laboratory as protection against contamination of the person or of the product. This may include gloves, laboratory coats, hair covers, face covers, shoe covers, and sterile sleeves.

Laboratory Director: A qualified individual holding a relevant doctoral degree who is responsible for all technical aspects of the cellular therapy product service.

Laboratory Medical Director: A qualified licensed physician who has overall responsibility and authority for all medical aspects of the cellular therapy product service.

Legal Custodian: A person legally responsible for the donor until the donor's age of majority.

Leukocyte-Rich Products: Leukocyte-rich products are defined at the time of collection/procurement, even if later processing might remove leukocytes. Some examples of leukocyte-rich products include but are not limited to: hematopoietic stem progenitor cells such as apheresis products, bone marrow, umbilical/placental cord blood or gestational materials, and nucleated cell preparations such as as mononuclear cell collected by apheresis (MNC,A). Some organs and tissues can be leukocyte-rich.

Life-Cycle Requirements: The stages and time span from initial planning of an information system software program to its retirement; ie, from concept, to software development, to business changes, to revisions, to retirement.

Lookback: The process of reviewing and, if necessary, removing from inventory any product that is potentially infectious or nonconforming.

Maintain: To keep in the current state; to preserve or retain; to keep in a state of validity.

Manufacture: All steps in the preparation and testing of a cellular therapy product, from donor evaluation to making the product available for distribution.

Materials: Goods or supply items used in a process or procedure to prepare the cellular therapy product or service. Reagents (whether purchased or prepared in-house) are a type of critical material.

Medical Suitability: Evaluation of cellular therapy donors for risks related to the donation process and potential noninfectious risks to the recipient.

Medical Therapy: The direct provision of a medical intervention ordered by a physician (eg, harvest of hematopoietic progenitor cells by apheresis, administration of a pharmaceutical agent to a patient, or administration of a cellular therapy product).

Mesenchymal Stem Cells: A cellular therapeutic product defined as multipotent cells with the ability to differentiate into nonhematopoietic tissues of mesodermal origin.

Mononuclear Cells (MNCs): Lymphocytes and monocytes in the collected product.

Myeloablative Therapy: Treatment of a patient with an agent (eg, chemotherapy or gamma irradiation) that causes irreversible bone marrow aplasia.

Noncompetent: With respect to donors, an individual who lacks the legal ability to make medical decisions for himself/herself.

Nonconformance: Failure to meet requirements.

Nonconforming Product or Service: A product or service that does not satisfy one or more specified requirements.

Novel Method: An innovative method or procedure being evaluated and introduced into practice at a facility. The method may not have undergone internal or external peer review or approval by an Independent ethics committee.

Off-Site Location: A physical storage facility or electronically supported storage medium that provides reliable redundancy of data.

Organization: An institution, a part thereof, or an entity bridging across several institutions that has its own functions and executive management.

Outer Shipping Container: A container made of material adequate to withstand leakage of contents, impact shocks, pressure changes, temperature changes, puncture, and other conditions incident to ordinary handling.

Output: The product, information, or service that results from performing a process or procedure.

Parties: Entities or individuals who have entered into an agreement.

Patient: An individual undergoing medical care. The individual may also be a research subject.

Patient-Specific Product: A product collected and/or prepared exclusively for a particular autologous or allogeneic recipient.

Policy: A documented general principle that guides present and future decisions.

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

Preparation for Administration: The preparation of a distributed cellular therapy product for administration. Preparation steps typically are minimal and occur immediately before a product is issued for administration.

Preparative Regimen: Any regimen of immunosuppressive and/or myelosuppressive chemotherapeutic agents and/or radiation therapy that is given to prepare the recipient before the administration of a cellular therapy product.

Preventive Action: An activity performed to eliminate the potential for nonconformance or other undesirable situations.

Procedure: A description of how an activity is to be performed; ie, a standard operating procedure.

Process: A set of related tasks and activities that accomplishes a work goal; ie, that transforms input into output products and services. This transformation can be achieved by an activity or a series of interrelated activities.

