Proposed Standards for Biotherapy Services, 13th Edition

Effective July 1, 2027

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 13th edition begins on page 2 and runs through page 31. The proposed 13th edition begins on page 32 and runs through page 190.

Significant Changes to the Proposed 13th ed of Standards for Biotherapies

Proposed Retitling of the Standards for Cellular Therapy Services

The Cellular Therapies Standards Committee proposes changing the title of this set of Standards from "*Standards for Cellular Therapy Services"* to "*Standards for Biotherapy Services*" effective with the 13th edition.

Cellular therapy refers to therapeutic modalities in which cells constitute the administered product. Biotherapy is a broader category encompassing therapeutic products derived from cells or tissues, including but not limited to cellular therapies. When these *Standards* were first developed, "cellular therapy" accurately described the field and the activities covered. Scientific and technological advances, however, have expanded the field to include increasingly complex cell- and tissue-derived products and services.

The Committee believes that retaining a title limited to "cellular therapy" may not adequately reflect this evolving filed. Retitling the publication as the *Standards for Biotherapy Services* would preserve the requirements applicable to traditional cellular therapies while providing an appropriate framework for addressing additional cell- and tissue-derived modalities as the science, regulatory environment, and professional practice mature.

The proposed title change is a forward-looking framing decision. The Standards Committee is not recommending a substantial expansion of the *Standards'* scope in the 13th edition. Rather, the change is intended to permit the orderly development of future requirements when sufficient scientific, regulatory, and operational consensus exists. Existing requirements addressing organizational responsibilities, resources, equipment, suppliers and customers, process control, documents and records, deviations and nonconformances, adverse events, assessments, process improvement, and facilities and safety are grounded in quality-management principles that are broadly relevant to cell- and tissue-derived products.

In an effort to be proactive, the definition of "biotherapies" has been edited to read:

Biotherapies: For the purposes of these Standards, biotherapies are products derived from cells or tissues that may be unmanipulated, manipulated, or manufactured and are intended for therapeutic use in accordance with applicable requirements of the appropriate Competent Authority. These Standards may also apply to cellular starting materials, intermediate products, and materials intended for nonclinical research that support the development of these therapies.

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

The committee replaced the term "cellular therapy" with "biotherapy" for consistency with the title change of the edition. This change has been made throughout the edition where appropriate.

C **1.1.3 Procurement Facilities**
The procurement facility shall have a medical director **who will be a member of executive management. When the medical director delegates these responsibilities to another qualified medical professional (designee), the medical director shall retain** ultimate responsibility**. Reference**

Standards 1.1A and 1.1B apply ~~who is ultimately responsible for ensuring that the determination of donor eligibility and medical suitability was performed, when applicable~~.

~~1.1.3.1 Procurement Medical Director~~

~~The procurement medical director shall be a member of executive management and 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 shall have responsibility and authority for the scope of accredited medical activities related to the procurement of cellular therapy products and services under these CT Standards. 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 at least 1 year of experience in the scope of procurement activities performed by that facility.~~

~~C1.1.3.1.2~~ ~~The procurement medical director shall have had active oversight of a minimum of 10 cell product procurement procedures related to their scope of responsibilities throughout the preceding 2-year accreditation cycle. Standard 2.1.2 applies.~~

***C*1.1.4 Processing Facilities**

The processing facility shall have a laboratory medical director and a laboratory director who will be **members of the executive management. When the laboratory medical director delegates these responsibilities to another qualified medical professional (designee), the medical director shall retain ultimate responsibility. Reference Standards 1.1A and 1.1B apply** ~~responsible for the processing, storage, and/or provision of the product under their responsibilities~~.*

*42 CFR 493.1405, 42 CFR 493.1407, 42 CFR 493.1443, and 42 CFR 49.1445.

For accredited facilities that are assessed by AABB for conformance with the Clinical Laboratory Improvement Amendments (CLIA), refer to the Verification of CLIA Compliance Form before on-site assessment.

1.1.4.1 In order for the laboratory director to also serve as laboratory medical director, the individual shall meet the requirements for the laboratory medical director.

***42 CFR 493.1443(b)(3), 42 CFR 493.1445(e).**

For accredited facilities that are assessed by AABB for conformance with the Clinical Laboratory Improvement Amendments (CLIA), refer to the Verification of CLIA Compliance Form before on-site assessment.

~~1.1.4.1Laboratory Medical Director~~

~~The laboratory medical director(s) shall be a member of executive management and shall be a licensed physician with relevant experience, and qualified by training. The processing laboratory medical director shall participate in continuing education in activities performed by the facility as required by these CT Standards. The laboratory medical director(s) shall have responsibility and authority for the scope of accredited medical activities related to the processing and provision of cellular therapy products and~~

services under these CT Standards. When the medical director delegates these responsibilities to another qualified medical professional (designee), the medical director shall retain ultimate responsibility.*

*42 CFR 493.1405, 42 CFR 493.1407, 42 CFR 493.1443, and 42 CFR 49.1445.

For accredited facilities that are assessed by AABB for conformance with the Clinical Laboratory Improvement Amendments (CLIA), refer to the Verification of CLIA Compliance Form before on-site assessment.

1.1.4.1.1 The laboratory medical director shall have at least 1 year of experience in the scope of processing activities performed by the facility.†

†42 CFR 493.1443.

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

***C*1.1.4.1.2** The laboratory medical director shall have had active oversight of a minimum of 10 cell product processing procedures related to their scope of responsibilities throughout the preceding 2-year accreditation cycle. Standard 2.1.2 applies.

1.1.4.2 Laboratory Director

The laboratory director shall be a member of executive management and have 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 technical aspects of the facility for the scope of accredited services that are related to the processing and provision of cellular therapy products and services under these CT Standards. When the laboratory director delegates these responsibilities to a designee, the laboratory director shall retain ultimate responsibility.*

*42 CFR 493.1405, 42 CFR 493.1407, 42 CFR 493.1443, and 42 CFR 493.1445.

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

1.1.4.2.1 The laboratory director shall have at least 1 year of experience in the scope of processing activities performed by the facility.†

†42 CFR 493.1443.

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

***C*1.1.4.2.2** The laboratory director shall have had active oversight of a minimum of 10 cell product processing procedures related to their scope of responsibilities throughout the preceding 2-year accreditation cycle. Standard 2.1.2 applies.

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.

***C* 1.1.5 Clinical Facility**

The clinical facility shall have a program director **who will be a member of executive management. When the clinical program director delegates these responsibilities to another qualified medical professional (designee), the clinical program director shall retain ultimate responsibility** ~~responsible for patient care and product administration.~~**. Reference Standards 1.1A and 1.1B apply.**

~~**1.1.5.2 Clinical Program Director**~~

~~The clinical program director shall be a member of the executive management and 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 1 year of experience in the scope of clinical services.~~

~~***C* 1.1.5.2.2** Relevant continuing education shall be obtained throughout the accreditation cycle in the scope of clinical activities performed in the facility.~~

Reference Standard 1.1A – Required Qualifications for Executive Management Directors

Facility Type	Role	License/ Degree	Experience and Training	Continuing Education (Annually)
Procurement Facility	Medical Director	Licensed Physician (MD or equivalent)	At least 1 year of relevant experience in the scope of procurement activities performed by the facility*	At least 10 hours of continuing medical educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility^
Processing Facility	Medical Director	Licensed Physician (MD or equivalent)	At least 1 year of relevant experience in the scope of processing activities performed by the facility*	At least 10 hours of continuing medical educational activities relevant to the role and the biotherapy activity or associated activities performed in the facility^
Processing Facility	Laboratory Director	Doctoral degree in a relevant biological science (PhD or equivalent)	At least 1 year of relevant experience in the scope of processing activities performed by the facility*	At least 10 hours of educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility^

		Advanced degree in a relevant biological science	**At least 10 years of relevant experience in the scope of processing activities performed by the facility***	**At least 10 hours of educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility^**
Clinical Program	**Clinical Program Director**	**Board-certified licensed physician (MD or equivalent)**	**At least 1 year of relevant experience in the scope of clinical activities**	**At least 10 hours of continuing medical educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility^**

***42 CFR 493.1443.**

^42 CFR 493.1413(b)(7) and 42 CFR 493.1451(b)(7).

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

Reference Standard 1.1B – Required Responsibilities of Executive Management Directors

Facility Type	Role	Scope of Duties	Documented Active Oversight
Procurement Facility	**Procurement Medical Director**	**Accredited medical activities related to the procurement of biotherapy products and services under these Biotherapies Standards, including:** • **verification that donor eligibility and medical suitability were performed, when applicable, and** • **management of procurement adverse events**	**At least 10 biotherapy product procurement procedures related to their scope of duties throughout the preceding 2-year accreditation cycle**
Processing Facility	**Laboratory Medical Director**	**Accredited medical activities related to the processing and provision of biotherapy products and services under these Biotherapies Standards, including:** • **processing,** • **storage, and/or** • **provision of the product**	**At least 10 cell product processing procedures related to their scope of duties throughout the preceding 2-year accreditation cycle**
Processing Facility	**Laboratory Director**	**Technical and operational aspects of the facility for the scope of accredited services that are related to the processing and provision of biotherapy products and services under these Biotherapies Standards**	**At least 10 cell product processing procedures related to their scope of duties throughout the preceding 2-year accreditation cycle**

Clinical Program	**Clinical Program Director**	**All aspects of the clinical program, including:** • **medical,** • **technical,** • **operational, and** • **quality management regarding the selection and care of patients and donors and product administration**	**At least 10 cell, gene, and tissue based therapy recipient cases related to their scope of duties throughout the preceding 2-year accreditation cycle**

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

In an effort to provide clarity, the committee has deleted the standards in strikethrough above and incorporated that content in two new reference standards, one focused on the qualification of the roles that are a part of executive management and one focused on the responsibilities of those same individuals. The elements in bold in the standards have been pulled from the standards deleted to ensure that elements that could not fit in the reference standards were represented.

1.2.1.2 On an annual basis, the quality representative shall complete a minimum of 10 hours of educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility.*

*42 CFR 493.1413(b)(7) and 42 CFR 493.1451(b)(7).
For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

The content of standard 1.2.1.2 is not new but appeared as a part of standard 2.1.6.1 which has now been deleted as for all other positions this requirement appears in the new reference standards.

1.4.2 Facilities shall perform a risk assessment for all critical activities during procurement, processing, storage, transport, testing, and distribution.

The committee created new standard 1.4.2 for completeness. While standard 1.4 exists, the committee felt that a specific standard directed at the activities specific to procurement, processing, storage, transport, and testing was important.

1.5.1 The facility shall have a policy to address critical ~~supply~~ shortages **that can affect the services provided by the organization**.

The committee edited standard 1.5.1 as the terminology that previously appeared felt to geared toward the BB/TS Standards where this standard originated.

✎**C** **2.1.6 Continuing Education**

The organization shall ensure that continuing education requirements applicable to these Biotherapies Standards are met when applicable. **Reference Standards 1.1A and 1.1B apply**.

~~**2.1.6.1** The facility shall ensure that the medical, laboratory, procurement, and clinical program directors, and the quality representative, annually complete a minimum~~

~~of 10 hours of educational activities relevant to the role and the associated cellular therapy activity or activities performed in the facility.* Standards 1.1.3.1, 1.1.4.1, 1.1.4.2, and 1.1.5.2 apply.~~

~~*42 CFR 493.1413(b)(7) and 42 CFR 493.1451(b)(7).~~
~~For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.~~

With the creation of the new reference standards at the end of chapter 1, the need for standard 2.1.6.1 was negated. The content has moved over to a "Continuing Education" column.

2.2 Access to Ancillary Services and Direct Patient Care

The clinical facility shall have an agreement in place to ensure comprehensive care and relevant resources required for patient care in ~~cellular~~ **bio**therapies, including, but not limited to:
2) ~~Services related to~~ Pharmacy **services**.

The committee edited subnumber 2 for clarity, the intent has not changed.

3.5.3 The organization shall:

7) Tracing of any given product or service to all equipment associated with the procurement, processing, storage, distribution, and administration of the product or service.
8) Identification and recall of all biotherapy products associated with a specific piece of equipment.

~~**C3.6 Equipment Traceability**~~
~~The organization shall maintain records of equipment use in a manner that permits:~~
~~1) Equipment to be uniquely identified and traceable.~~
~~2) Tracing of any given product or service to all equipment associated with the procurement, processing, storage, distribution, and administration of the product or service.~~
~~3) Identification and recall of all cellular therapy products associated with a specific piece of equipment.~~

Based on a review of chapter 3, it was deemed that this standard is redundant to many standards in chapter 3, specifically the 3.5 thread and standard 6.2.2 in chapter 6. While this is a QSE, it is causing issues for accredited facilities and will be struck from the other standards as they are being set, starting with the proposed 17th ed of RT Standards. The committee did request to keep elements of 3.6 into standard 3.5.3

3.5.4.1 When a nonconformance cannot be attributed to a specific piece of equipment, all potentially affected pieces of equipment shall be assessed to determine expected performance measures based on the manufacturer's written instructions.

The committee created new standard for clarity. This clarifies that in the case where a malfunction cannot be attributed to one piece of equipment, all other equipment has to be assessed. Note this standard is being incorporated into all sets of AABB Standards.

F **3.7.1 Artificial Intelligence Oversight**

The organization shall establish and maintain a framework for the responsible use of Artificial Intelligence (AI) technologies. This framework shall apply to all processes where AI influences policy development, critical decision making, or donor/patient/staff safety. The facility shall maintain documentation of intended use, validation of output, including evidence, and audit trails for AI-driven decisions.

F **3.7.2 Risk Management of AI Output(s)**

The facility shall:

1) Define roles and responsibilities of the individual(s) for the oversight and use of AI.

2) Determine the intended use of AI.

3) Perform risk assessments of the AI software before implementation.

4) Ensure compliance with ethical principles, privacy, and applicable regulations.

3.7.3 Verification of AI Output(s)

The facility shall verify the AI fitness for the intended use, including bias checks, and performance metrics.

Standard 3.3 applies.

3.7.4 Monitoring of AI

The organization shall monitor and manage the performance of AI models including inputs and outputs.

3.7.4.1 The facility shall monitor AI performance on a scheduled basis to detect unintended outcomes. Standards 3.5.4 and 3.5.4.1 apply.

Recognizing that AABB members are using artificial intelligence as a part of their day to day activities, the committee felt that it was important to include standards that could apply to all AABB members with regard to implementation, risk management, verification of the output, and monitoring of AI as part of their usage of the tool. The impetus for this was a memo drafted by the SPC and APC to the Board, and their assent to the committees to spearhead this. Whatever the final language, the standards will be implemented across all AABB Standards in the future.

4.2.3.2.5 Specifications and requirements for **donor and recipient** ~~patient~~ care, quality, safety, and other facility-defined critical parameters.

The committee replaced "patient" with "donor and recipient" as this allows the entire continuum to be covered in a way that "patient" did not. This change has been made throughout the edition.

4.2.3.2.6 Adherence to all applicable CGMP and CGTP requirements for third party service providers.

Based on a comment, the committee created the new standard 4.2.3.2.6 to ensure that all third part providers of a service to a facility is doing so in accordance with the current GMP and GTP regulations where appropriate.

4.2.5.2.1 **For facilities that distribute biotherapy products for further manufacture or storage, there shall be an order that conforms to the quality agreement.**

The committee created the new standard 4.2.5.2.1 for clarity. This ensures that distribution facilities follow the quality agreement in place according to its supplier and customer expectations.

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

The committee edited standard 4.5.2.2 for clarity. The committee felt that the clause in strikethrough was redundant and could potentially cause confusion.

4.5.3 The terms and length of storage, possible transfer to another facility, and disposition, including discard, of the 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~~ **gestational parent**, ~~biologic mother~~ **genetic parent**, and, where applicable, gestational surrogate).

Genetic Parent ~~**Biologic Mother:**~~ The person who is the source of the ovum.

Gestational Parent ~~**Birth Mother:**~~ The person carrying the fetus to term.

The committee has replaced the terms "biologic mother" and "birth mother" with "genetic parent" and "gestational parent" to ensure that the standards represent the most up to date verbiage. This terminology is in use by the American College of Obstetricians and Gynecologists, and a better reflection of these individuals.

Reference Standard 4.5A—Donor Informed Consent or Authorization
I. General Informed Consent

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

Throughout the edition, where the term "health-care professional" appears, the committee added the term "qualified" for clarity.

III. Authorization for Cadaveric Donors

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~~ **donor eligibility and medical** suitability ~~and eligibility~~.

Throughout the edition, the committee has adjusted the order of the terms "eligibility and suitability" to mirror common understanding. The intent of the standard(s) has not changed.

5.1.1.1 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 product shall be validated before the change is implemented. Standard **1.4 and** 2.1.4 **apply** ~~applies~~.

The committee added a crossreference to standard 1.4 (risk assessment" for clarity.

F **5.1.9.1.1**The facility shall have a policy for the use/**distribution** ~~issue~~ of a **biotherapy** ~~cellular therapy~~ product provided by a supplier and/or received by a consignee that lacks a complete chain of custody. Standards 7.2.4 and 7.2.6.2 apply.

After a review of the edition, the committee elected to replace the term "issue" with "distribution". The term "issue" as it was used in the edition is consistent with the newly revised definition of "distribution". The removal of "issue" from the edition brings the Standards in line with all other accrediting organizations as well as the FDA. The committee felt after reviewing its use and the definition that this was a remnant of the BB/TS Standards from which the Biotherapies Standards were derived from.

The committee rewrote the definition of "distribution" and "distributing facility" to ensure there was clarity of the intent.

Distribution: The transportation or shipment of a biotherapy product or its precursor that meets facility defined release criteria, or urgent medical need as applicable.

Distributing ~~Issuing~~ Facility: The facility that distributes the biotherapy product or its precursor for further manufacturing, storage, or clinical use.

5.1.10.2 In the absence of an approved external proficiency testing program, **an alternative assessment process shall be used and approved by the appropriate medical director at least twice annually** ~~proficiency testing shall include comparison of test results from an outside laboratory~~.

The committee edited standard 5.1.10.2 recognizing that in some countries many proficiency testing are not available, and that the alternative assessment is the standard at this time.

C **5.1.11 Investigational Products**

The organization shall ensure that processes are carried out in conformance with the Investigational New Drug (IND) application or equivalent as approved by the FDA or relevant Competent Authority. Standard 1.1.2 applies.

The committee added this standard for completeness wanting to ensure that all accredited organizations follow the processes as outlined by their IND (or equivalent) as indicated. This will be a benefit for our assessors.

5.2.2 For the clinical **program** ~~facility~~, this shall include the clinical outcomes as specified by the clinical protocols and as applicable:

6) Immune effector cell endpoints.*

7) Gene therapy product endpoints.*

*** FDA Guidance for Industry: Long Term Follow-Up After Administration of Human Gene Therapy Products (January 2020)**

The committee added new subnumber 7 for completeness and to mirror the expanded scope of the Standards. The addition of the link to the FDA Guidance provides support to the inclusion of new subnumber 7 and supports existing subnumber 6.

5.4.1 Biotherapy ~~Cellular Therapy~~ Product Manipulation

Biotherapy ~~Cellular therapy~~ Product manipulation shall address the following:

2) Use of biological safety cabinets or other environmentally controlled spaces, if applicable.^

5) Facility defined time limits for each phase of manufacturing, if applicable.*

10) Labeling.

11) Disposition of **processing and/or manufacturing by-products** ~~cellular therapy by products and waste~~.

^ FDA Guidance for Industry: Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (December 2011)

*** 21 CFR 211.111**

The committee added a reference to the FDA Guidance of the GTPs to subnumber 2 for completeness.
The committee added new subnumber 5 (along with a reference to the CFR) to ensure that facilities define the time phases for each phase of product manipulation.
The committee also added a new subnumber 10 for completeness recognizing this step is integral in the manipulation.
Finally, subnumber 11 was edited for clarity. This better meets the current framework of the current edition of the Standards.

5.4.2 Aseptic Methods

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

6) Sterilization of equipment **and supplies**, as applicable.

Standards 5.3.5, 5.12 and 10.1 apply.

21 CFR 1271.150.

The committee added the clause "and materials" to subnumber 6 for completeness.
The committee added the crossreferences to the standards cited to for completeness.

✎C **5.4.3 Operational Controls**

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

6) Cleaning and setup of spaces and equipment between **manufacturing** ~~production~~ runs.

The committee replaced the term "production" with "manufacturing" for clarity and accuracy.

5.5 Product Identification and Traceability

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

✎C **5.5.1 Traceability and Unique Identification**

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

The committee added the clause, "and by-products" for completeness to ensure that the samples and their by products were included in the traceability process.

5.6.1.2 Apheresis and marrow **cellular starting materials** ~~products~~ shall be labeled with ISBT 128 or Eurocode labels at the time of procurement.

The committee replaced the term "products" with "cellular starting materials" for clarity.

5.6.1.3.~~2.1~~ ~~Other cellular therapy~~ **If the information required for a complete ISBT 128 label is not available at the time of procurement,** products shall be labeled with the proper name and a unique alpha or numeric identifier, at a minimum, at the time of procurement.

The committee edited standard 5.6.1.3 for clarity. This recognizes that there are times when a biotherapy product does not have all the contents of an ISBT 128 label at the time of procurement and ensures that the biotherapy product in question is labeled with the critical information.

5.6.1.4.1 For biotherapy products that are procured but do not require further processing/manufacture, an ISBT 128 or Eurocode compliant label shall be applied before distribution or administration.

The committee created new standard 5.1.6.1.4.1 for completeness. This ensures that products that need further manipulation are labeled appropriately before distribution or administration.

5.6.1.7 Special Labeling Requirements of Investigational Products
Investigational products shall be labeled with ISBT 128, Eurocode labels or a label approved by the FDA or relevant Competent Authority.

5.6.1.7.1 If an ISBT 128 or Eurocode label has not been approved by the FDA or relevant Competent Authority the label shall include the following at a minimum:
1) For procurement facilities:
-Product name.
-Unique alpha or numeric product identifier.
-Product type.
-Two unique donor identifiers.
-Chain of identity identifier, if applicable.
-Date and time of procurement.
2) For processing facilities, additionally:
-Processing facility identifier.
-Product expiration date and time, if applicable.

The committee added new standard 5.6.1.7 and 5.6.1.7.1 recognizing that there are instances where some investigational products cannot be labeled with an ISBT 128 or Eurocde label, and in those instances that these are the minimum requirements to appear on the label until such time as the appropriate label can be applied to the product.

5.6.3.4 When labeling a licensed biotherapy product, the information contained on the label shall be consistent with the distributor's accompanying information.

5.6.3.4.1 If a label cannot display all required product attributes, an additional label with the remaining information shall be attached. Reference Standard 5.6.2A, Requirements for Labeling of Products applies.

The committee added new standards 5.6.3.4 and 5.6.3.4.1 for completeness. These standards ensure that the product label contains all the appropriate information, and in cases where it cannot due to issues of size or content, they will ensure the additional information shall be contained on an additional label.

✎***C*5.8 Inspection and Testing of Cellular Starting Materials and Final Biotherapy 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.

The committee edited the standard for clarity and completeness.

✎C **5.8.1 Receipt of Incoming ~~Cells, Tissues, and Organs~~ Cellular Starting Materials**
At the time of receipt, incoming ~~cells, tissues, and organs~~ **cellular starting materials** shall be inspected, sampled, and/or tested, as appropriate, to determine their acceptability. Standards 5.6.1, 5.6.3, and 5.7.6 apply. Records of the following shall be maintained:
14) Certificate of analysis, **summary of records**, or manufacturer's insert or equivalent, if applicable.

The committee edited standard 5.8.1 for clarity and completeness. The inclusion of "summary of records" in subnumber 14 ensures conformance with FDA requirements.

5.8.1.1 Identification of ~~Cells, Tissues, and Organs~~ Cellular Starting Materials upon Receipt
The facility shall require verification of the chain of identity of ~~cells, tissues, and organs~~ **cellular starting materials**.

5.8.1.2 **Cellular starting materials** ~~Cells, tissues, and organs~~ shall be quarantined upon receipt and their disposition determined by a qualified individual when any of the following occur:
2) The **cellular starting materials** ~~cells, tissues, and organs~~ are judged as not meeting acceptance criteria.
3) The **cellular starting materials** ~~cells, tissues, and organs~~ require further sampling, labeling, processing, or testing before disposition.
4) The **cellular starting materials** ~~cells, tissues, and organs~~ are determined to be nonconforming, or donor eligibility has not been determined, or the donor is ineligible.

For consistency the committee edited standards 5.8.1.1 and 5.8.1.2 to mirror the standards cited above.

✎C **5.9.1** Storage areas shall have the capacity and design to ensure that proper temperature, humidity, **and light*, as applicable** are maintained.
***21 CFR 211.142(b)**

The committee added "and light" to the standard to recognize that this is an environmental condition that the FDA requires to be regulated.

✎C **5.9.1.1** If **biotherapy** ~~cellular therapy~~ products are stored in an open storage area, the ambient temperature and humidity shall be recorded **at facility defined intervals based on the product's stability profile(s) and a risk assessment** ~~at a minimum of every 4 hours~~. Standard 1.4 applies.

The committee edited standard 5.9.1.1 recognizing that the 4 hour time frame was not based in science and could be different based on environment and facility practices. This edit ensures that the standard meets all potential member needs.

5.9.3.1 The temperature and/or liquid nitrogen levels of freezers where **biotherapy** ~~cellular therapy~~ products are immersed in liquid nitrogen **or stored in vapor phase** shall be recorded **at manufacture defined intervals, or if not provided, at facility defined intervals based on the biotherapy product's stability profile(s) and a risk assessment** ~~every 24 hours, at a minimum~~. **Standard 1.4.2 applies**.

The committee edited standard 5.9.3.1 for clarity and to mirror the changes made to standard 5.9.1.1. The committee added "or stored in vapor phase" for completeness.

5.9.3.2 The temperature of refrigerators and freezers where **biotherapy** ~~cellular therapy~~ products ~~are not immersed in liquid nitrogen~~ **are stored** shall be recorded **at manufacturer defined intervals, or if not provided, at facility defined intervals based on the product's stability profile(s) and a risk assessment. Standard 1.4.2 applies** ~~every 4 hours, at a minimum~~.

In line with the changes to standards 5.9.1.1 and 5.9.3.1 the committee updated standard 5.9.3.2 accordingly.

✎C **5.9.4** Storage devices containing **cellular starting materials, intermediate products, and final biotherapy** ~~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.

The committee edited standard 5.9.4 to ensure parallel construction with other standards throughout the edition.

5.10.1 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 **starting material or biotherapy product**. This evaluation shall be conducted by a **qualified** health-care professional and shall include, based on examination, clinical history, and relevant medical record(s):

The committee edited the standard for consistency with other standards in the edition.

5.10.1.1 The ability to tolerate the **collection** ~~donation~~ procedure.

The committee replaced the term "donation" with "collection" for clarity.

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

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

21 CFR 1271.80.

The committee added the term "donor blood" for clarity.

***F** **5.10.4 Evaluation of Cellular ~~Therapy Products~~ Starting Materials and Biotherapy Products**

Before shipment or transport of cellular ~~therapy products~~ **starting materials, and biotherapy products** the receiving facility shall review the donor screening and infectious disease testing records for compliance with applicable local and FDA or relevant Competent Authority regulations of the receiving facility, to ensure the product meets specified requirements.

The committee edited standard 5.10.4 for parallel construction with other changes in the edition.

5.10.6 ~~Abnormal~~ Indeterminate or Reactive Results on Donor Screening and Testing

5.10.6.1 The facility shall establish policies, processes, and procedures for notification of **indeterminate** ~~abnormal~~ or reactive infectious disease test results. Standard 7.2.4 applies.

***F** **5.10.6.2** **Indeterminate or reactive** ~~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.

***F** **5.10.6.3** **Indeterminate or reactive** ~~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 biotherapy product shall be communicated to the recipient's physician and to the recipient before distribution of the biotherapy product for clinical use. Reference Standards 4.5A, Donor Informed Consent or Authorization, and 4.7A, Patient Informed Consent, apply.

***F** **5.10.7 Products from Ineligible Donors**

The biohazard label shall be attached to any allogeneic product for which there are ~~abnormal~~ **incomplete** donor screening or **indeterminate or reactive** testing results. All allogeneic products from ineligible donors shall be provided only under urgent medical need and according to local and/or FDA or relevant Competent Authority regulations. The product shall be labeled with the phrase "WARNING: Advise patient of communicable disease risks." Reference Standard 5.6.2A, Requirements for Labeling of Biotherapy Products, applies.

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

To remain in conformance with the current language, the committee replaced the term "abnormal" with "indeterminate" or "reactive" where appropriate.

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

The committee removed the term "marker" as it was deemed superfluous.

F **5.12.1 Medical Order for Procurement**

The procuring facility shall obtain a medical order before the procurement procedure for all **cellular starting materials** ~~cellular therapy products other than for cord blood or gestational materials~~. The medical order shall include procurement goals. Standard 5.13 applies.

5.12.1.1 **Cellular starting materials** ~~Cord blood, gestational materials, or tissue or cellular starting materials~~ collected via a noninvasive procedure and before identification of an intended recipient do not require a medical order before procurement. Standard 5.22 applies.

The committee edited standards 5.12.1 and 5.12.1.1 to ensure parallel construction with other changes to the edition.

F **5.12.5 Procurement Records**

A procurement record shall include:

5) Chain of identity identifier, if applicable.

The committee added #5 for completeness.

F **5.15.1 Medical Order for Processing, Preservation, or Storage**

The facility performing processing, preservation, or storage shall obtain a **medical** order from a health-care provider, if applicable. The **medical** order shall contain information that uniquely identifies the donor and the recipient. Specific instruction for processing and preservation shall be provided in the order as appropriate.

The committee added the term "medical" to the standard for completeness. In this case this would be a medical order and should reflect that accordingly.

F **5.15.2 Processing Record**

A complete processing record shall include:

1) Donation identification number.

2) Product description code, type of collection, and division code.
3) Product name and attributes.
4) Unique donor and/or patient identifier, if available.
5) Unique, traceable, chain-of-identity identifier, if applicable.
6) Date and time of procurement.
7) Name and address of processing facility.
8) All details of critical processing, preservation, and storage steps.* Records shall include:
a) Date and time (if applicable) of critical steps.
b) Names of persons responsible for each step.
c) Names, manufacturers, lot numbers, and expiration dates of all critical materials used in processing, preservation, and storage.
d) Quantities of reagents used.
e) Identifiers of equipment used.
9) Documentation of product distribution or final disposition.
10) Final review as defined by the facility's policies, processes, and procedures.

***5.17.3 applies**

The committee added a crossreference to standard 5.17.3 which is focused on records of cryopreserved products as an element to review as part of the processing record.

✎*F* **5.15.4 Managing Red Cell Antigen Incompatibility**

The processing facility shall manage red cell antigen incompatibility **between the donor and the recipient**, as applicable ~~between the donor and the recipient~~.

The elements in bold that were moved within the standard were done based on the addition. This ensures that assessors can review the procedures in place.

5.15.5 Processing Records

Each facility or the facilities performing processing, preservation, or storage shall provide a copy of the product processing record ~~insofar as the processing records~~ concerning the safety, purity, and potency of the product or cellular starting material involved, or a summary of the product processing record to the facility(ies) receiving the product, while maintaining chain of custody **and chain of identity**. Chapter 4, Suppliers and Customers, applies.

The committee added the clause in bold for completeness. The elements in strikethrough were removed as they were deemed redundant to the title and section the standard appears in.

✎*C* **5.16 Storage of Noncryopreserved Biotherapy Products or Cellular Starting Materials**

The facility shall establish, for each type of product or cellular starting material, the storage specifications and defined storage conditions, including temperature range and length of storage to maintain facility-defined ~~attributes~~ **critical characteristics, including viability, to ensure integrity and suitability for use** ~~(eg, viability)~~.

The committee replaced the term "attributes" with "critical characteristics" as the committee could not define the term and its use. The term "critical characteristics" is more well known in the community and better reflects current practice.

5.17 Cryopreservation of Biotherapy ~~Cellular Therapy~~ Products

Biotherapy ~~Cellular therapy~~ products ~~or cellular starting materials~~ shall be cryopreserved using a controlled-rate freezing procedure or equivalent procedure validated to maintain **critical characteristics, including viability**. The temperature of the product(s) and/or freezing process shall be monitored.

To committee edited standard 5.17 to mirror the edits to standard 5.16 for parallel construction.

5.17.2.1 Cord blood products shall have at least two integrally attached segments cryopreserved with the product **for further testing**. Standard 5.5.1.3 and Reference Standard 5.15B, Processing Tests for HPC, Cord Blood Products or Gestational Materials (#5), apply.

The committee added the clause in bold for clarity.

5.18.1 The facility shall define and validate expiration dates **for each biotherapy product type based on facility-defined critical characteristics**. Reference Standard 5.6.2A, Requirements for Labeling of **Biotherapy** ~~Cellular Therapy~~ Products (#13), applies.

The committee edited standard 5.18.1 for completeness and in line with edits to standard 5.16 and 5.17.

5.18.2.1 For each critical quality characteristic, statistical criteria for sample size and test intervals shall be established to demonstrate stability.*
***21 CFR 211.166**

The committee created new standard 5.18.2.1 to remain in line with FDA requirements to ensure that all products are demonstrating stability, beyond just cryopreserved products.

5.21 Distribution

F **5.21.1** Upon request for distribution, the following items shall be reviewed:
1) Documentation that the product was requested. Standards 4.2.3.1 and 4.2.5 apply.
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) **including.**
-Recipient's name and unique identifier(s).
-Donation identification number.
-Product description code, type of collection, and division code.
-Product name and attributes.
-Unique donor identifier, if available.
- Chain of identity identifier, if applicable.
- Chain of custody, if applicable.
3) Product condition by visual inspection, including container closure and integrity.

~~4) Recipient identification, if applicable.~~

4) 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 **5.21.2 The processing facility shall document the following at the time of distribution:**

1) Identity of person(s) verifying that the product is intended for the recipient.

2) Identity of the person distributing the product.

3) Identity of the person to whom the product was distributed.

4) Date(s) and time(s) of distribution.

~~***F*** **5.22 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, including container closure and integrity.~~

~~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*** **5.22.1** The issuing facility shall review and verify the following items at the time of final cellular therapy product distribution/issue:~~

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

~~2) Donation identification number.~~

~~3) Product description code, type of collection, and division code.~~

~~4) Product name and attributes.~~

~~5) Unique donor identifier, if available.~~

~~6) Product condition by visual inspection, including container closure and integrity.~~

~~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(s) and time(s) of issue.~~

In line with the committee's decision to remove the term "issue" from the standards (as noted in standard 5.1.9.1.1 above), the elements of former standard 5.22 (product issue) have been incorporated into standard 5.21.1 focused on "distribution." For those element that could not fit into 5.21.1, new standard 5.21.2 has been created to ensure that the focus of distribution from the processing facility perspective was included. The content of the standards are not new.

5.21.4 ~~**5.22.2**~~At distribution ~~and issue~~ of allogeneic products, the following information shall accompany the product or be readily available wherever the product is located to maintain the chain of custody:

In line with the edits made above, the committee removed the term "issue" from the standard.

✎F **5.22 Return of Biotherapy ~~Cellular Therapy~~ Products**

The facility shall have a policy for the return of biotherapy products that includes:
3) Determination of the acceptability and disposition of the **biotherapy** product, such as **redistribution** ~~reissue~~, storage, further manufacturing, or discard.

In line with the edits made above, the committee replaced the term "reissue" with "redistribution" in the standard for parallel construction.

✎F **5.23 Redistribution of Returned ~~Cellular Therapy~~ Biotherapy Products**

The facility shall have a policy for the ~~reissue~~ **redistribution** of ~~cellular therapy~~ **biotherapy** products that includes:
1) Criteria for **redistribution** ~~reissue~~ eligibility.
4) Product preparation for **redistribution** ~~reissue~~, including label verification.

Standards 5.21.1 and 5.21.2 apply.

In line with the edits made above, the committee replaced the term "reissue" with "redistribution" in the standard for parallel construction.

5.23.1 ~~Patient (Recipient) Evaluation~~

The facility shall define clinical indications and ensure that **recipient** evaluation criteria are met and continue to be met before treatment. This evaluation shall be conducted by a **qualified** health-care professional and approved by a physician.

The committee edited the standard for clarity.

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

The committee edited the standard for parallel construction with the standards cited above.

✎F **5.28.4 Administration Records**

Records of administration shall include:
9) Date and time of expiration, if applicable.
10) Chain of identity identifier, if applicable.

To ensure consistency with other standards concerning records, subnumbers 9 and 10 have been added for completeness.

Reference Standard 5.6.2A—Requirements for Labeling of Biotherapy Products

*(For labeling of regulated investigational products or licensed products, Standards 5.6.2.1 and 5.6.2.2 apply.)**

Item No.	Element	Completion of Procurement[1]	In-Process Label[1]	Completion of Processing	Distribution ~~and Issue~~[2]

To remain consistent with edits made to the edition, the committee removed the clause "and issue" from the reference standard header.

Reference Standard 5.6.2A—Requirements for Labeling of Biotherapy Products
*(For labeling of regulated investigational products or licensed products, Standards 5.6.2.1 and 5.6.2.2 apply.)**

3	Product attributes[4]	A[5] **or P**	R	A[5] **or P**	P[6]

A = attached ~~(may be permanently affixed)~~

The committee added "or P" (permanently affixed) to the reference standard in line 3 (and others where appropriate, 5, 11, 12, 13, 17, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28) recognizing that labels that are attached can also be permanently affixed as noted in the footnote. The committee felt that it was more appropriate to include the "P" into the table than to use the footnote.

Reference Standard 5.6.2A—Requirements for Labeling of Biotherapy Products
*(For labeling of regulated investigational products or licensed products, Standards 5.6.2.1 and 5.6.2.2 apply.)**

12	~~Patient/~~Recipient name and/or identifier (if known)[9]	R	R	R	A[5] or P

In conjunction with edits made to the edition, the committee removed the term "patient" for consistency.

Reference Standard 5.6.2A—Requirements for Labeling of Biotherapy Products
*(For labeling of regulated investigational products or licensed products, Standards 5.6.2.1 and 5.6.2.2 apply.)**
* **When more than one element is indicated, either option is suitable.**

The committee added the new footnote for the title to indicate that in either case where of labeling investigational or licensed products, that either the "A" or "P" are appropriate.

Reference Standard 5.6.2A—Requirements for Labeling of Biotherapy Products
[2]The final labeling information for distribution shall be on or included with the container before the product is **distributed** ~~issued or transported~~.

The committee replaced "issued or transported" with "distributed" for parallel construction with other edits to the edition.

Reference Standard 5.6.2A—Requirements for Labeling of Biotherapy Products
[5]If ~~affixing or~~ **attaching** the applicable warnings and statements to the container is physically impossible, then the label **element(s)** must accompany the human cells, tissues, and cellular and tissue-based products.

The committee edited the footnote for consistency with the other edits to the table.

Reference Standard 5.6.2B—Requirements for Labeling Shipping Containers

Item No.	Element	Shipping Document*	Outer Shipping Container
2	Phrase: "Do Not Irradiate" (if applicable)	R	A **or P**

In line with edits to reference standard 5.6.2A, the element of "permanently affixed" "P" has been added to the outer shipping container requirements where attached using a tie tag was included (3,4, 5, 6, 7).

Reference Standard 5.10A—General Requirements for Biotherapy Product and Cellular Starting Material Donors[1]

III. Determination of Donor Eligibility and Medical Suitability

4) **Donor** eligibility and medical suitability determination shall be performed and approved in a manner and time frame that provides current relevant information and protects the safety of the intended recipient and donor.

The committee added the term "donor" for completeness.

Reference Standard 5.10A—General Requirements for Biotherapy Product and Cellular Starting Material Donors[1]

III. Determination of Donor Eligibility and Medical Suitability

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 **determination** could not be completed.

The committee added the term "determination" for completeness.

Reference Standard 5.10A—General Requirements for Biotherapy Product and Cellular Starting Material Donors[1]

III. Determination of Donor Eligibility and Medical Suitability

4) Cadaveric Donors

c) Organs, tissues, or cells procured from cadaveric donors shall be within 24 hours after death if the body is cooled or refrigerated within 12 hours of death, or 15 hours after death if the body was not cooled or refrigerated.

The committee added subletter c to the edition for completeness. This ensures that all organs, tissues, or cells are procured within a timeframe that ensures viability.

Reference Standard 5.10B—Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors

~~[8]FDA Guidance for Industry: Recommendations to Reduce the Risk of Transmission of *Mycobacterium tuberculosis* (Mtb) by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (January 2025).~~

The committee deleted the footnote as the FDA guidance has since been removed.

Reference Standard 5.10D—Clinical Evaluation and Laboratory Testing of Cord Blood or Gestational Material Donors

~~[8]FDA Guidance for Industry: Recommendations to Reduce the Risk of Transmission of *Mycobacterium tuberculosis* (Mtb) by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (January 2025).~~

The committee deleted the footnote as the FDA guidance has since been removed.

Reference Standard 5.10E—Clinical Evaluation and Laboratory Testing of Cadaveric Donors

~~[7]FDA Guidance for Industry: Recommendations to Reduce the Risk of Transmission of *Mycobacterium tuberculosis* (Mtb) by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (January 2025).~~

The committee deleted the footnote as the FDA guidance has since been removed.

Reference Standard 5.15A—Processing Tests for HPC, Apheresis and HPC, Marrow

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

The committee added the clause "if applicable" for recognizing that there are instances when an ABO and Rh typing is not performed, specifically for autologous donors.

Reference Standard 5.15B—Processing Tests for HPC, Cord Blood

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

The committee edited subnumber 4 to include the clause in bold for clarity, recognizing that this would not take place if no microbial contamination is detected. This mirrors the language in the previous paragraph.

Reference Standard 5.15B—Processing Tests for HPC, Cord Blood

5) The following tests shall be performed before **distribution** ~~issue~~:

The committee edited subnumber 5 for parallel construction with other edits made to the edition.

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

The committee removed the clause in strikethrough as it was deemed guidance and will be moved there accordingly.

Reference Standard 5.15C—Processing Tests for Biotherapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood

2) Testing specific to the **biotherapy** ~~cellular therapy~~ product shall include:
   a) For T cells, CD3+ cell count.
   b) For islets, islet equivalents (IEQ).
   c~~d~~) **Relevant** cell viability, if applicable.
   d~~e~~) For other **biotherapy** ~~cellular therapy~~ products, the relevant cell count shall be defined by the facility and **shall define appropriate product characterization criteria and measurements be defined, if** applicable.

The committee edited subletter d (previously c) for clarity.

6.2.5.3 The ~~actual~~ result of each action performed shall be recorded immediately, and the final interpretation shall be recorded upon completion of testing.

The committee removed the term "actual" as it was deemed superfluous.

6.2.6.1 The record shall identify the work performed, the individual performing the activity, and ~~when~~ **the date and if applicable, time** it was performed.

The committee replaced "when" with "date and if applicable time" as that is what would be expected by "when".

6.3.1.2 **The facility shall define and identify which** individuals ~~shall be identified and defined by job description~~ are authorized to create, modify, maintain, or transmit records in a controlled and approved manner in conformance with the FDA or relevant Competent Authority requirements.

The committee replaced the clause with the element in bold for clarity. The standard now reads more clearly.

8.3.1 When corrective action is taken, it shall be developed, implemented, and evaluated in accordance with Chapter 9, Process Improvement.

The committee added standard 8.3.1 which appears in other sets of AABB Standards.

***C*8.5 Monitoring Clinical Activities**

Facilities performing clinical activities shall have a program that addresses, evaluates, and monitors patient care practices for all biotherapies. The following shall be monitored:

8) ~~Compliance~~ **Conformance** with peer-reviewed recommendations.

10) Critical process points ~~(eg, hand-offs, confirmation of patient identification before medical intervention)~~ for conformance with policies, processes, procedures, and protocols.

Subnumber 8 has been edited to mirror the language that best reflects AABB, in this case conformance. Compliance is a term predominantly used in the biotherapy space with the FDA.

Subnumber 10 has removed the eg as it was deemed guidance and will be moved there accordingly.

10.1.1 Policies, processes, and procedures shall identify and take appropriate intervention to limit exposure ~~and address the~~ **to** hazards present in the facility including, **but not limited to**:
1) Biological,
2) Chemical, and,
3) Radiation safety, if applicable.

The intent of the standard has not changed; however, the standard was reordered to appear as a list for legibility purposes.

10.1.1.1 The facility shall maintain a system for monitoring ~~training and compliance~~ **exposures and for minimizing potential exposure to hazards.**

Standard 10.1.1.1 previously appeared as the second sentence of standard 10.1.1, however the committee felt it would be more appropriate as a stand alone substandard. The committee added the clause in bold to provide specificity.

10.1.5 The clinical facility shall have either on-site or ready access to services, **resources, and personnel** to manage anticipated adverse events and provide emergency medical care.

The committee added the elements in bold for completeness.

Autologous Donor: An **individual** ~~person~~ who acts as **their** ~~his or her~~ own biotherapy product(s) donor.

The committee edited this definition for clarity.

~~**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.~~

The committee elected to remove the term from the glossary as it was deemed unnecessary.

~~**Bacteremia:** Systemic inflammatory response due to an infectious agent and accompanied by characteristic clinical and laboratory findings.~~

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

The committee removed these terms from the glossary as they do not appear in the Standards.

Biotherapies: For the purposes of these Standards, biotherapies are products derived from cells or tissues and intended for therapeutic use. Biotherapies may include cellular therapies, gene-modified cellular therapies, tissue-based therapies, and cell- or tissue-based regenerative medicine products. These Standards may apply to starting materials, intermediate products, and materials intended for nonclinical research that support the development or manufacture of these therapies.

The committee created this definition based on the definition that exists on the AABB website, however it is has been edited to better reflect the edition.

~~**Cellular Therapy:** Cell-based products that may be minimally or more than minimally manipulated, including cellular immunotherapies, regenerative medicines, and other types of autologous and allogeneic cells, tissues or organs.~~

Based on the new definition of "Biotherapies" the committee felt that the definition for the product was no longer necessary as it was including as an element in that definition.

By-Products: Portions of the original **biotherapy** ~~cellular therapy~~ product (**eg, cells, tissues or organs)** retained for **further** ~~nonclinical~~ use.

The committee edited the definition for clarity.

Characterization: A process by which the molecular, physical, and/or functional attribute(s) of cells, tissues, or organs are defined ~~cell's identity by the expression, or activity, of certain genes in its DNA and the resulting production of particular proteins~~.

Based on edits to the edition, the committee updated the definition of characterization to include the concept of attributes.

Compliance (Biotherapy Standards): The act of adhering to regulatory requirements.

The QSEs define compliance as "see conformance" but for the purposes of these Standards, the committee wished to provide a definition of the term to reflect adherence to appropriate regulations.

Continuing Education: Ongoing adult learning and training after initial qualification/education has been granted. Relevant continuing education consists of educational activities related to the activities performed at the facility that serve to enhance professional development related to the job functions by maintaining, developing, or increasing, the knowledge and skills of an individual.

Continuing Medical Education: Ongoing adult learning and training after completion of medical training. Continuing medical education is received from an accredited organization with the goal of maintaining competency or increasing the knowledge, skills, and professional abilities that a physician uses to provide services in the relevant field of work.

The committee created new definitions for continuing education and continuing medical education for completeness and to ensure a differentiation between the two terms.

Cryopreservation: The process of ~~low temperature~~ freezing and storage of **biotherapy** ~~cellular therapy~~ products **at low temperature** in **the presence of a cryoprotectant** ~~order~~ to preserve **their key critical characteristics** ~~cells that, after thawing, retain a significant measure of their prefreeze viability and function~~.

The committee edited the definition for clarity, better reflecting the expectations of the community.

Designee: An individual with appropriate experience or expertise who is given the authority to assume a specific responsibility **and who is not the primary individual responsible by job description**.

The committee added the element in bold to reflect the requirements in the standards in chapter 1.

Donation Identification Number (DIN): A 13-character code that identifies products from a single donation event that allows each event to be uniquely identified. The DIN contains three elements: the five-character alphanumeric facility identification number (FIN), the two **digit** ~~character numeric DIN code~~ year **the DIN was assigned**, and the six **digit** ~~character numeric DIN~~ sequence number.

The committee edited this definition based on the definition from ICCBBA for accuracy.

Final Biotherapy ~~Cellular Therapy~~ Product: A **biotherapy** ~~cellular therapy~~ product that is ready for **distribution** ~~issue or final distribution~~.

Based on edits made throughout the edition, the committee edited this definition for parallel construction.

Handling: The various operations involved in the preparation, processing, and movement of materials and products. This includes actions such as receiving, transporting, **shipping**, unpacking, sorting, and preparing items for manufacturing or further distribution.

The committee added the term "shipping" to the definition for completeness.

In Vitro: Biological or chemical processes that are performed outside a living organism ~~Observable in an artificial environment~~.

The committee edited this definition for clarity.

In Vivo: Biological or chemical processes that are performed inside a living organism ~~within the living body~~.

The committee edited this definition for clarity.

Information System Life-Cycle Requirements: The stages and time span from initial planning of an information system software program to its retirement; that is, from concept, to software development, to business changes, to revisions, to retirement.

The committee added the clause "Information System" to the definition to reflect the fact that the term in question only appeared in terms of software, the definition itself has not changed.

~~**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.~~

Based on the edits made to the edition, the committee deleted these definitions.

Leukocyte-Rich Products: Leukocyte-rich products are **products that contain a high number of leukocytes/white blood cells. They 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 and progenitor cells such as apheresis products, marrow, umbilical/placental cord blood or gestational materials, and nucleated cell preparations such as mononuclear cells collected by apheresis (MNC, Apheresis). Some organs and tissues can be leukocyte-~~

~~rich.~~

The committee edited the definition of this term for clarity. The elements in strike through will be included in the guidance.

Medical Suitability: Refers to the health status of an individual to donate or receive a product. ~~Evaluation of cellular therapy donors for risks related to the donation process and potential noninfectious risks to the recipient.~~

The committee edited this definition for clarity.

~~**Mesenchymal Stem Cells:** A cellular therapeutic product defined as multipotent cells with the ability to differentiate into nonhematopoietic tissues of mesodermal origin.~~

~~**Mononuclear Cells (MNCs):** Lymphocytes and monocytes in the collected product.~~

The committee deleted the terms as they do not appear in the edition.

Offsite Location: A location that is not within the same contiguous building as the facility's primary site of activity ~~physical storage facility or electronically supported storage medium that provides reliable redundancy of data.~~**.**

The committee edited the definition of the term above for clarity.

~~**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.~~

The committee deleted the term as it did not appear in the edition.

Qualification (equipment or suppliers): A documented process of verifying that equipment and/or systems are properly installed, function as intended, and are fit for their designated use ~~specified attributes required to accomplish the desired task have been met~~**.**

The committee edited the definition of the term above for clarity.

Reference Sample: A sample collected from a donor or product that is retained and used for future testing to establish identity, compatibility, or quality of the product.

The committee added this new definition for clarity and based on its use in the edition.

~~**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.~~

The committee removed the term from the glossary as they felt it was deemed unnecessary.

Shipping: The physical act of transferring a biotherapy product within or between facilities. During shipping, the product **is not under** ~~leaves~~ the control of trained personnel at the originating or receiving facility.

The committee edited this definition to mirror the definition of transport.

Sterility: Being free of ~~An aseptic condition, meaning an absence~~ living microorganisms.

The committee edited this definition for clarity.

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 **biotherapy** product is available and the ~~recipient~~ **patient** is likely to suffer **death or** serious **illness** ~~morbidity or~~ without receiving the **biotherapy** ~~cellular therapy~~ product.

The committee edited this definition for clarity.

Viability: The measurement of living cells ~~Demonstrated capability of living; indicating (either in-vivo or in-vitro) ability to perform physiologic functions~~.

The committee edited this definition for clarity.

QSE 1 - Organization

Key Concepts

This quality system essential (QSE) describes the responsibilities of executive management, the nature of the quality system, and the need for ongoing attention to operational and quality issues through demonstrated management commitment.

Key Terms

Customer: The recipient of a product or service. A customer may be internal (eg, another organizational unit within the same organization) or external (eg, a patient, client, donor, or another organization).

Emergency Management: Strategies and specific activities designed to manage situations in which there is a significant disruption to organization operations or a significantly increased demand for the organization's products or services.

Executive Management: The highest-level personnel within an organization, including employees, clinical leaders, and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or a group of individuals.

Organization: An institution, or a location or operational area within that organization; the entity assessed by the AABB and receiving AABB accreditation for specific activities.

Policy: A set of basic principles or guidelines that direct or restrict the organization's plans, actions, and decisions.

Procedure: A defined series of tasks and instructions that specify how an activity is to be performed.

Process: A set of related activities that transform inputs into outputs.

Quality Management System: The organizational structure, responsibilities, policies, processes, procedures, and resources established by executive management to achieve quality.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Organizational charts or documents describing roles, responsibilities, and decision-making authority.
- Evidence of executive management review of a quality system.
- Applicable federal, national, state, and local laws and regulations, as well as copies of any required certificates.
- Defined quality system.
- Process for approving exceptions to policies, processes, and procedures, as well as documented examples, if applicable.
- Risk assessments and mitigation strategies.
- Emergency operation and disaster continuity plan(s).

- Executive management review of customer feedback.

1. Organization

1.0 Organization

The organization shall define the parties responsible for the provision of products or services.

1.1 Executive Management

The organization shall have a defined executive management. Executive management shall have:
1) Responsibility and authority for the quality system and operations.
2) Responsibility for compliance with these Biotherapies Standards and applicable laws and regulations, including all applicable current good manufacturing practice (CGMP) requirements.
3) Authority to establish or make changes to the quality system.

1.1.1 The facility shall demonstrate institutional support for the biotherapy program.

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

C **1.1.3 Procurement Facilities**

The procurement facility shall have a medical director who will be a member of executive management. When the medical director delegates these responsibilities to another qualified medical professional (designee), the medical director shall retain ultimate responsibility. Reference Standards 1.1A, Required Qualifications for Executive Management Directors and 1.1B, Required Responsibilities of Executive Management Directors apply.

C **1.1.4 Processing Facilities**

The processing facility shall have a laboratory medical director and a laboratory director who will be members of the executive management. When the laboratory medical director delegates these responsibilities to another qualified medical professional (designee), the medical director shall retain ultimate responsibility. Reference Standards 1.1A, Required Qualifications for Executive Management Directors and 1.1B, Required Responsibilities of Executive Management Directors apply. *

*42 CFR 493.1405, 42 CFR 493.1407, 42 CFR 493.1443, and 42 CFR 49.1445.

For accredited facilities that are assessed by AABB for conformance with the Clinical Laboratory Improvement Amendments (CLIA), refer to the Verification of CLIA Compliance Form before on-site assessment.

1.1.4.1 In order for the laboratory director to also serve as laboratory medical director, the individual shall meet the requirements for the laboratory medical director.*

*42 CFR 493.1443(b)(3), 42 CFR 493.1445(e).

For accredited facilities that are assessed by AABB for conformance with the Clinical Laboratory Improvement Amendments (CLIA), refer to the Verification of CLIA Compliance Form before on-site assessment.

✎C **1.1.5 Clinical Facility**

The clinical facility shall have a program director who will be a member of executive management. When the clinical program director delegates these responsibilities to another qualified medical professional (designee), the clinical program director shall retain ultimate responsibility. Reference Standards 1.1A, Required Qualifications for Executive Management Directors and 1.1B, Required Responsibilities of Executive Management Directors apply.

1.1.5.1 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 System

The organization shall have a quality system. The organization's executive management shall ensure that this quality system is implemented and followed at all levels of the organization.

1.2.1 Quality Representative

The quality system shall be under the supervision of a designated person who reports to executive management.

1.2.1.1 The quality representative shall have defined independent authority for ensuring that the facility establishes, implements, and maintains a quality system that meets the requirements of these Biotherapies Standards. When the quality representative delegates these responsibilities to a designee, the quality representative shall retain ultimate responsibility.

✎C **1.2.1.1.1** This individual shall report to executive management at least quarterly on quality system activities and to other staff as appropriate.

✎C **1.2.1.1.2** These reports shall be used for management review and improvement of the quality system.

1.2.1.2 On an annual basis, the quality representative shall complete a minimum of 10 hours of educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility.*

*42 CFR 493.1413(b)(7) and 42 CFR 493.1451(b)(7).

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

✎*C* **1.2.2 Management Reviews**

Management shall assess the effectiveness of the quality system at defined intervals.

✎*C* **1.2.2.1** The review of the quality system shall occur at a minimum on an annual scheduled basis to ensure that the system meets the requirements of these Biotherapies Standards.

1.2.3 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.

✎**C1.3 Policies, Processes, and Procedures**

Policies, processes, and procedures shall be implemented and maintained to satisfy the applicable requirements of these *Biotherapies Standards*. All such policies, processes, and procedures shall be in writing or captured electronically and shall be followed.

1.3.1 The medical director and/or laboratory director (as applicable) shall approve all medical and technical policies, processes, and procedures.

✎*C* **1.3.1.1** The procurement medical director shall review and approve all procurement policies, processes, and procedures.

✎*C* **1.3.1.2** The laboratory medical director shall review and approve all medical laboratory policies, processes, and procedures.

✎*C* **1.3.1.3** The laboratory director shall review and approve all technical laboratory policies, processes, and procedures.

✎*C* **1.3.1.4** The clinical program director shall review and approve all clinical policies, processes, and procedures related to administration and patient care.

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

✎**C** **1.3.2** Any exceptions to medical and technical policies, processes, and procedures shall require justification and preapproval by the medical director and/or laboratory director, as applicable.

✎**C1.4 Risk Assessment**

The facility shall have a process to perform risk assessments for activities at defined intervals. Standards 5.1.1 and 6.1.5 apply.

1.4.1 Mitigation strategies shall identify, assess, and address the level of risk associated with quality and safety.

1.4.2 Facilities shall perform a risk assessment for all critical activities during procurement, processing, storage, transport, testing, and distribution.

1.5 Operational Continuity

The organization shall address continuity in the event that operations are at risk.

1.5.1 The facility shall have a policy to address critical shortages that can affect the services provided by the organization.

1.6 Emergency Preparedness

The organization shall have an emergency operation plan(s) to respond to the effects of internal and external disasters.

✎**C** **1.6.1** The emergency management plan, including emergency communication systems, shall be tested at defined intervals.

1.6.1.1 This evaluation shall occur, at a minimum, on an annual scheduled basis.

1.7 Communication of Concerns

The organization shall have a process for personnel to anonymously communicate concerns about quality or safety. Personnel shall be given the option to communicate such concerns either to their organization's executive management, AABB, or both. AABB's contact information shall be readily available to all personnel.

1.8 Customer Focus

Executive management shall identify the organization's customers and their needs and expectations for products or services.

1.9 Facility Status Changes

The facility shall communicate to AABB within 30 days of any change(s) that directly or indirectly impacts a facility's accreditation status.

1.9.1 If the organization is the subject of regulatory enforcement action by a relevant Competent Authority, the organization shall notify AABB within 7 days of the receipt of notification.

1.10 Unanticipated Event Notification

Within 30 days, the organization shall notify AABB of the discovery of an event that has caused, is causing, or is likely to cause serious injury or harm, or death, to an individual resulting from any deviation(s) related to the scope of these Biotherapies Standards.

1.11 Human Subject 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.

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

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

Reference Standard 1.1A – Required Qualifications for Executive Management Directors

Facility Type	Role	License/ Degree	Experience and Training	Continuing Education (Annually)
Procurement Facility	Medical Director	Licensed Physician (MD or equivalent)	At least 1 year of relevant experience in the scope of procurement activities performed by the facility*	At least 10 hours of continuing medical educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility^
Processing Facility	Medical Director	Licensed Physician (MD or equivalent)	At least 1 year of relevant experience in the scope of processing activities performed by the facility*	At least 10 hours of continuing medical educational activities relevant to the role and the biotherapy activity or associated activities performed in the facility^
Processing Facility	Laboratory Director	Doctoral degree in a relevant biological science (PhD or equivalent)	At least 1 year of relevant experience in the scope of processing activities performed by the facility*	At least 10 hours of educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility^
		Advanced degree in a relevant biological science	At least 10 years of relevant experience in the scope of processing activities performed by the facility*	At least 10 hours of educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility^
Clinical Program	Clinical Program Director	Board-certified licensed physician (MD or equivalent)	At least 1 year of relevant experience in the scope of clinical activities	At least 10 hours of continuing medical educational activities relevant to the role and the associated biotherapy activity or activities performed in the facility^

*42 CFR 493.1443.

^42 CFR 493.1413(b)(7) and 42 CFR 493.1451(b)(7).

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

Reference Standard 1.1B – Required Responsibilities of Executive Management Directors

Facility Type	Role	Scope of Duties	Documented Active Oversight
Procurement Facility	Procurement Medical Director	Accredited medical activities related to the procurement of biotherapy products and services under these Biotherapies Standards, including: • verification that donor eligibility and medical suitability were performed, when applicable, and • management of procurement adverse events	At least 10 biotherapy product procurement procedures related to their scope of duties throughout the preceding 2-year accreditation cycle
Processing Facility	Laboratory Medical Director	Accredited medical activities related to the processing and provision of biotherapy products and services under these Biotherapies Standards, including: • processing, • storage, and/or • provision of the product	At least 10 cell product processing procedures related to their scope of duties throughout the preceding 2-year accreditation cycle
Processing Facility	Laboratory Director	Technical and operational aspects of the facility for the scope of accredited services that are related to the processing and provision of biotherapy products and services under these Biotherapies Standards	At least 10 cell product processing procedures related to their scope of duties throughout the preceding 2-year accreditation cycle
Clinical Program	Clinical Program Director	All aspects of the clinical program, including: • medical, • technical, • operational, and • quality management regarding the selection and care of patients and donors and product administration	At least 10 cell, gene, and tissue based therapy recipient cases related to their scope of duties throughout the preceding 2-year accreditation cycle

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

Excerpt of Reference Standard 6.2.9A Relevant to Organization

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/ Management Issues	Unit/ Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
1.1.3	Procurement medical director management or review of 10 cell procurement procedures	X	X	X	C	10
1.1.4	Laboratory medical director and laboratory director management or review of 10 cell product processing procedures	X	X	X	C	10
1.1.5	Relevant continuing education of the clinical program director	X	X	X	C	10
1.2.1.1.1, 1.2.1.1.2	Quarterly reports by quality representative to executive management	X	X	X	C	10
1.2.2	Management review of effectiveness of the quality system	X	X	X	C	10

1.2.2.1	Yearly review of the quality system	X	X	X	C	10
1.3	Policies, processes, and procedures	X	X	X	C	10
1.3.1.1	Procurement medical director review and approval of all medical policies, processes, and procedures	X	X	X	C	10
1.3.1.2	Laboratory medical director review and approval of all medical policies, processes, and procedures	X	X	X	C	10
1.3.1.3	Laboratory director review and approval of all technical policies, processes, and procedures	X	X	X	C	10
1.3.1.4	Clinical program director review and approval of all clinical policies, processes, and procedures	X	X	X	C	10

1.3.2	Exceptions to policies, processes, and procedures	X	X	X	C	10
1.4	Risk assessment	X	X	X	C	10
1.6.1	Emergency operation plan tested at defined intervals	X	X	X	C	2 years, or two organizational testing intervals (whichever is longer)

[1]Applicable federal, state, or local law may exceed this period.

QSE 2 – Resources

Key Concepts

This QSE describes the need for resources—human, financial, and otherwise—to support the work performed. It also describes personnel issues such as the qualification of staff, assessments of competence [including those performed under Clinical Laboratory Improvement Amendment (CLIA) regulations], and continuing education requirements.

Key Terms

Competence: An individual's demonstrated ability to apply knowledge and skills needed to perform the job tasks and responsibilities.

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.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Current job descriptions.
- Evaluation of staffing levels and workload, if performed.
- Process for recruiting and hiring.
- Personnel records (eg, certifications, qualifications, competence assessments, diplomas, transcripts).
- Training records.
- Evaluations of competence records.
- Evidence that job qualifications are met.
- Continuing education records.

2. Resources

2.0 Resources

The organization shall have adequate resources to perform, verify, and manage all the activities described in these Biotherapies Standards.

2.1 Human Resources

The organization shall employ an adequate number of individuals qualified by education, training, and/or experience.*

*21 CFR 1271.170.

✎C **2.1.1 Job Descriptions**

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

✎C **2.1.2 Qualification**

Personnel performing critical tasks shall be qualified to perform assigned activities on the basis of appropriate education, training, and/or experience.†

†42 CFR 493.1403, 42 CFR 493.1409, 42 CFR 493.1415, 42 CFR 493.1421, 42 CFR 493.1441, 42 CFR 493.1447. 42 CFR 493.1453, 42 CFR 493.1459, 42 CFR 493.1461, and 42 CFR 493.1487.

For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

✎C **2.1.3 Training**

The organization shall provide training for personnel performing critical tasks.‡

‡21 CFR 211.25.

✎*C* **2.1.3.1** This training shall include:

1) Orientation.
2) Initial job-specific training to perform assigned responsibilities.
3) Quality-systems-related training.
4) Ongoing job-specific training for employee assigned responsibilities.

Standards 2.1.4, 2.1.6, and 5.1.1 apply.

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

✎C **2.1.4 Competence**

Evaluations of competence shall be performed before independent performance of assigned activities and at specified intervals.

✎C **2.1.4.1** Action shall be taken when competence has not been demonstrated. Standard 9.1 applies.

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

*21 CFR 211.25, 42 CFR 493.1413(b)(8), and 42 CFR 493.1451(b)(8).
For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

2.1.4.3 For individuals who perform moderate- and high-complexity testing, semiannual reviews of competence shall be performed in their first year of employment. For facilities located in the United States, specified requirements apply.†

†42 CFR 493.1413(b)(9) and 42 CFR 493.1451(b)(9).
For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

2.1.4.4 Competence shall be assessed when new or novel processes or procedures are introduced. Standard 5.1.4 applies.

✎C **2.1.5 Personnel Records**

Personnel records for each employee shall be maintained.

2.1.5.1 For those authorized to perform or review critical tasks, records of names, signatures, initials or identification codes, and inclusive dates of employment shall be maintained.

✎C **2.1.6 Continuing Education**

The organization shall ensure that continuing education requirements applicable to these Biotherapies Standards are met when applicable. Reference Standards 1.1A and 1.1B apply.

2.1.6.1 Requirements for the relevant continuing education activities performed by the facility as required by these Biotherapies Standards shall be defined for employees who perform critical tasks.

2.2 Access to Ancillary Services and Direct Patient Care

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

1) Transfusion medicine.
2) Pharmacy services.
3) Radiology.
4) Laboratory services.
5) Acute care or medical facilities.
6) Social and psychological support.
7) Long-term follow-up based on protocol or treatment plan.

Excerpt of Reference Standard 6.2.9A Relevant to Resources

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/ Management Issues	Unit/ Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
2.1.1	Job descriptions	X	X	X	C	10
2.1.2	Qualification of personnel performing critical tasks	X	X	X	C	10
2.1.3	Training records of personnel	X	X	X	C	10
2.1.3.1	Identification of qualifications required for trainers	X	X	X	C	10
2.1.4	Evaluations of competence	X	X	X	C	10
2.1.4.1	Corrective action when competence has not been demonstrated	X	X	X	C	10
2.1.5	Personnel records of each employee	X	X	X	C	10
2.1.6, 2.1.6.1	Continuing education requirements	X	X	X	C	10

[1]Applicable federal, state, or local law may exceed this period.

QSE 3 – Equipment

Key Concepts

This QSE describes the selection, use, maintenance, and monitoring of equipment, including information systems. It also describes the use and testing of alternative systems when primary systems fail.

Key Terms

Backup: Digital data and/or physical storage containing copies of relevant data.

Calibrate: To set or align measurement equipment against a known standard**.**

Corrective Action: Actions taken to address the root cause(s) of an existing nonconformance or other undesirable situation in order to reduce or eliminate recurrence.

Critical Equipment/Materials: A piece of equipment or material that can affect the quality of the organization's products.

Data Integrity: The accuracy, completeness, and consistency of information resources.

Equipment: A durable item, instrument, or device used in a process or procedure.

Installation Qualification: Verification that the correct equipment is received and that it is installed according to specifications and the manufacturer's recommendations in an environment suitable for its operation and use.

Operational Qualification: Verification that equipment will function according to the operational specifications provided by the manufacturer.

Performance Qualification: Verification that equipment performs consistently as expected for its intended use in the organization's environment, using the organization's procedures and supplies.

Validation: Establishing evidence that a process, executed by users in their environment, will consistently meet predetermined specifications.

Verification: Confirmation by examination and provision of objective evidence that specified requirements have been met.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Processes for equipment selection, qualification, and maintenance.
- List or tool used for critical equipment identification.
- Equipment calibration and maintenance records, if applicable.
- Equipment qualification records.
- Manufacturer's written instructions
- Records of investigation of equipment malfunction, failure, repair, and requalification, if applicable.

- Alarm system testing and records of alarm management, if appropriate.
- Evidence of information system backup and records of testing.

3. Equipment

3.0 Equipment

The organization shall define and control critical equipment.

3.1 Equipment Specifications

Equipment specifications shall be defined before purchase.

C3.2 Qualification of Equipment

All critical equipment shall be qualified for its intended use. Equipment shall be requalified, as needed, after repairs and upgrades.

3.2.1 Installation Qualification

Equipment shall be installed per manufacturer specifications.

3.2.2 Operational Qualification

Each piece of equipment and component of an information system shall be verified before actual use.

3.2.3 Performance Qualification

Equipment shall perform as expected for its intended use.

3.2.3.1 Facility-developed predetermined criteria shall meet the specifications established by the manufacturer or be qualified for its intended use.

3.3 Use of Equipment

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

C3.4 Unique Identification of Equipment

Equipment shall have unique identification.

3.5 Equipment Monitoring and Maintenance

Equipment shall be monitored and maintained in accordance with the manufacturer's written instructions.

C 3.5.1 Calibration and Accuracy of Equipment

Calibrations and/or adjustments shall be performed using equipment and materials that have adequate accuracy and precision. At a minimum, calibrations and/or adjustments shall be confirmed as described below unless otherwise indicated by the manufacturer:

1) Before use.
2) After activities that may affect the calibration.
3) At prescribed intervals.

3.5.1.1 Calibration of equipment shall include details of equipment type, unique identification, location, frequency of checks, check method, acceptance criteria, and specified limitations.

3.5.1.2 Equipment used for calibration, inspection, measuring, and testing shall be certified to meet nationally recognized measurement standards. Certification shall occur before initial use, after repair, and at prescribed intervals. Where no such measurement standards exist, the basis for calibration shall be described and recorded.

3.5.1.3 Equipment shall be safeguarded from adjustments that would invalidate the calibration setting.

3.5.1.4 The organization shall identify equipment that is to be maintained in a calibrated state.

3.5.1.5 The organization shall determine the measurements to be made and the accuracy and precision required.

✎**C** **3.5.2** When equipment is found to be out of calibration or specification, the validity of previous inspection and test results and the conformance of potentially affected products or services (including those that have already been released or delivered) shall be verified.

3.5.3 The organization shall:
1) Define cleaning and sanitization methods and intervals for equipment.
2) Ensure that environmental conditions are suitable for the operations, calibrations, inspections, measurements, and tests carried out.
3) Remove equipment from service that is malfunctioning/ out of service and communicate to appropriate personnel.
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 equipment maintenance and repairs are performed by qualified individuals and in accordance with the manufacturer's recommendations.
7) Tracing of any given product or service to all equipment associated with the procurement, processing, storage, distribution, and administration of the product or service.
8) Identification and recall of all biotherapy products associated with a specific piece of equipment.

Standard 3.2 applies.

3.5.4 Investigation and Follow-Up
Investigation and follow-up of equipment malfunctions, failures, or adverse events shall include:
1) Assessment of products or services provided since the equipment was last known to be functioning per the manufacturer's written instructions or organization-defined specifications.
2) Assessment of the effect on the safety of individuals affected.

3) Removal of equipment from service, if indicated.
4) Investigation of the malfunction, failure, or adverse event, and a determination if other equipment is similarly affected, as applicable.
5) Requalification of the equipment.
6) Reporting the nature of the malfunction, failure, or adverse event to the manufacturer, when indicated.

3.5.4.1 When a nonconformance cannot be attributed to a specific piece of equipment, all potentially affected pieces of equipment shall be assessed to determine expected performance measures based on the manufacturer's written instructions.

C3.6 Information Systems

The organization shall have controls in place for the implementation, use, ongoing support, and modifications of information system software, hardware, and databases. Elements of planning and ongoing control shall include:
1) Numeric designation of system versions with inclusive dates of use.
2) Validation/verification/qualification of system software, hardware, databases, and user-defined tables before 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 the donor, the product, or the service, and the recipient (as applicable).
11) Training and competency of personnel who use information systems.
12) Procedures to ensure confidentiality of protected information.

F 3.6.1 Alternative Systems

An alternative system shall be maintained to ensure continuous operation in the event that computerized data and computer-assisted functions are unavailable. The alternate system shall be tested at defined intervals. Processes and procedures shall address mitigation of the effects of disasters and include recovery plans.

3.6.2 Personnel responsible for management of information systems shall be responsible for compliance with the regulations that affect the use of the system.

3.6.3 The organization shall support the management of information systems.

3.6.4 A system designed to prevent unauthorized access to computers and electronic records shall be in place.

3.6.5 The organization shall have measures in place to minimize the risk of internal and external data breaches.

***F*3.7 Technology Infrastructure**

The organization shall have an active program to ensure that critical technology and communication infrastructures function as intended, including risk-based monitoring or testing at facility-defined intervals. Standards 1.4, 1.5, and 1.6 apply.

F **3.7.1 Artificial Intelligence Oversight**

The organization shall establish and maintain a framework for the responsible use of Artificial Intelligence (AI) technologies. This framework shall apply to all processes where AI influences policy development, critical decision making, or donor/patient/staff safety. The facility shall maintain documentation of intended use, validation of output, including evidence, and audit trails for AI-driven decisions.

F **3.7.2 Risk Management of AI Output(s)**

The facility shall:

1) Define roles and responsibilities of the individual(s) for the oversight and use of AI.
2) Determine the intended use of AI.
3) Perform risk assessments of the AI software before implementation.
4) Ensure compliance with ethical principles, privacy, and applicable regulations.

3.7.3 Verification of AI Output(s)

The facility shall verify the AI fitness for the intended use, including bias checks, and performance metrics.

Standard 3.3 applies.

3.7.4 Monitoring of AI

The organization shall monitor and manage the performance of AI models including inputs and outputs.

3.7.4.1 The facility shall monitor AI performance on a scheduled basis to detect unintended outcomes. Standards 3.5.4 and 3.5.4.1 apply.

***F*3.8 Alarm Systems**

Storage devices for biotherapy products shall have alarms and shall conform to the following standards:

3.8.1 The alarm shall be set to activate under conditions that will allow enough time for proper action to be taken before biotherapy products reach unacceptable conditions.

3.8.2 Activation of an alarm shall initiate a process for immediate action, investigation, and appropriate corrective action.

Excerpt of Reference Standard 6.2.9A Relevant to Equipment

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/ Management Issues	Unit/ Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
3.2	Equipment qualification	X	X	X	C	10 years after retirement of the equipment
3.4	Unique identification of equipment	X	X	X	C	10
3.5.1	Equipment calibration activities	X	X	X	C	10
3.5.2	Equipment found to be out of calibration	X	X	X	C	10
3.5.3	Equipment monitoring, maintenance, calibration, and repair	X	X	X	C	10
3.6	Implementation and modification of software, hardware, or databases	X	X	X	C	2 years after retirement of system
3.6.1	Testing of alternative systems	X	X	X	F	10
3.7	Monitoring of technology infrastructure	X	X	X	F	10
3.7.1	Artificial intelligence oversight	X	X	X	F	10
3.7.2	Artificial intelligence risk assessment	X	X	X	F	10
3.8	Alarm system check	X	X	X	F	10

[1]Applicable federal, state, or local law may exceed this period.

QSE 4 – Suppliers and Customers

Key Concepts

This QSE describes the need for agreements between the organization and its suppliers and customers. The agreements define expectations between both parties and measures taken when one entity fails to meet the expectations of an agreement.

Key Terms

Agreement: A contract, order, or understanding between two or more parties, such as between an organization and one of its customers.

Agreement Review: Systematic activities carried out before finalizing the agreement to ensure that requirements are adequately defined, free from ambiguity, documented, and achievable.

Customer: The receiver of a product or service. A customer may be internal (eg, another organizational unit within the same organization) or external (eg, a patient, client, donor, or another organization).

Quality: Characteristics of a product or service that bear on its ability to fulfill customer expectations. The measurable or verifiable aspects of a product or service that can be used to determine if requirements have been met.

Quality Control: Testing routinely performed on materials and equipment to ensure their proper function.

Supplier: An entity that provides a material, product, or service.

Supplier Qualification: Evaluation of a supplier to assess its ability to consistently deliver products or services that meet specified requirements.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Processes for defining and updating or changing agreements.
- Process for recording verbal agreements, if practiced.
- Agreement records.
- Agreement review records.
- Supplier qualification records.
- Supplier evaluation records.
- Supplier selection process.
- Evidence of action taken when a supplier fails to meet expectations, if applicable.
- Evidence of receipt of product(s) as stipulated in agreements.
- Records of inspection and testing.

4. Suppliers and Customers

4.0 Suppliers and Customers

The organization shall ensure that agreements to provide or receive products or services are reviewed, approved, and meet supplier and customer expectations.

✎C4.1 Supplier Qualification

The organization shall evaluate the ability of suppliers of critical materials, equipment, and services to meet specified requirements.

4.1.1 The organization shall evaluate and participate in the selection of suppliers. If executive management is not included in the selection process, there shall be a mechanism to provide feedback to management with contracting authority.

4.1.2 When a supplier fails to meet specified requirements, it shall be reported to the management with contracting authority.

4.1.3 When biotherapy services involve more than one facility, each facility shall be qualified to perform the scope of activities defined in the agreement in accordance with these *Biotherapies Standards*.

✎C4.2 Agreements

Agreements and any incorporated changes shall be reviewed and communicated.

✎C **4.2.1** Agreements shall be reviewed at defined intervals to ensure that the terms of the agreement continue to meet requirements.

4.2.1.1 This review shall occur at a minimum of every 2 years.

4.2.2 Changes to agreements shall be communicated to affected parties.

4.2.3 The responsibilities for activities covered by these Biotherapies Standards when more than one organization is involved shall be specified by agreement.

4.2.3.1 Before acceptance of a documented verbal or written agreement, the agreement shall be reviewed by all involved parties to ensure that:
1) The customer's requirements are adequately defined in compliance with these Biotherapies Standards and in accordance with applicable FDA or relevant Competent Authority requirements.
2) Any differences between the agreement requirements and the biotherapy products or services offered under the agreement are resolved.
3) The facility has the capability to meet the requirements detailed in the agreement.
4) Chain of identity is maintained.
5) Chain of custody is maintained.
6) Cellular starting material or biotherapy product quality is maintained under the scope of

activities covered by the parties' agreement per specified requirements.
7) Conformance with accepted policies and procedures is maintained.
8) Conformance with safety requirements is maintained.

4.2.3.2 Agreements shall define and describe the following:

4.2.3.2.1 Roles and responsibilities of key personnel.

4.2.3.2.2 Roles and responsibilities of each party involved in the procurement, processing, labeling, storage, distribution, or administration of a biotherapy product to maintain the chain of identity and chain of custody.

4.2.3.2.3 Communication of critical information, including deviations, nonconformances, and adverse events, and changes in facility status. Standards 1.9 and 5.5 apply.

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

4.2.3.2.5 Specifications and requirements for donor and recipient care, quality, safety, and other facility-defined critical parameters.

4.2.3.2.6 Adherence to all applicable CGMP and CGTP requirements for third party service providers.

4.2.3.2.7 Incorporation of quality system essentials required by these *Biotherapies Standards*.

✎*C* **4.2.4 Changes to Agreements**
The parties shall define how changes to agreements are proposed, accepted, and communicated to affected parties.

✎*C* **4.2.5 Agreements Relating to Biotherapy Products, Materials, and Services**
When the responsibilities for activities covered by these Biotherapies Standards involve more than one party or department, there shall be agreements that define the following for the biotherapy product from point of origin to administration, including, but not limited to, the following:

✎*F* **4.2.5.1 Authorization for Procurement and Processing**
The facility shall have authorization for procurement and processing of biotherapy products, except where the recipient is unknown and the procurement of the product is noninvasive. The facility shall ensure that agreements 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 of the clinical facility to provide the medical order for procurement or processing.

Standards 5.12.1 and 5.15.1 apply.

4.2.5.2 Authorization for Distribution

The facility shall ensure that agreements define the following:
1) Responsibility for the distributing facility to obtain a medical order before distribution for clinical use.
2) Responsibility for the receiving facility to provide a medical order for distribution for clinical use.

4.2.5.2.1 For facilities that distribute biotherapy products for further manufacture or storage, there shall be an order that conforms to the quality agreement.

✎**C4.3 Incoming Receipt, Inspection, and Testing**

Incoming products, equipment, and materials shall be received, inspected, and tested, as necessary, before approval for use. Standard 3.2 applies.

✎***F*** **4.3.1 Transfer of Products**

When products are transferred between departments or facilities, the following items shall be defined:
1) Responsibility for maintaining the chain of identity during transfer.
2) Responsibility for maintaining the chain of custody during transfer.
3) Timing of product delivery and administration.
4) Agreement by all parties to provide the necessary documentation, including timing of the following, as applicable:
a) Mobilization.
b) Procurement.
c) Recipient conditioning.

✎***F*** **4.3.2 Instructions**

When products are transferred between departments or facilities, instructions shall be provided for the following:
1) Collection, transport, receipt, handling, and administration of the biotherapy product(s).
2) Reporting postinfusion outcomes data and adverse events to the issuing facility and other parties.

✎***C*** **4.3.3 Records**

When products are transferred between facilities, the following items shall be defined:
1) Responsibility of the administering facility or registry for the creation and retention of records of outcomes data listed in Standards 5.2 through 5.2.4.1.

2) Responsibilities of each facility involved to provide records of the procurement, processing, labeling, storage, distribution, or administration of a biotherapy product.
3) Time frames for making records available for review or transfer upon request.

✎*C* **4.3.4 Conditions for Product Storage and Disposition**

When products are transferred between departments or facilities, the following conditions shall be defined:
1) Maintenance of the chain of identity.
2) Maintenance of the chain of custody.
3) Terms and lengths of storage.
4) Possible transfer to another facility.
5) Disposition of the biotherapy product, including discard.

4.3.5 Information about Product Administration

When products are transferred between departments or facilities, the following items shall be obtained:
1) Summary record of biotherapy product administration.
2) Summary of adverse events suspected to be linked to the biotherapy product. Standard 7.3 applies.

✎*F* **4.3.6 International Requests for Biotherapy Products**

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

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

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

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

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

✎*F* **4.5 Donor Informed Consent**

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

*21 CFR Part 11.

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

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

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

4.5.2.2 There shall be a process to provide a qualified interpreter when applicable.

4.5.3 The terms and length of storage, possible transfer to another facility, and disposition, including discard, of the biotherapy 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 gestational parent, genetic parent, and, where applicable, gestational surrogate).
2) If known, the intended recipient and the recipient's physician.

*F*4.6 Authorization for Cadaveric Donors

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

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

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

4.6.3 The terms and length of storage, the possible transfer to another facility, and the disposition, including discard, of the biotherapy product shall be addressed with:
1) The donor's legally authorized representative.
2) If known, the intended recipient and the recipient's physician.

*F*4.7 Patient Informed Consent

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

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

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

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

4.8 Obtaining Materials, Services, and Biotherapy Products

The facility shall ensure that purchased, donated, or otherwise acquired materials, services, or biotherapy products conform to specified requirements.

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

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

1) Training and qualifications of personnel who perform activities related to the provision of materials and/or services are addressed.

2) Facilities providing tests or manufacturing services required by these Biotherapies Standards are accredited by AABB or other relevant standard setting organizations.

3) The supplier is appropriately qualified or authorized to provide such service as required by the relevant Competent Authority.

4.8.1.1 The facility shall review package inserts for all infectious disease test reagents and kits, including their sample requirements, to verify they are approved for their intended use in testing of biotherapy products. Standards 5.10.2.6 and 5.10.2.10 apply.

F **4.8.2 Evaluation and Qualification of Suppliers of Biotherapy Products**

The facility shall ensure that suppliers of biotherapy products are qualified and selected based on the following requirements:

1) The source facility is authorized, designated, licensed, registered, and/or accredited.

2) Specified product procurement requirements are met when these activities are performed by a supplier.

3) Training and qualifications of personnel who perform activities related to the supply of biotherapy products are addressed.

4) Facilities providing biotherapy products are accredited by AABB or another accrediting body.

F **4.8.3 Monitoring of Suppliers of Materials, Services, and Biotherapy 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 biotherapy 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, Nonconformances, and Adverse Events, applies.

Reference Standard 4.5A—Donor Informed Consent or Authorization

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

I. General Informed Consent

A. Description of participation, including:

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

B. The consenter(s) shall acknowledge in writing that they have received information concerning the risks, benefits, discomforts, and alternatives to human biotherapy product donation; that they have had an opportunity to have access to donor advocacy and/or translation services when applicable; 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 biotherapy 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 qualified health-care professional who is knowledgeable about the 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. The individual providing consent shall be able to make an informed, autonomous decision without coercion or undue influence.

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

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

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

III. Authorization for Cadaveric Donors

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

B. Authorization shall be expressed in either of two ways:

1) Document of gift made before death such as in a donation registry or other legally acceptable method that produces a record.

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 donor eligibility and medical suitability.

Reference Standard 4.7A—Recipient Informed Consent

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

I. General Informed Consent

A. Description of participation, including:

1) The individual's rights as a recipient and, where applicable, as a research subject.

2) Risks associated with the selected medical interventions, including the administration of biotherapy products and side effects of drugs and other treatment that is part of the regimen.

3) General explanation of the indications for, and expected outcome of, the biotherapy.

4) Discussion of confidentiality, including the need for disclosure to other entities of personal and family health information.

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

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

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

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

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

Excerpt of Reference Standard 6.2.9A Relevant to Suppliers and Customers

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/ Management Issues	Unit/ Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
4.1	Evaluation and participation in selection of suppliers	X	X	X	C	10
4.2	Agreements	X	X	X	C	10
4.2.1	Agreement review	X	X	X	C	10
4.2.3	Agreements concerning activities involving more than one organization	X	X	X	C	10
4.2.4	Agreement changes communicated to affected parties	X	X	X	C	10
4.2.5	Review of agreements before acceptance and at facility defined intervals	X	X	X	C	10
4.2.5.1	Agreements for the timing and responsibility of medical orders	X	X	X	F	10
4.3	Inspection of incoming critical materials	X	X	X	C	10
4.3.1	Agreements between departments	X	X	X	F	10

	or facilities regarding the transfer of products					
4.3.2	Agreements for the collection, transport, receipt, handling, and administration of the cellular therapy product, reporting adverse events, and obtaining outcome data	X	X	X	F	10
4.3.3	Agreement between processing/ issuing facility and the administering facility or registry for creation and retention of records; agreements for each facility to access relevant records	X	X	X	C	10
4.3.4	Conditions for product storage and disposition	X	X	X	C	10
4.3.6	Shipment of products	N/A	N/A	X	F	10
4.4	Claims in educational and promotional materials	X	X	X	F	10
4.5	Donor informed consent	X	X	X	F	10
4.6	Authorization for cadaveric donors	X	X	X	F	10

4.7	Patient informed consent	X	X	X	F	10
4.8.1, 4.8.2	Evaluation, qualification, and selection of suppliers of materials, services, and products	X	X	X	F	10
4.8.3	Monitoring of suppliers (including reporting to management of a supplier's failures to meet specified requirements)	X	X	X	F	10
4.8.4	Notification of shipping facility And manufacturer (if applicable) when materials are received in an unacceptable condition	X	X	X	C	10

[1]Applicable federal, state, or local law may exceed this period.

QSE 5 – Process Control

Key Concepts

This QSE covers the organization's operations and production functions. It describes the need to ensure that this work is controlled, that processes function as expected, and that expected outcomes are met. This QSE encapsulates what occurs in each organization and forms the basis of its accreditation.

Key Terms

Change Control: A structured method of revising a policy, process, or procedure, including hardware or software design, transition planning, and revisions to all related documents.

Critical Equipment/Materials/Tasks: A piece of equipment, material, service, or task that can affect the quality of the organization's products.

Executive Management: The highest-level personnel within an organization, including employees, clinical leaders, and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or a group of individuals.

Process Control: Activities designed to ensure that processes are stable and consistently operate within acceptable limits of variation in order to produce predictable output that meets specifications.

Product: A tangible output from a process.

Reference Standard: Specified requirements defined by the AABB. Reference standards define how or within what parameters an activity shall be performed and are more detailed than quality system requirements.

Service: An intangible output of a process.

Standard: A set of specified requirements upon which an organization may base its criteria for the products, components, and/or services provided.

Validation: Establishing evidence that a process, executed by users in their environment, will consistently meet predetermined specifications.

Verification: Confirmation by examination and provision of objective evidence that specified requirements have been met.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Implementation records.
- Records enabling traceability.
- Storage records.
- Quality control records.
- Process planning, process validation, and change control records.

- Records of material storage, handling, and use.
- Records of inspection of materials.
- Product inspection records.
- Testing records.

5. Process Control

5.0 Process Control

The organization shall ensure the quality of products or services.

5.1 General Elements

The organization shall ensure that processes are carried out under controlled conditions.

✎C **5.1.1 Change Control**

When the organization develops new processes or procedures or changes existing ones, they shall be validated before implementation.

5.1.1.1 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 biotherapy product shall be validated before the change is implemented. Standard 1.4 and 2.1.4 apply.

✎C **5.1.2 Quality Control**

A program of quality control shall be established that is sufficiently comprehensive to ensure that products, equipment, materials, and analytical functions perform as intended. Standard 1.2.2 applies.

5.1.2.1 Quality control results shall be reviewed and evaluated against acceptance criteria.

5.1.2.2 Quality control failures shall be investigated before release of test results, products, or services.

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

5.1.2.4 Processing facilities shall prevent contamination of cellular starting materials and final biotherapy products; maintain the biotherapy product's identity, function, safety, purity and potency, and integrity; and prevent the transmission of infectious disease. This shall include:
1) Defining criteria for acceptable results of in-process tests and final biotherapy product characteristics.
2) Monitoring and control of suitable process parameters and biotherapy product characteristics.
3) Use of statistical techniques required for establishing, controlling, and verifying process requirements and product characteristics.

5.1.3 Process Planning

Quality requirements shall be incorporated into new or changed processes, products,

services, and novel methods. Planning and implementation activities 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/or literature).
3) Evaluation of risk.* Standard 1.4 applies.
4) Identification of affected internal and external parties and mechanism to communicate relevant information.
5) Identification of performance measures 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 organization (or program) processes. Standards 2.1.3 and 10.0 apply.
8) Evaluation of the need to create or revise documents for the new or changed process, product, or service.
9) Review and approval of the output of process development and design activities (eg, pilot or scale-up study results, process flow charts, procedures, data forms).
10) Evaluation of the extent and scope of process validation or revalidation depending on the level of risk and impact of the new or changed products or services.

*21 CFR 1271.180.

5.1.4 Process Validation

Before implementation, the new or changed processes and procedures shall be validated.

5.1.4.1 Validation activities shall include the following:

1) Identification of objectives, 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 objectives are not met.

Standards 2.1.3 and 2.1.4 apply.

5.1.5 Process Implementation

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

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

5.1.6 Use of Materials

All materials shall be stored and used in accordance with the manufacturer's written instructions and shall meet specified requirements.

5.1.7 Inspection

The organization shall ensure that products or services are inspected at organization-defined stages.

✎C **5.1.8 Identification and Traceability**

The organization shall ensure that all products or services are identified and traceable.

5.1.9 Handling, Storage, and Transportation

The organization shall ensure that products or services are handled, stored, and transported in a manner that prevents damage, limits deterioration, and provides traceability.*

*21 CFR 1271.290.

✎C **5.1.9.1** The facility shall ensure that suppliers and/or consignees of biotherapy products provide evidence of processes for traceability, tracking, and recall of products. Standard 7.2.5 applies.

✎F **5.1.9.1.1** The facility shall have a policy for the use/distribution of a biotherapy product provided by a supplier and/or received by a consignee that lacks a complete chain of custody. Standards 7.2.4 and 7.2.6.2 apply.

✎C **5.1.10 Proficiency Testing**

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

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

*42 CFR 493.801.

5.1.10.1.1 Laboratories shall ensure that no interlaboratory communications pertaining to proficiency test events occur until after the submission deadline.†

†42 CFR 493.801(b)(4).
For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

5.1.10.1.2 The laboratory shall ensure that no portion of a proficiency testing sample is sent to another laboratory for analysis.*

*42 CFR 493.801(b)(5).
For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

5.1.10.1.3 Any laboratory that receives a proficiency testing sample from another laboratory shall notify CMS of the receipt of the sample.†

†42 CFR 493.801(b)(5).
For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

5.1.10.2 In the absence of an approved external proficiency testing program, an alternative assessment process shall be used and approved by the appropriate medical director at least twice annually.

✎*C* **5.1.10.3** Proficiency testing results shall be reviewed by the medical or laboratory director or designee.‡

‡42 CFR 493.1236.
For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

5.1.10.3.1 Proficiency testing shall be successful. Failures shall be investigated and corrective actions taken, including the notification of potentially affected parties and appropriate regulatory bodies, as applicable. § Standard 1.4 applies.

§42 CFR 493.803 and 42 CFR 493.1236(b).
For accredited facilities that are assessed by AABB for CLIA conformance, refer to the Verification of CLIA Compliance Form before on-site assessment.

✎*C* **5.1.11 Investigational Products**
The organization shall ensure that processes are carried out in conformance with the Investigational New Drug (IND) application or equivalent as approved by the FDA or relevant Competent Authority. Standard 1.1.2 applies.

✎*F* **5.2 Outcome Data**
The facilities shall have a program to obtain, audit, and monitor clinical outcomes of biotherapy products at defined intervals. Standard 5.28 applies.

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

5.2.2 For the clinical program, this shall include the clinical outcomes as specified by the clinical protocols and as applicable:
1) Mortality and survival rates.
2) Disease status and/or relapse.
3) Adverse events and complications.
4) Disease-modifying activity.
5) Engraftment.
6) Immune effector cell endpoints.*
7) Gene therapy product endpoints.*
8) Hematopoietic reconstitution.
9) Monitoring of patient safety.

* FDA Guidance for Industry: Long Term Follow-Up After Administration of Human Gene Therapy Products (January 2020)

5.2.2.1 The clinical program shall determine the criteria for biotherapy product safety, product efficacy, and/or clinical outcome data and collect these data for analysis at defined intervals.

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

5.2.4 The sharing and review of data shall be defined. Standard 4.2.5 and Chapter 7, Deviations, Nonconformances, and Adverse Events, apply.

F **5.2.4.1** There shall be defined processes and procedures for the issuing facility and/or product manufacturer to obtain information on adverse events and patient outcomes appropriate for each product type.

C **5.3 Materials Management**

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

5.3.1 All critical materials, including containers and solutions used for collection, processing, preservation, and storage of biotherapy 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.

5.3.2 Receipt of Materials

The facility shall ensure that incoming materials that come into contact with the patient or

biotherapy product or that directly affect the quality of a biotherapy product are not used until they have been inspected or otherwise verified as conforming to requirements. Standard 4.8 applies.

✎C **5.3.2.1 Quarantine of Critical Materials**
The facility shall establish a process for quarantine and disposition of critical supplies and materials.

✎C **5.3.2.2** Records of the following shall be maintained:
1) Identification of the material.
2) Name of the manufacturer.
3) Lot number.
4) Date of receipt.
5) Date of manufacture and/or expiration date.
6) Results of visual inspection upon receipt, if applicable.
7) Identity of the person receiving the material, if applicable.
8) Indication of acceptance or rejection.
9) Identity of the person determining acceptance or rejection of the material.
10) Certificate of analysis, manufacturer's insert, or equivalent, if applicable.
11) Quantity.

✎C **5.3.2.3 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.

5.3.3 Qualification of Critical Materials
Materials that come into contact with the patient or biotherapy product shall be sterile and of appropriate grade for the intended use and shall be approved for human use by the FDA or relevant Competent Authority. Standard 4.2 applies.

5.3.3.1 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.

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

5.3.3.1.2 The facility shall qualify, verify, and validate critical materials for their intended use.

✎C **5.3.4** Reagents prepared in-house shall be produced using a validated method. Such reagents shall be inspected before release. Standards 5.3.2.2, 5.3.5, and 5.3.6 apply.

C **5.3.5 Utilization**

Non-single-use materials that come into contact with the patient or biotherapy products during procurement, processing, or administration shall be cleaned and sterilized. Sterilization methods shall be validated and monitored, according to specified requirements.

F **5.3.6** Use of critical materials shall be recorded in a manner that ensures complete and accurate traceability of any given biotherapy product to all critical materials that come into contact with the patient or biotherapy product. Chapter 7, Deviations, Nonconformances, and Adverse Events, applies.

C **5.3.6.1** 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.

5.4 Methods and Operational Controls

5.4.1 Biotherapy Product Manipulation

Biotherapy product manipulation shall address the following:

1) Staff attire, gowning, and use of personal protective equipment.
2) Use of biological safety cabinets or other environmentally controlled spaces, if applicable.^
3) Materials and equipment for each specific process.
4) Manipulation of materials.
5) Facility defined time limits for each phase of manufacturing, if applicable.*
6) