PROPOSED Standards for Cellular Therapy Services
10th Edition

Effective July 1, 2021

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 10th edition begins on page 2 and runs through page 26. The proposed 10th edition begins on page 27 and runs through page 137.
Significant Changes to the Proposed 10th edition of Standards for Cellular Therapy Services

1.1.2 The facility shall register for all applicable products and activities with the FDA or relevant Competent Authority. When applicable, the facility shall obtain licensure for all products and activities.

This standard is new to the proposed edition and in conjunction with the creation of new standard 1.5 was added to ensure that accredited facilities remain in compliance with FDA regulations (or regulations pertaining to non-US facilities) as it relates to contamination (suspected or actual) or loss of cell function. This standard was put in place due to many facilities receiving Warning Letters concerning risk points that can directly impact the cellular therapy product and will allow assessors to cite facilities who are not in conformance accordingly.

1.1.3.1 Procurement Medical Director

The procurement medical director(s) shall be a licensed physician with relevant experience and qualified by training, and/or experience and relevant.

The procurement medical director(s) shall participate in continuing education in 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.

The committee moved the clause “relevant” to appear before “experience” and created a second sentence focused solely on “continuing education” to ensure users knew that both concepts were required and that the term “relevant” appeared in both sentences.

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 two year accreditation cycle and have at least one year of experience in the scope of procurement activities performed by that facility.

The committee replaced the term “overseen” with “managed or reviewed” for clarity; the change provides more specificity. The requirement of reviewing 5 procedures was shifted to 10, to require 5 per annum, while matching the normal accreditation cycle. Finally, the clause “throughout the preceding two year accreditation cycle” was added to the standard to ensure that it was understood that this requirement applies for each edition and not just one time.

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 procurement laboratory medical director shall participate in experience and relevant 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.

The changes in standards 1.1.4.1 and 1.1.4.1.1 were made to match the changes made to standards 1.1.3.1 and 1.1.3.1.1.

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 experience and relevant 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 two year accreditation cycle and have at least one year of experience in the scope of processing activities performed by the facility.

The changes in standards 1.1.4.2 and 1.1.4.2.1 were made to match the changes made to standards 1.1.3.1 and 1.1.3.1.1.

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 and relevant 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 one year of experience. Relevant continuing education shall be obtained throughout the accreditation cycle in the scope of clinical activities performed in the facility.
The changes in standards 1.1.5.2 and 1.1.5.2.1 were made to match the changes made to standards 1.1.3.1 and 1.1.3.1.1.

**C 1.2.5 Executive Management Review**

The facility’s executive management shall review the quality system on an annual basis to ensure that the system meets the requirements of these CT Standards. Standard 6.1.5 applies.

The committee added the clause in bold to ensure that executive management reviews the entire quality system annually. This will ensure that executive management participates and are aware of changes to the quality system at least twice per accreditation cycle.

**C1.5 Assessment of Risk**

The facility’s executive management shall ensure there are continuous risk assessments of the operations or changes to operations that affect product quality and safety. Standard 5.2.1 applies.

1.5.1 Mitigation strategies shall address these level of risks associated with activities in accordance with the FDA or relevant Competent Authority.

This standard is new to the proposed edition and in conjunction with the creation of new standard 1.1.2 was added to ensure that accredited facilities remain in compliance with FDA regulations as it relates to contamination or causing a loss of cell function. Placing risk assessment, in Chapter 1 Organization, means it will be considered "a key quality function" as stated in Standard 1.0

This new standards above will address the need for a facility to perform a comprehensive review of their processing processes and identify areas that might be at risk of introducing contamination or causing loss of cell function, etc.. Then, as with a process validation (Standard 5.0, 5.2.3), corrective action must be devised and implemented to ensure the risk is minimized or eliminated, and addressed in policies, processes, and procedures in order to ensure product integrity. Finally, an assessment to ensure the corrective action has been effective should be performed. All these activities must be documented and approved by the medical and/or laboratory director, and quality director as applicable and ultimately executive management.

These standards were put in place due to many facilities receiving “Warning Letters” concerning risk points that can directly impact the cellular therapy product and will allow assessors to cite facilities who are not in conformance accordingly. These standards added together (1.1.1.1, 1.5 and 1.5.1) give facilities a more solid framework for direction in performing a robust consideration of the risk points throughout the activities which directly impact the cellular therapy product; and provides standards for assessors to confirm compliance with applicable regulations for HCTPs, those classified as both 351 and 361 products.

**C 2.1.6 Competence**

Evaluations of competence shall be performed before independent performance of assigned activities and annually thereafter for defined tasks and 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.^

^42 CFR 493.1413(b)(9), 42 CFR 493.1451(b)(9)

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

The change and proposed addition to the proposed edition were added based on a request from the CLIA liaison to the Standards Committee. These additions will ensure that the Standards remain in compliance with current regulations, cited along with the standards.

2.2 Access to Ancillary Services and Direct Patient Care Services

The clinical facility shall ensure access to medical specialty services and resources as needed for patient care, including but not limited to:

4) Laboratory services.

#4 is new to the proposed edition and was added for completeness.

3.0 Equipment

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

The committee added the term “operate” for completeness.

3.1 Equipment Specifications

Equipment specifications shall be defined before purchase.

3.1.1 Elements of Control

The facility shall:

1) Define equipment specifications before purchase.

2) Qualify each piece of equipment for its intended use, including specifications for accuracy and precision, as applicable.

3) Ensure all equipment has unique identification.

After reviewing the content of standards 3.2 – 3.2.3, the committee noted that everything in standard 3.1 was redundant to the content below it. Therefore, the committee deleted standard 3.1 and added new standard 3.1 to cover equipment specifications, the only novel concept in the former standard 3.1.

3.2.2 Operational Qualification

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

The committee replaced the term “computer” with “information” matching the changes made in the 5th edition of Standards for Molecular Testing for Red Cell, Platelet and Neutrophil Antigens.

3.3 **Use of Equipment**

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

The committee included new standard 3.3 in this edition. This standard exists in all other sets of Standards AABB provides for voluntary accreditation.

*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.**

The committee created new subnumber 1 to standard 3.5 for completeness.

*F* 3.6 **Information Systems**

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

3.6.1 **Alternative Systems**

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

The committee replaced the term “computer” with “information” matching the changes made in the 5th edition of Standards for Molecular Testing for Red Cell, Platelet and Neutrophil Antigens.

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

This standard is new to this edition and was pulled from the 32nd edition of Standards for Blood Banks and Transfusion Services.

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

Except for HPC, Cord Blood banks when the recipient is not known, There shall be agreements that define the following:

2) **Responsibility of the processing facility to obtain a medical order before the processing procedure, if applicable.**

4) **These orders are not required for cord blood banks where the recipient is not known at the time of collection.**

**Standards 5.14.1 and 5.17.1 apply.**
The committee re-formatted the standard for clarity and as such created new subnumber 4 to replace the clause that previously began the standard. The crossreferences were added for completeness. The clause “if applicable” was added to #2 recognizing that there are instances where processing facilities do not have this medical order on hand.

\( F \) 4.3.3 Transfer of Products

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

3) Agreement by all parties to provide the necessary documentation concerning timing of procurement and pre transplant regimens.

The committee created new subnumber 3 for completeness.

\( C \) 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 to another upon request. **Standard 5.7 applies.**

The committee edited subnumber 2 for clarity.

\( F \) 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

The committee added a crossreference to the FDA regulation to ensure users knew what types of signatures for consent were appropriate; especially in light of the COVID-19 pandemic.

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.

In standard 4.5.2 (and throughout the standards) the committee added the clause “or gestational materials” where appropriate. This allows the standards to apply more broadly to other gestational materials that can be procured during/after cord blood.

4.5.2.1 There shall be a process to identify vulnerable donor populations that require a donor advocate to address informed consent issues.
This standard is new to the edition and was included for completeness. It requires the facility to identify their vulnerable donor populations and to determine who needs access to a donor advocate. The term “vulnerable donor populations” is an industry understood term.

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 acceptability of use. Standard 5.12.2.10 applies.

The elements in bold were added to standard 4.8.1.1 for completeness. It is important that samples sent to testing labs are meeting sample requirements as stated in the package inserts. This addition ensures that will occur. The crossreference in standard 4.8.1.1 was moved from standard 4.8.1 to standard 4.8.1.1 where it fits more appropriately.

Reference Standard 4.5A – Donor Informed Consent or Authorization

The committee removed any gender specific clause from the reference standard (and throughout the standard) replacing “he or she” with “they” and “his or her” with “their.”

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

G is new to the proposed edition and was included for completeness. This addition was included based on feedback from the committee ethicist.

Reference Standard 4.7A – Patient Informed Consent

The committee removed any gender specific clause from the reference standard (and throughout the standard) replacing “he or she” with “they” and “his or her” with “their.”

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

F is new to the proposed edition and was included for completeness. This addition was included based on feedback from the committee ethicist.

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

*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

The committee added the references to the CFR for completeness at the request of the CLIA.
representative to the committee. The committee edited standard 5.1.2.3.1 to craft the standard in a positive frame, noting that proficiency testing should be the goal and if it does not happen to investigate.

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

The committee replaced the term “computer” with “information” matching the changes made in the 5th edition of Standards for Molecular Testing for Red Cell, Platelet and Neutrophil Antigens.

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 attributed to procurement.

5.3.2 For processing facilities, this shall include but is not limited to adverse events and complications attributed to processing.

The committee elected to remove standard 5.3.2 and added the content to standard 5.3.1.

5.3.2 For the clinical facility, this shall include but is not limited to:
5) Engraftment.

The committee added new number 5 to standard 5.3.2 to remain parallel to standard 5.3.1 which calls out engraftment as an outcomes measure to monitor.

5.3.5 For facilities that process or administer islet products, there shall be a process for recording and monitoring recipient safety and reviewing clinical outcomes as specified by the clinical protocols. Clinical outcomes shall include, but are not limited to:
1) C-peptide.
2) Loss of serious hypoglycemia unawareness.
3) Hemoglobin A1c.
4) Durability of islet transplantation.
5) Insulin independence.
6) Insulin requirements.
7) Quality of life.

Based on comments from the islets expert on the committee elected to remove the elements in standard 5.3.5 as they were deemed inadequate and not uniform across accredited facilities. The committee will include these as elements in guidance.

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.

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FOR COMMENT PURPOSES ONLY
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The committee added the clause in bold for completeness.

5.9.1 The facility shall control packaging to the extent necessary to ensure conformance with specified requirements. Local, national, and/or international transport/shipping regulations apply.

The committee removed the clause in strike through as it was deemed unnecessary and impossible to assess.

\[ C \] 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:
3) Product description code and division code.

The committee edited subnumber 3 for accuracy with proper ISBT nomenclature. This change was made throughout the document as needed as the Product code is comprised of the product description code, donation type code and division code.

\[ C \] 5.10.2 In-Process and Final Product Inspection and Testing
In-process testing and monitoring shall be defined. The facility shall:
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.

The committee added the term “processing” to standard 5.10.2 for completeness.

5.12.1 Donor Medical Suitability
The facility shall define donor medical suitability criteria to protect the safety of the donor and the intended recipient. Donor 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, and relevant clinical history, and relevant medical record(s):

The committee replaced the term “donor” as it relates to “suitability” with “medical.” Medical suitability is a more accurate term and removes any potential stigma being associated with donors being deemed “unsuitable.” This does not change the requirement contained in this standard and throughout the document and does not allow for individuals who are not medically suitable to donate products.
would be given to another human being. The committee also moved the clause in strike through to be a part of the new requirements concerning the medical record that is used as a part of a donor evaluation.

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

In line with the change to standard 5.12.1, the committee replaced the term “donor” with “medical” as it relates to suitability.

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

The committee added the clause “and emerging infectious diseases” to standard 5.12.2.10 to ensure that facilities have policies, processes and procedures in place to ensure that they take action when a new diseases emerge.

5.14.2 Verification of Donor Medical Suitability

5.14.2.1 Before procurement, the procurement facility shall verify that the determination of donor 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, 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.

In line with the change to standard 5.12.1, the committee replaced the term “donor” with “medical” as it relates to suitability.

5.14.2.4 On each the 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 the 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.

The committee replaced the term “the” with “each” recognizing that there are instances where procurement can take place on more than one day.
5.14.5 Procurement Records for Processing Facilities

Procurement facilities and/or procurement personnel shall make procurement data available to processing facilities receiving the cellular therapy products as needed. Chapter 4, Agreements, applies.

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5.14.5.1 Procurement Records

A procurement record shall include:
1) Donation identification number.
2) Product description code and division code.
3) Product name and attributes.
4) Unique donor 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.

The committee elected to merge standards 5.14.5 and 5.14.5.1 as standard 5.14.5 did not fit appropriately for what was being required. A new standard below (5.14.7) will discuss this further. The edits to entry #2 was made to match ISBT product nomenclature, and #7 was expanded to ensure that the product procured was included in the record.

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5.14.6 Review of Procurement Records

After completion of procurement, the facility shall ensure that the procurement record for each cellular therapy product is accurate and complete shall be reviewed in a specified time frame.

The committee edited this standard for clarity. The committee felt that the clause “after completion of procurement” implied an action had to be taken immediately which is not the case.

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5.14.7 Procurement Record Availability

Each facility performing procurement shall provide a product procurement record to the facility receiving the product. Chapter 4, Agreements, applies.

5.14.7.1 Records shall include:
1) Donation identification number.
2) Product code.
3) Product name and attributes.
4) Unique donor identifier, if available.
5) Date and time of procurement, including time zone.
if applicable.
6) Name and address of the procurement facility.

Standards 5.14.7 and 5.14.7.1 are new to the proposed edition and were included to parallel the language in standard 5.14.5. These standards focus however on what the minimum requirements are needed to be shared from a procurement facility for a product that is in process.

**5.15 Procurement Endpoints Goals**

Procurement goals and endpoints shall be defined.

5.15.1 Unrealized Endpoints Goals

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

5.15.1.1 If expected endpoints goals are not met for cells, tissues, or organs procured for autologous use or cells designated for a specific patient, the intended recipient’s physician, the processing facility, and other relevant appropriate parties shall be notified.

The committee replaced the term “endpoints” with “goals” as this is realistically what is articulated in procurement facilities. The term “relevant” replaced “appropriate” as this better fit the sentiment and appropriate has been deemed difficult to assess. The elements in strike through in standard 5.15.1.1 was deemed unnecessary and will be included in guidance along with other examples.

**5.17.2 Processing Record**

A complete processing record shall include:

2) Product description code and division code.

The committee made this edit to parallel similar changes previously noted in the document.

5.17.5 Processing Records

Each facility(ies) performing processing, preservation, or storage shall provide a copy with of the complete 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. Chapter 4, Agreements, applies.

The committee removed “complete” as it was deemed unnecessary.

5.19 Cryopreservation

Cellular therapy products shall be cryopreserved using a controlled-rate freezing procedure or equivalent procedure known 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.
The committee replaced the term “known” with “validated” as this is the term that is in concert with FDA recommendations.

**F** 5.19.3 Records for Cryopreserved Products
In addition to the items required by Standard 5.17.2, cryopreservation records shall include:
2) Product description code and division code.

The committee made this edit to parallel similar changes previously noted in the document.

**F** 5.24.1 The issuing facility shall review and verify the following items at the time of final cellular therapy product distribution/issue:
3) Product description code and division code.

The committee made this edit to parallel similar changes previously noted in the document.

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.

The committee added the clause in bold to the standard, as in the clinical setting a health-care professional can perform the evaluation, however it has to be approved by a physician.

**F** 5.26.1.2 Orders for cellular therapy product administration shall uniquely identify the recipient, and 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.

The committee added the term “the dose” for completeness.

5.28.1 Receipt and Administration of Cellular Therapy Products
The patient care service administering the final cellular therapy product clinical facility shall have procedures for the receipt, and preparation, and administration of products. Standards 5.7, 5.8, 5.10, and 5.22 apply.

The committee edited this standard noting that administration of products did not appear until standard 5.29.

**F** 5.28.2 The administering service clinical facility shall review and verify the following items at the time of final cellular therapy product receipt:
3) Product description code and division code.
The committee made this edit to parallel similar changes previously noted in the document. The term “clinical facility” replaced “administering service” understanding that this standard appears in the clinical section and they would be the facility performing the administration.

**F5.29 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 patient care service shall confirm the identity of the product and the intended recipient. Intended recipients shall be identified using at least two identifiers.

The term “clinical facility” replaced “patient care service” for completeness and parallel construction.

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.

The committee reformatted this standard for consistency with AABB standards setting norms.

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

5.29.3 The clinical facility shall have policies, processes, and procedures for the following:

1) Infusional toxicities and adverse reactions due to 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 cell products.

6) Treatment of or prophylaxis for infectious disease.

7) Use of blood products.


9) **Complications of immune effector cellular therapy.**

The committee deleted the first sentence in former standard 5.29.3 as it was deemed duplicative of what was included in standard 5.29.2. The committee also edited subnumber 1 for clarity. Subnumber 9 is new to this edition and was added to ensure that the complications referenced were covered, this addition is in line with subnumbers 2 and 3.

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

The edits made to standard 5.29.3 were made for consistency in language.

F 5.29.4 Records of Administration
Records of administration shall include:
3) Product description code and division code.

F 5.29.5 Recipient Records
Recipient records shall include the following:
3) Product description code and division code.

The committee made this edit to parallel similar changes previously noted in the document.

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.

This standard is new to the proposed edition and as created to ensure that clinical facility’s that need to provide data to a registry (e.g. CIBMTR) do so in a manner that is consistent and appropriate.

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

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Line 3 has added a new footnote to the “Distribution and Issue” column which requires that in times
where the label size does not allow for everything to be on the label, said label will refer to the accompanying documentation.

The footnote reads as such:

7 If label size precludes displaying all product attributes, the label shall refer to accompanying documentation for details.

In line with changes throughout the Standards, entry #4 has been updated to match ISBT nomenclature, and the additional elements included on the label as required by ISBT. Entry 5 was then deemed redundant.

Entry #26 is new to this edition and was made to mimic what is required (and has been) in the Standards for Blood Banks and Transfusion Services.

Reference Standard 5.9.5A – Labeling and Packing Requirements Upon Shipping of Cellular Therapy Products

4) Current Circular of Information for the Use of Cellular Therapy Products, certificate of analysis, manufacturer’s insert, investigator’s brochure, or equivalent or product package insert and product information.

The committee elected to edit the standard for clarity and accuracy.

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

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. The prospective donor [or legally authorized representative(s), if applicable] shall acknowledge in writing that he or she has read or viewed the educational material, has been given the opportunity to ask questions, and has had those questions answered satisfactorily.

The committee edited this standard to ensure that the standard remains gender neutral. The clause “or viewed” was included understanding that some consent documents are virtual or on an IPad, and the term read implies holding a piece of paper.

B. Educational materials shall include the following elements:

3) For marrow donors:
   a) Information about the bone marrow donation procedure.
   b) Risks and discomforts of marrow donation of anesthesia.
   c) General risks and discomforts of anesthesia.
   b) Risks and discomforts of marrow donation, including infection, mechanical injury, and transfusion.
Elements a, b, and c were created to mirror the language that appears for apheresis donors in number 4.

4) For apheresis donors:
   a) Detailed Information about the apheresis procedure for cell procurement by apheresis.
   d) Risks and discomforts side effects of growth factor and/or other pharmacologic agent(s), where applicable.

These standards were updated to match the language in number 3 above. The intent of the standard has not changed.

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.

   In line with the change to standard 5.12.1, the committee replaced the term “donor” with “medical” as it relates to suitability.

   2) The Medical suitability of the donor shall be determined by the donor’s physician or by a physician who, in the case of allogeneic donors, is not cannot be directly involved with the care of the recipient.
      a) For cord blood or gestational material donors, the medical suitability shall be determined by a health-care professional.

      The committee edited this entry to ensure that allogeneic donors do not have their ability to donate performed by a physician who is involved with the care of the recipient.
      For autologous donors, this would not apply.

      In line with the change to standard 5.12.1, the committee replaced the term “donor” with “medical” as it relates to suitability.

   3) The facility shall evaluate donor eligibility and medical suitability according to defined risk-based clinical and laboratory testing criteria.

      In line with the change to standard 5.12.1, the committee replaced the term “donor” with “medical” as it relates to suitability.

   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.

      The committee added the clause “and donor” for completeness.

      In line with the change to standard 5.12.1, the committee replaced the term “donor” with “medical” as it relates to suitability.
5) Donor eligibility and medical suitability records shall be reviewed before administration of a conditioning regimen to the recipient and the beginning of mobilization.

The committee added the clause “and the beginning of mobilization” for completeness. In line with the change to standard 5.12.1, the committee replaced the term “donor” with “medical” as it relates to suitability.

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 final disposition of previously collected products, if it is discovered that the donor does not meet eligibility criteria subsequent to procurement.

The committee edited this standard for clarity. The committee felt that letter “c” was unnecessarily wordy.

B. Specific Donor Requirements
   2) Autologous Donors
      A health assessment specific to the donation procedure shall be performed by the autologous donor’s physician, a health-care professional and approved by a physician before the scheduled procurement.

This change was made to mirror a change made to standard 5.25.1, allowing for a health assessment to be performed by a health-care professional but approved by a physician.

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

III. Laboratory Testing for required of Allogeneic Donors

The committee edited this header for clarity.

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

III. Laboratory Testing for required of Allogeneic Donors

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<thead>
<tr>
<th>WNV</th>
<th>Yes</th>
<th>No</th>
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4In 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.

The committee edited the entry for West Nile Virus moving it from not required as a test for allogeneic donors to a required one based on the current FDA Guidance. This is in line with current FDA thinking.

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

III. Laboratory Testing

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<tr>
<td>WNV(^4)</td>
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\(^4\)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.

The committee edited the entry for West Nile Virus moving it from not required as a test for allogeneic donors to a required one based on the current FDA Guidance. This is in line with current FDA thinking.

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

History and behavioral risk for exposure to the following infectious agents or diseases\(^1\):

| Rabies (contact with potentially rabid animal)\(^4\) | Yes |

The committee removed this requirement as it is not required by the FDA for HCT/Ps, nor is it exactly relevant to the products and practices covered by this set of Standards.

Reference Standard 5.17A – Processing Tests for HPC, Apheresis, and HPC, Marrow Cellular Therapy Products other than HPC, Cord Blood

The committee elected to separate the reference standards into three distinct tables, focused on traditional HPCs, Cord Blood (in 5.17B) and then all other products in (5.17C). Many of the elements that have been removed from 5.17A now exist in newly created 5.17C.

1) Cell count and viability specific to the cellular therapy product. This includes:
   a) For HPC, Marrow, the total nucleated cell count.
   b) For HPC, Apheresis, CD34+ cell count.
   c) For T Cell, CD3+ cell count.
   d) For islets, islet equivalents (IEQ).
   e) For other cellular therapy products, the relevant cell count shall be defined by the facility.

2. Antigen expression analysis specific to the cellular therapy product, if applicable.

The committee removed the elements in strikethrough have been moved to new reference standard 5.17C.
2) Microbial contamination (culture for aerobic and anaerobic bacterial and fungal elements) at the completion of processing.

   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.**

The committee added the clause “as determined by the appropriate medical director” understanding that the standards contain different directors for each discipline and that they alone determine when a notification is released.

Letter c is new to the edition and was added to parallel “b” which focused only on the donor.

4. Potency assay specific to the cellular therapy product. This includes:

   a) A test for viability.

   b) For HPCs, CD34 analysis or comparable assay (except for marrow).

   c) For other cellular therapy products, the relevant potency assay shall be defined by the facility.

Number 4 has been removed from 5.17A and moved to 5.17C.

3) If the final product contains red cells, after receipt or before administration, ABO group 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.

The committee edited number 3 for clarity as the clause in strikethrough would not apply to the newly revised products covered in reference standard 5.17A; the clause would apply only to products now in reference standard 5.17C.

6) Testing of cultured cells shall include endotoxin and mycoplasma testing, unless not required under an investigational new drug or license application or as approved by the Competent Authority.

This clause would not apply to the newly revised products covered in reference standard 5.17A; the clause would apply only to products now in reference standard 5.17C.


1) Testing for ABO group and Rh type shall be performed on the cord blood obtained before and the results reported within 7 days of cryopreservation.

The committee edited this entry as it was deemed redundant to standard 5.12.2.2.
3) The following processing tests shall be performed on a sample obtained after processing but before the addition of cryoprotectant:
   b) Total cell and/or CD45 cell viability

*3 has been edited for clarity. The element in bold in “b” has been edited for clarity and accuracy.*

4) Tests for microbial contamination (culture for aerobic and anaerobic bacterial and fungal elements) shall be performed on a sample obtained after processing but 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.**

*The committee added the sentence in bold for completeness. All facilities perform this action and lead assessors noted that facilities are cited for not performing this activity even without the requirement spelled out.*

4) If results affect the donor’s health as determined by the appropriate medical director, notify the mother and/or the mother’s physician and recipient’s physician of positive culture results.

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

*The elements in the first sentence were added to parallel the sentence that appears below it. The first sentence is focused on the donor, while the second sentence is focused on the recipient of the product. This change, to reference both donors has been made throughout the Standards where appropriate.*

5) The following tests shall be performed before issue:
   c) Colony-forming unit and/or Viable CD34 (direct measurement) assay from an integrally attached segment on products that will be used for hematopoietic reconstitution.

*The committee edited this standard for clarity. The committee noted that viable CD34 is the most common test and most accurate so it felt that making this change would put the Standards in line with what our members are doing.*

5) The following tests shall be performed before issue:
   d) Other tests as required by the applicable registry.

*The committee added new subletter “d” in conjunction with new standard 5.30.1 for those facilities participating in a registry.*

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

PROPOSED Standards for Cellular Therapy Services, 10th edition
FOR COMMENT PURPOSES ONLY
JULY 3, 2020 – SEPTEMBER 3, 2020
This reference standard is new to the proposed edition and was added to focus on “other products” outside of the traditional HPCs the Standards cover. This format was used previously in the 6th edition and as the CT Standards continue to expand their scope the return of this reference standard made sense. Note, that many of the elements included in 5.17C previously appeared as a part of 5.17A.

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.

*Number 1 was built off of the same requirement in reference standard 5.17B and expanded upon.*

2) Testing specific to the cellular therapy product shall include:
   a) For T Cell, 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.

*Number 2 previously appeared as number 1 in reference standard 5.17A.*

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.

*Number 3 previously appeared as number 2 in reference standard 5.17A.*

4) Antigen expression analysis specific to the cellular therapy product, if applicable.

*Number 4 previously appeared as number 2 in reference standard 5.17A.*

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

*5a previously appeared as number 4c in reference standard 5.17A.*

6) If the final product contains red cells, after receipt or before administration, ABO group 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.
Number 6 previously appeared as number 5 in reference standard 5.17A.

7) Testing of cultured cells shall include endotoxin and mycoplasma testing, unless not required under an investigational new drug or license application or as approved by the Competent Authority.

Number 7 previously appeared as number 4 in reference standard 5.17A.

6.2.11 Storage of Records
Records shall be stored to:
3) Permit ready identification
4) Allow retrieval in a defined timeframe.

Subnumber 3 is new to standard 6.2.11 and was added for completeness.
Subnumber 4 was expanded to ensure that facilities had validated retrieval times for records.

6.3.2.2.1 The facility shall have a process to access archived records on media and platforms no longer in use.

This standard is new to the proposed edition and was added understanding that some media are no longer supported, but that records do still exist in this fashion and that facilities need to have the ability to access and read them.

6.3.4.1 Back-up data shall be stored in a secured off-site location.

The committee added the term "secured" for completeness.

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.

Standard 7.1.3.1 is new to the proposed edition but the content is not. The content of standard 7.1.3.1 previously appeared as the second sentence in standard 7.1.3. The committee felt that splitting the concept out would be more appropriate as a standalone standard.

7.3.1 The procurement facility shall have a process to detect, monitor, report, evaluate, and manage, and report donor adverse events.
7.3.2 The clinical facility shall have a process to detect, monitor, report, evaluate, and manage, and report recipient adverse events related to the cellular therapy.

The term “monitor” was added to standards 7.3.1 and 7.3.2 for completeness. The reporting aspect contained in the standards were moved so that they would appear in line with proper workflow.

8.0 Internal and External Assessments
The facility shall perform assessments that verify whether the quality system and operational activities comply with specified requirements.

Standard 8.0 was edited for clarity.

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.

The committee added the clause in bold for clarity.

8.5 Quality Monitoring
The facility shall have a process to collect and evaluate quality indicator data on a scheduled basis, including adverse events.

The committee added new standard 8.5 to the proposed edition for completeness. This standard exists in all other sets of Standards that AABB provides accreditation for.

The committee also included the definition of “Quality Indicator Data” to the Glossary that reads as follows:

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.

The definition is taken from the Standards mentioned above.

9.1 Corrective Action
The process for corrective action shall include:

4) Ensuring that corrective action is reviewed and found to be effective.

The committee added the clause in bold for clarity.

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. National, state, and local regulations apply. **Standard 2.1.4 applies.**

The committee added a cross reference to standard 2.1.4 to ensure that all employees are trained on the elements covered in standard 10.0.

**Glossary**

**Gestational Material:** Any intact tissue procured at or near the time of birth e.g., umbilical cord tissue, placental tissue, amniotic fluid.

The committee (as noted earlier) added the clause “or gestational materials” to “cord blood” where appropriate throughout the Standards. As such a definition was created, which will allow the Standards scope to expand.

**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.

The three definitions for “Label” have been created for clarity.

**Procurement Endpoint:** The product characteristics (eg, volume or number of cells) that meet the procurement goal or that can safely be obtained.

As noted earlier, the committee reviewed the term “procurement endpoint” from the Standards and as such removed the definition.
1. ORGANIZATION

C1.0 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 FDA or relevant Competent Authority. When applicable, the facility shall obtain licensure 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.
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 two year accreditation cycle and have at least one 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 procurement 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.

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.

1.1.4.2.1 The laboratory 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.
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.

1.1.5.2.1 The clinical program director shall have at least one 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 healthcare 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 postadministration 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.

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

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.

C 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 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.

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

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

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.

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.

1.5 Assessment of Risk
The facility’s executive management shall ensure there are continuous risk assessments of the operations or changes to operations that affect product quality and safety. Standard 5.2.1 applies.

1.5.1 Mitigation strategies shall address the level of risk associated with activities in accordance with the FDA or relevant Competent Authority.

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 apply.
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 orientation and initial and ongoing job-specific and quality-systems-related training needs. The facility shall define the qualifications required for trainers.

*C 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.\(^\uparrow\)

\(^\uparrow\)42 CFR 493.1413(b)(9), 42 CFR 493.1451(b)(9)

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

2.1.6.4 Action shall be taken when competence has not been demonstrated.

\(\checkmark\) 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 medical, laboratory, procurement, clinical program directors and quality representative complete 10 hours of educational activities annually related to the accredited activity or activities. Standards 1.1.3.1, 1.1.4.1, 1.1.4.2, and 1.1.5.2 apply.

2.2 Access to Ancillary Services and Direct Patient Care

The clinical facility shall ensure access to medical specialty services and resources as needed for patient care, including but not limited to:

1) Leukoreduced/irradiated blood components for patients receiving hematopoietic stem cell transplants.
2) Pharmacy.
3) Radiology.
4) Laboratory services.
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
Equipment specifications shall be defined before purchase.

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 and manufacturer recommendations.

3.2.1 Installation Qualification
Equipment shall be installed per 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.

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 that, at a minimum, is in accordance with manufacturer’s written instructions.

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 recommendations.

\[F\] 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 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.

3.6.1.1 The alternative systems shall be tested periodically.

3.6.2 A process shall be in place to ensure that the facility has measures to minimize the risk of an internal or 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

4.1.1 Before acceptance of a 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.
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 agreement requirements.

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

4.2 Changes to Agreements
The facility shall define how changes to agreements are made 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 including but not limited to, the following:

F 4.3.1 Medical Orders for Procurement and Processing
There shall be agreements that define the following:
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.
4) These orders are not required for cord blood and gestational banks where the recipient is not known at the time of collection.

Standards 5.14.1 and 5.17.1 apply.
4.3.2 Medical Orders 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.

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 custody during transfer.
2) Timing of product delivery and administration.
3) Agreement by all parties to provide the necessary documentation concerning timing of procurement and pre transplant regimens.

4.3.4 Providing 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.

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 5.3.7.1.
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 upon request. Standard 5.7 applies.

4.3.6 Conditions for Product Storage and Disposition
When products are transferred between departments or facilities, the following conditions shall be defined:
1) Terms and lengths of storage.
2) Possible transfer to another facility.
3) Disposition of the cellular therapy product, including discard.
4.3.7 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.

4.3.8 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 national 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 national 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.

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 cell therapies for administration outside the context of an independent ethics committee-approved protocol.

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 and approved by the 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.

4.5.3 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.

/F4.6 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 and approved by the 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.

/F4.7 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 and approved by the 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.

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 performs 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. Standard 5.12.2.10 applies.

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.

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 Requirements

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. Sample procurement and storage for possible future testing.
   5. Sample 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.
   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.

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 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 cell 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 a:
   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 Requirements

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 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.
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.

5.1.2 Proficiency Testing
The facility shall participate in an external proficiency testing program for each analyte measured by the laboratory.

5.1.2.1 In the United States, for each analyte requiring proficiency testing under CLIA*, each laboratory shall participate in a CMS-approved proficiency testing program.

*42 CFR 493.801

5.1.2.2 In the absence of an external proficiency testing program, proficiency testing shall include comparison of test results from an outside laboratory.
5.1.2.2.1 Proficiency testing for each analyte shall be performed twice a year at a minimum.

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

*C

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

*42 CFR 493.1236

42 CFR 493.803

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 applies.
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 (e.g., pilot or scale-up study results, process flow charts, procedures, data forms).

10) Evaluation of the extent and scope of process validation or re-validation 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.

5.3 Outcomes Data
The facility 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.

5.3.2 For the clinical facility, this shall include 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.
5.3.4 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.

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

5.3.6 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.

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

5.4 Quality Control

The facility shall establish a program of quality control that is sufficiently comprehensive to ensure that materials (including reagents), equipment, and analytical procedures function 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.

5.5 Materials 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.

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.

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 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 Food and Drug Administration (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, gowns, 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 CO₂, 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 patient. 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.

5.6.2.1 The effectiveness of such measures shall be monitored and reviewed on a regular basis.

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.
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 identification and traceability of each cellular therapy product and all related samples from their initial source, through all processing and/or 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.

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 identification 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 cell 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.
2) Verification that the label stock meets facility-defined specifications.
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.
5) The control of label inventory and templates, including discard. Chapter 6,

PROPOSED Standards for Cellular Therapy Services, 10th edition
FOR COMMENT PURPOSES ONLY
JULY 3, 2020 – SEPTEMBER 3, 2020
Cellular therapy products shall be labeled in conformance with the current versions of ISBT 128 or Eurocode labeling.* Standard 5.7 applies.

*Chttp://www.iccbba.org

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

5.8.1.1 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 national regulations.

5.8.2.2 Products approved or licensed by applicable local and/or national governments shall be labeled according to the terms of licensure or approval.

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.iccbba.org

F5.9 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.

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

C 5.9.2 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** The receiving facility shall maintain records of product 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 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.
   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 identification 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 person 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 shall be recorded at least 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.

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

°F5.12 Donor Evaluation


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, 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 Standard 5.12B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors and Reference Standard 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 Bloodapply.

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 transplant, 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 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 the privacy and confidentiality of the donor eligibility determination process.

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 national or local regulations are more stringent:
1) HPC, Cord Blood: Collect maternal sample within 7 days before or after delivery.
2) HPC, Marrow; HPC, Apheresis: Collect from the donor within 30 days before procurement.
3) All other cell therapy products: Collect from the donor within 7 days before or after procurement.

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.

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).”

21 CFR 1271.80

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 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)


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

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 a
Competent Authority (e.g., Centers for Medicare and Medicaid Services) 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 Competent Authority and specifically labeled for cadaveric specimens, when available.

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 national regulations of the receiving facility and to ensure the product meets specified requirements.

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. Standard 5.12.8 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 the Clinical Laboratory Improvement Amendments (CLIA) or that has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS). For facilities located outside of the United States, the use of a laboratory authorized as a testing center by the 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.

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 required by law or regulation, and test results shall be made available to the donor’s legal next of kin if the test result(s) could affect the health of others.

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.

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.

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].”

5.12.8 Donors with Incomplete Eligibility Determinations
Allogeneic donors who were not screened or tested in conformance with requirements of the 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.

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 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 was 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 in accordance with the requirement of the Competent Authority, 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.

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.

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.

\( \textbf{F} \) 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, 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.

\( \textbf{F} \) 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.

\( \textbf{C} \) 5.14.2.3 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.
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.

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.

5.14.5 Procurement Records
A procurement record shall include:
1) Donation identification number.
2) Product code.
3) Product name and attributes.
4) Unique donor 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.

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. Chapter 4, Agreements, applies.
5.14.7.1 Records shall include:
1) Donation identification number.
2) Product code.
3) Product name and attributes.
4) Unique donor identifier, if available.
5) Date and time of procurement, including time zone if applicable.
6) Name and address of the procurement facility.

F5.15 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.

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 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.

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.

5.17.2 Processing Record

A complete processing record shall include:

1) Donation identification number.
2) Product code.
3) Product name and attributes.
4) Unique donor 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.

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. Chapter 4, Agreements, applies.

\[ C \] 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 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 cell 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.

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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 code.
3) Product name and attributes.
4) Unique donor 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 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) Specified requirements, as defined in applicable policies, processes, and procedures, 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.

**C5.23 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.

**F5.24 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 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:
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.
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 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.

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.

5.25.2 The facility shall ensure that orders and responsibility for the provision of patient care are defined and communicated whenever responsibility changes.
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-vs-host disease, cytokine release syndrome and other cellular therapy-associated complications.

5.26.1 Medical Orders

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

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

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.

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 patient for administration of cellular therapy product(s) which shall address, at a minimum, the following:

1) Administration of the preparative regimen, if applicable.

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. Standards 5.7, 5.8, 5.10, and 5.22 apply.

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 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.

F5.29 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 cell products.
6) Treatment of or prophylaxis for infectious disease.
7) Use of blood 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
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:
1) Recipient’s name and unique identifier(s).
2) Donation identification number.
3) Product code.
4) 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 appropriate 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 Recipient Records

Recipient records shall include the following:
1) Recipient’s name and unique identifier(s).
2) Donation identification number.
3) Product 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 cell therapy product.
8) Unique cell 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.
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.

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.)

<table>
<thead>
<tr>
<th>Item No.</th>
<th>Element</th>
<th>Completion of Procurement¹</th>
<th>In-Process Label¹</th>
<th>Completion of Processing</th>
<th>Distribution and Issue²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Donation Identification Number (Unique alpha and/or numeric identifier of the product)³</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>2</td>
<td>Name of the product</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>3</td>
<td>Product attributes⁴</td>
<td>A⁶</td>
<td>R</td>
<td>A⁶</td>
<td>P⁷</td>
</tr>
<tr>
<td>4</td>
<td>Product Code³</td>
<td>P</td>
<td>N/A</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>5</td>
<td>Donor identifier or name⁵</td>
<td>A</td>
<td>N/A</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>6</td>
<td>Date of procurement</td>
<td>R</td>
<td>N/A</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>7</td>
<td>Time of completion of procurement (time zone, if applicable)⁸</td>
<td>R</td>
<td>N/A</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>8</td>
<td>Name of procurement facility/donor registry</td>
<td>R</td>
<td>N/A</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>9</td>
<td>Approximate product volume or weight (if applicable)</td>
<td>R</td>
<td>N/A</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>10</td>
<td>Names/volumes of anticoagulants and other additives (if applicable)</td>
<td>R</td>
<td>N/A</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>11</td>
<td>Recipient name and/or identifier (if known)</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>A⁶</td>
</tr>
<tr>
<td>12</td>
<td>Expiration date and time (if applicable)</td>
<td>N/A</td>
<td>N/A</td>
<td>A⁹</td>
<td>A</td>
</tr>
</tbody>
</table>

¹ Completion of Procurement: P = Present, A = Absent
² Distribution and Issue: P = Present, A = Absent
³ Product Code: Product Description Code, Collection Type Code, Division Code
⁴ Product attributes include: Name, Volume, Weight, Anticoagulants, Additives
⁵ Donor identifier or name: Unique identifier associated with the donor
⁶ Approximate values: A = Absent, P = Present
⁷ Time zone information: R = Present, N/A = Not Applicable
⁸ Date and time information: R = Present, N/A = Not Applicable
⁹ Recipient name and/or identifier: Present, N/A = Not Applicable

PROPOSED Standards for Cellular Therapy Services, 10th edition
FOR COMMENT PURPOSES ONLY
JULY 3, 2020 – SEPTEMBER 3, 2020
<table>
<thead>
<tr>
<th></th>
<th>ABO and Rh of the donor (if applicable)</th>
<th>N/A</th>
<th>N/A</th>
<th>R</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>Red cell compatibility (if applicable)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>R</td>
</tr>
<tr>
<td>15</td>
<td>Recommended storage temperature (in degrees Celsius)</td>
<td>R</td>
<td>N/A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>16</td>
<td>Name and address of the facility that determines the product has met release criteria and makes the product available for distribution</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>R</td>
</tr>
<tr>
<td>17</td>
<td>Biohazard label (if applicable; see Reference Standard 5.8.2B, Requirements for Labeling Shipping Containers)</td>
<td>A</td>
<td>A⁶</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>18</td>
<td>Phrase: “Do Not Irradiate” (if applicable)</td>
<td>N/A</td>
<td>R</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>19</td>
<td>Phrase: “Do Not Use Leukoreduction Filters” (if applicable)</td>
<td>N/A</td>
<td>N/A</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>20</td>
<td>Phrase: “NOT EVALUATED FOR INFECTIOUS SUBSTANCES” and the statement “WARNING: Advise Patient of Communicable Disease Risks” (if applicable)</td>
<td>A</td>
<td>A⁶</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>21</td>
<td>Phrases: “Warning: Reactive Test Results for [name of disease agent or disease]” and “WARNING: Advise Patient of Communicable Disease Risks” (if applicable)</td>
<td>A</td>
<td>A⁶</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>22</td>
<td>Phrase: “For Autologous Use Only” (if applicable)</td>
<td>A</td>
<td>A⁶</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>23</td>
<td>Phrase: “For Use by Intended Recipient Only” (if applicable)</td>
<td>N/A</td>
<td>A⁶</td>
<td>A⁶</td>
<td>A⁶</td>
</tr>
<tr>
<td>Phrase</td>
<td>P</td>
<td>A</td>
<td>R</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>24 “Properly Identify Intended Recipient and Product”</td>
<td>N/A</td>
<td>A⁶</td>
<td>A⁶</td>
<td>A⁶</td>
<td></td>
</tr>
<tr>
<td>25 “Caution: New Drug – Limited by Federal (or United States) Law to Investigational Use” (if applicable)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>A⁶</td>
<td></td>
</tr>
<tr>
<td>26 “For Nonclinical Use Only” (if applicable)</td>
<td>N/A</td>
<td>R</td>
<td>A⁶</td>
<td>A⁶</td>
<td></td>
</tr>
</tbody>
</table>

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 cell 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 Procurement Facility is different from the Processing Facility
9. 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

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

*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).

¹21 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).
²Includes, but is not limited to, a written description of product.
I. Donor Advocacy Services
   All allogeneic donors or their legally authorized representatives shall be provided with the opportunity to access donor advocacy 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. The prospective donor [or legally authorized representative(s), if applicable] shall acknowledge in writing that they have read or viewed the educational material, has been given the opportunity to ask questions, and has 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 material 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 health assessment specific to the donation procedure shall be performed by a 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.

1FDA Guidance, August 8, 2007, “Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps).”
### Reference Standard 5.12B—Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors

#### I. Clinical Evaluation to protect the safety of the donor

<table>
<thead>
<tr>
<th>Required (Yes/No)</th>
<th>Physical examination and health history</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hemoglobinopathy risk(^1)</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Anesthesia risk, if applicable</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Vascular access</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Pregnancy in female donors</td>
<td>Yes</td>
</tr>
</tbody>
</table>

#### II. Clinical Evaluation to protect the safety of the recipient\(^2\)

<table>
<thead>
<tr>
<th>Required (Yes/No)</th>
<th>Donor screening for clinical and physical evidence of risk for, or symptoms of, relevant communicable disease(^3)</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hemoglobinopathy risk(^1)</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Risk of any condition, such as malignancy or any inherited condition that could be transferred to the recipient by transplant</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Evaluate for recent immunization and vaccination history.</td>
<td>Yes</td>
</tr>
</tbody>
</table>

#### History and behavioral risk for exposure to the following infectious agents or diseases\(^2\):

<table>
<thead>
<tr>
<th>Infection</th>
<th>Required (Yes/No)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>Yes</td>
</tr>
<tr>
<td>HBV</td>
<td>Yes</td>
</tr>
<tr>
<td>HCV</td>
<td>Yes</td>
</tr>
<tr>
<td>HTLV (viable, leukocyte-rich products only)</td>
<td>Yes</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Yes</td>
</tr>
<tr>
<td>WNV(^4)</td>
<td>Yes</td>
</tr>
<tr>
<td>Vaccinia (smallpox vaccine)</td>
<td>Yes</td>
</tr>
<tr>
<td>Human TSEs</td>
<td>Yes</td>
</tr>
<tr>
<td>Malaria (travel or residence in malaria-endemic areas)(^5)</td>
<td>Yes</td>
</tr>
</tbody>
</table>
### Trypanosoma cruzi (Chagas disease)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

### Sepsis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

### Zika

<table>
<thead>
<tr>
<th>Disease</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

## III. Laboratory Testing for Allogeneic Donors

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1/2</td>
<td>Yes</td>
</tr>
<tr>
<td>HBV</td>
<td>Yes</td>
</tr>
<tr>
<td>HCV</td>
<td>Yes</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Yes</td>
</tr>
<tr>
<td>HTLV-I/II (viable, leukocyte-rich products only)</td>
<td>Yes</td>
</tr>
<tr>
<td>CMV (viable, leukocyte-rich products only)</td>
<td>Yes</td>
</tr>
<tr>
<td>HLA Type, if applicable&lt;sup&gt;8,9&lt;/sup&gt;</td>
<td>Yes</td>
</tr>
<tr>
<td>ABO/Rh, if applicable&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Yes</td>
</tr>
<tr>
<td>CBC, if applicable</td>
<td>Yes</td>
</tr>
<tr>
<td>WNV&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Yes</td>
</tr>
<tr>
<td>Trypanosoma cruzi (Chagas disease)&lt;sup&gt;5&lt;/sup&gt;</td>
<td>No</td>
</tr>
<tr>
<td>Zika&lt;sup&gt;6&lt;/sup&gt;</td>
<td>No</td>
</tr>
</tbody>
</table>

<sup>1</sup> Applies only to donors where hemoglobinopathy will put the donor or recipient at risk.

<sup>2</sup> Relevant medical records as described in 21 CFR 1271.3(s).

<sup>3</sup> The relevant communicable disease agents or diseases are described in 21 CFR 1271.3(r)(1)(i)(ii) and 1271.3(r)(2).

<sup>4</sup> 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.

<sup>5</sup> 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 federal regulations which 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

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical examination and health history</td>
<td>Yes</td>
</tr>
<tr>
<td>Hemoglobinopathy risk(^1)</td>
<td>Yes</td>
</tr>
<tr>
<td>Anesthesia risk, if applicable</td>
<td>Yes</td>
</tr>
<tr>
<td>Vascular access</td>
<td>Yes</td>
</tr>
<tr>
<td>Pregnancy in female donors</td>
<td>Yes</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Yes</td>
</tr>
</tbody>
</table>

#### II. Laboratory Testing

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO/Rh, if applicable(^2)</td>
<td>Yes</td>
</tr>
<tr>
<td>CBC, if applicable</td>
<td>Yes</td>
</tr>
</tbody>
</table>

\(^1\)Applies only to donors where 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 federal regulations which 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 \(^2,7\)
<table>
<thead>
<tr>
<th>Disease/Agent</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1/2</td>
<td>Yes</td>
</tr>
<tr>
<td>HBV</td>
<td>Yes</td>
</tr>
<tr>
<td>HCV</td>
<td>Yes</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Yes</td>
</tr>
<tr>
<td>HTLV-I/II (viable, leukocyte-rich products only)</td>
<td>Yes</td>
</tr>
<tr>
<td>CMV (viable, leukocyte-rich products only)</td>
<td>Yes</td>
</tr>
<tr>
<td>WNV</td>
<td>Yes</td>
</tr>
<tr>
<td>Trypanosoma cruzi (Chagas disease)</td>
<td>No</td>
</tr>
<tr>
<td>Zika</td>
<td>No</td>
</tr>
</tbody>
</table>

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).
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 federal regulations which 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

<table>
<thead>
<tr>
<th>Required (Yes/No)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor screening for clinical and physical evidence of risk for, or symptoms of, relevant communicable disease</td>
<td>Yes</td>
</tr>
<tr>
<td>Risk of any condition, such as malignancy or any inherited condition that could be transferred to the recipient by transplant.</td>
<td>Yes</td>
</tr>
<tr>
<td>Evaluate for recent immunization and vaccination history</td>
<td>Yes</td>
</tr>
<tr>
<td>Coroner and/or autopsy report (if available)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### History and behavioral risk for exposure to the following infectious agents or diseases

<table>
<thead>
<tr>
<th>Required (Yes/No)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>Yes</td>
</tr>
<tr>
<td>HBV</td>
<td>Yes</td>
</tr>
<tr>
<td>HCV</td>
<td>Yes</td>
</tr>
<tr>
<td>HTLV (viable, leukocyte-rich products only)</td>
<td>Yes</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Yes</td>
</tr>
<tr>
<td>WNV&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Yes</td>
</tr>
<tr>
<td>Vaccinia (smallpox vaccine)</td>
<td>Yes</td>
</tr>
<tr>
<td>Human TSEs</td>
<td>Yes</td>
</tr>
<tr>
<td>Malaria (travel or residence in malaria-endemic areas)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Yes</td>
</tr>
<tr>
<td><em>Trypanosoma cruzi</em> (Chagas disease)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Yes</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Yes</td>
</tr>
<tr>
<td>Zika&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### II. Laboratory Testing

<table>
<thead>
<tr>
<th>Required (Yes/No)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1/2</td>
<td>Yes</td>
</tr>
<tr>
<td>HBV</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
</tr>
<tr>
<td>HCV</td>
<td>Yes</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Yes</td>
</tr>
<tr>
<td>HTLV-I/II (viable, leukocyte-rich products only)</td>
<td>Yes</td>
</tr>
<tr>
<td>CMV (viable, leukocyte-rich products only)</td>
<td>Yes</td>
</tr>
<tr>
<td>HLA Type, if applicable⁷</td>
<td>Yes</td>
</tr>
<tr>
<td>ABO/Rh, if applicable⁷</td>
<td>Yes</td>
</tr>
<tr>
<td>WNV</td>
<td>No</td>
</tr>
<tr>
<td>Trypanosoma cruzi (Chagas disease)⁴</td>
<td>No</td>
</tr>
<tr>
<td>Zika⁵</td>
<td>No</td>
</tr>
</tbody>
</table>

¹Relevant medical records as described in 21 CFR 1271.3(s).
²The 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).
³In 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.
⁴As 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.
⁵In 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.
⁶In 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).
⁷Testing 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 federal regulations which 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:
   f) Total nucleated cell count.
   g) 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 group 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.
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 cell and/or CD45 viability
   c) CD34 assay.
   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 but 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, notify the mother and/or the mother’s physician and recipient’s physician of positive culture results.

   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) Hemoglobinopathy testing of allogeneic cord blood units on a sample obtained from the product or from the donor.
   c) Viable CD34 (direct measurement) 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 or license application or as approved by the 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 Cell, 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) Antigen expression analysis specific to the cellular therapy product, if applicable.

5) Potency 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 group 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) Testing of cultured cells shall include endotoxin and mycoplasma testing, unless not required under an investigational new drug or license application or as approved by the 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.

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) Invalid or obsolete documents are not used.
6) Any archived or obsolete documents are suitably identified as such.

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.

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.
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.

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, Records, shall be retained.

6.2.1.1 Record Traceability
The records system shall ensure the traceability 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.
6.2.4 Record Change
Facilities shall establish and maintain appropriate 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.

6.2.5 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.

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 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 creation (C) or the final disposition (F) of the cellular therapy product with which they are associated. Applicable 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 national, state, or local law may exceed this period.

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.

6.3 Electronic 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 The authorization to access and release data and information shall be defined, and individuals authorized to enter, change, and release results shall be identified.

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 Back-Up Data
The facility shall define and routinely back up all critical data.

6.3.4.1 Back-up data shall be stored in a secure off-site location.

6.3.4.2 Back-up data shall be protected from unauthorized access, loss, or modification.
6.3.4.3 The ability to retrieve data from the back-up system shall be tested periodically.
### Reference Standard 6.2.1A—Records

<table>
<thead>
<tr>
<th>Item No.</th>
<th>Relevant Standard</th>
<th>Record to Be Retained</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Quality System Records</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.0</td>
<td>Responsibility, authority, and relationship of personnel who perform, verify, or manage work covered by the <em>CT Standards</em></td>
</tr>
<tr>
<td>2</td>
<td>1.1.3.1</td>
<td>Procurement medical director management or review of 10 cell procurement procedures</td>
</tr>
<tr>
<td>3</td>
<td>1.1.4.1.1</td>
<td>Laboratory medical director management or review of 10 cell product processing procedures</td>
</tr>
<tr>
<td>4</td>
<td>1.1.4.2.1</td>
<td>Laboratory director management or review of 10 cell product processing procedures</td>
</tr>
<tr>
<td>5</td>
<td>1.1.5.2.1</td>
<td>Relevant continuing education of the clinical program director</td>
</tr>
<tr>
<td>6</td>
<td>1.2.2</td>
<td>Established quality system</td>
</tr>
<tr>
<td>7</td>
<td>1.2.3.1</td>
<td>Policies, processes, and procedures (current and obsolete archived versions) and other documentation related to the quality system</td>
</tr>
<tr>
<td>8</td>
<td>1.2.3.2</td>
<td>Procurement medical director review and approval of all medical policies, processes, and procedures</td>
</tr>
<tr>
<td>9</td>
<td>1.2.3.3</td>
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7. DEVIATIONS, NONCONFORMING PRODUCTS OR SERVICES, AND ADVERSE EVENTS

F7.0 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.

F7.2 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 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.

7.2.2 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.

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

7.3.1 The procurement facility shall have a process to detect, monitor, evaluate, manage, and report donor adverse events.

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.

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.

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.

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.

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.

8.4 Monitoring Clinical Activities
Facilities performing clinical activities shall have a program that monitors and addresses 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.
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.

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.

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. National, state, and 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.

� 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.
The degree of environmental monitoring shall be specific to the cellular therapy product manipulation performed.

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:** The time when the parturient’s contractions are $\leq 5$ minutes apart, lasting up to 60 seconds.

**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 possesses working knowledge of cellular therapy and whose interest is centered on the well-being of the subject and speaks on their 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 (e.g., 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 cell 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.

**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 Therapy Product**: Somatic cell-based products (ie, stem or differentiated cells) that are procured from a donor and intended for manipulation and/or administration.

**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.

**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.

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 directly affect the quality of the 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 (i.e., another department or person within the same organization) or external (i.e., 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 transferring a cellular therapy product that has been determined to meet applicable requirements or which is an authorized nonconforming product.

**Document (noun):** Written or electronically generated information (i.e., 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 comprises 3 elements: the 5 character alphanumeric Facility Identification number (FIN), the 2 character numeric DIN year code, and the 6 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 Material: Any intact 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 cell 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 cell 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 non-medical 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 MNCs. 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.

**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 non-hematopoietic 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 treatment. 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.

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 prior to 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 as 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 cell 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 8 character ISBT 128 code that comprises the 5 character Product Description Code, the 1 character Collection Type Code, and the 2 character Division Code.
**Proficiency Testing:** The structured external evaluation of laboratory methods that assesses the performance of the test system.

**Protected Health Information:** 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 United States Food and Drug Administration (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, in a physically separate area clearly identified for such use, or 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:** 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.

**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 national, state, 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.

**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.

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 cell therapy, intended for transplantation or implantation.
Total Nucleated Cell (TNC): 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 is calculated by the following formula: \( \text{TNC} = (\text{WBCs} + \text{NRBCs}) \times \text{volume} \). 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.