Processing: Any activity performed on a cellular therapy product, other than recovery, donor screening, donor testing, storage, labeling, packaging, or distribution. Such processing activities include, testing for microorganisms, preparation, sterilization, steps to inactivate or remove adventitious agents, preservation for storage, and removal from storage.

Processing Facility: The facility involved in receipt of the product from the procurement facility. The processing facility may perform further manufacturing, testing, and/or distribution of the product.

Process Control: Efforts made to standardize and control processes in order to produce predictable output.

Procurement: The act of obtaining a cellular therapy product(s) from a donor by facility-approved methods, including, but not limited to, apheresis, marrow harvest, cord blood or gestational materials collection, or organ or tissue harvest from a donor.

Procurement-Associated Intervention: Any event intended to assist with the procurement of a cellular therapy product, such as medications given to mobilize cells, placement of a line for easier access, etc.

Procurement Container: Any receptacle suitable for the procurement of a specific product.

Procurement Facility: Either a facility that is directly responsible for the performance of donor eligibility determination, donor screening, and the procurement of cellular therapy products or a facility that ensures, through agreements, that one or more of these activities is/are performed in conformance with these *CT Standards*.

Procurement Goal: The desired outcome of the procurement process.

Product: A tangible result of a process or procedure. Note: the cellular therapy product provided to an intermediate facility by the procurement facility is a product for the procurement facility but a material for the intermediate facility.

Product Code: An eight character ISBT 128 code that comprises the five character Porduct Description Code, the one character collection type code, and the two character division code.

Proficiency Testing: The structured external evaluation of laboratory methods that assesses the performance of the test system.

Protected Health Information (PHI): Individually identifiable health information that can be linked to a particular person that is related to the physical or mental health status, type of health-care provided, or payment for the health-care provided. Common identifiers of health information include names, social security numbers, addresses, and birth dates. PHI can be in electronic, oral, or written format.

Purity: Dominance of a targeted cellular population defined by specific cell markers and with minimal to no contamination of cells negative for the same markers.

Qualification (equipment or suppliers): Verification that specified attributes required to accomplish the desired task have been met.

Qualification (individuals): The aspects of an individual's education, training, and experience that are necessary for the individual to successfully meet the requirements of a position.

Qualification (materials): For materials that come into contact with the patient or cellular therapy product, verification that the materials are sterile, the appropriate grade and suitability

for the intended use and, whenever possible, approved for human use by the FDA or relevant Competent Authority.

Quality: Characteristics of a product or service that affect its ability to meet requirements, including those defined during agreement review.

Quality Assurance: Confidence that the policies, processes, and procedures that influence the quality of the product and service are working as expected, both individually and collectively.

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 reagents, materials, analytical procedures, and equipment to ensure their proper function.

Quality Indicator Data: Information that may be collected and used to determine whether an organization is meeting its quality objectives as defined by top management in its quality policy. Indicators are measured by data for movement or regression with regard to those quality intentions. The data used for monitoring a quality indicator may consist of single-source data or multiple-source data, as long as it is clear how the data will come together to define the indicator.

Quality Manual: A document that describes a facility's quality system.

Quality Policy: The overall vision, intentions, and direction of an organization to achieve quality, formally expressed by executive management.

Quality System: The organizational structure, responsibilities, policies, processes, procedures, and resources established by executive management to achieve the quality policy.

Quarantine: Storage of cellular therapy products, reagents, or materials, in order to prevent improper release and/or cross contamination, either in a physically separate area clearly identified for such use, or by identification of a product through the use of other procedures, including automated designation, for the same purpose.

Reagent: A substance used to perform an analytical or manufacturing procedure. A substance used (as in detecting or measuring a component or preparing a product) because of its biological or chemical activity. Reagents can be either purchased ready for use or prepared within the facility (in house).

Receiving Facility: A facility receiving products or services.

Record (noun): Information captured in writing or electronically that provides objective evidence of activities that have been performed or results that have been achieved, such as test records or audit results. Records do not exist until the activity has been performed.

Recipient: The patient receiving a cellular therapy product.

Reference Standard: Specified requirements defined by the AABB (see Specified Requirements). Reference standards define how or within what parameters an activity shall be performed and are more detailed than system requirements contained in these *CT Standards*.

Registry: An organization that maintains a database of cellular therapy donors or products and coordinates the acquisition of cellular therapy products for transplantation.

Regulation: A rule promulgated by Competent Authority , or local authorities to implement laws enacted by legislative bodies.

Release: Removal of a product from quarantine or in-process status for the purpose of distribution.

Rework: May include reprocessing, retesting (other than infectious disease testing), or other steps in the manufacturing process that are out of the normal processing sequence or that are not specifically provided for in the process.

Risk Assessment: A process that results in a report that analyzes the potential for deviations or nonconformances to occur and the corrective and preventive actions to be taken to prevent or minimize risk.

Service: Work or activities performed to fulfill the needs of a customer. The intangible result of a process.

Shall: A term used to indicate a requirement.

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 originating or receiving facility.

Shipping Facility: A facility responsible for delivering a product in its custody to another location.

Source Material: Cells, tissue, or organs procured from a donor that have not been manipulated or processed.

Specified Requirements: The expectations for products or services. Specified requirements may be defined by customers, regulatory agencies (such as the FDA), practice standards, or accrediting organizations (such as AABB).

Stability: The ability of a product to maintain quality characteristics and resist change or deterioration.

Stability Program: An ongoing sampling program intended to assess the capacity of a cellular therapy product to remain within specifications throughout the retest period or expiration date, as

appropriate. Parameters assessed in a stability program may include all or any of the following: identity, viability, potency, sterility, and container integrity.

Standard: A set of specified requirements upon which a facility may base its criteria for the products, components, and/or services provided.

Statistical Techniques: Established mathematical methods used to collect, analyze, and present data.

Sterility: An aseptic condition, meaning an absence of living microorganisms.

Storage: The state of being kept in a place while not being used or transferred, shipped, or transported.

Storage Device: A piece of equipment used to keep a product in the physical state of storage.

Subject Matter Expert: A person who is qualified, competent and experienced in a particular task or functional area.

Summary of Records: A condensed version of the required testing and screening records that contains the identity of the testing laboratory, the listing and interpretation of all required infectious disease tests, a listing of the documents reviewed as part of the relevant medical records, and the name of the person or establishment determining the suitability of the human tissue for transplantation.

Supplier: An organization or individual that provides a product or service. A supplier can be both.

Surrogate Mother: The female who carries the fertilized ovum of another woman.

System: A subgroup of related activities performed by a particular organization. Activities dealing with maintaining product and service quality are organized into a quality system.

Tissue: Any aggregation of cells and/or associated intercellular matter that usually form a functional unit, and in the context of cellular therapy, intended for transplantation or implantation.

Total Nucleated Cell (TNC Count): The total number of nucleated cells in a volume of a cellular therapy product. Nucleated cells include white blood cell (WBC) populations such as neutrophils, monocytes, lymphocytes, eosinophils, and basophils, and nucleated red blood cells (NRBCs). The TNC count is calculated by the following formula: TNC = (WBCs + NRBCs) × volume. The contribution of NRBCs, if any, should be separately noted.

Traceability: The ability to follow the history of a process, product, critical material or supply, or service in both directions through review of documents and records.

Transfer: The act of relocating a final cellular therapy product or its intermediate in-process precursors.

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

Urgent Medical Need: Procurement and use of a cellular therapy product from an ineligible donor or a donor whose eligibility is incomplete when no comparable product is available and the recipient is likely to suffer serious morbidity or death without receiving the product.

Validation: Demonstration through objective evidence that the requirements for a particular application or intended use have been met. Validation provides assurance that new or changed processes and procedures are capable of consistently meeting specified requirements before implementation.

Verification: Confirmation, by examination of objective evidence, that specified requirements have been met.

Viability: Demonstrated capability of living; indicating (either in vivo or in vitro) ability to perform physiologic functions.

Workflow: The planned physical movement of people, materials, or data associated with a process, or the planned temporal sequence of activities associated with a process.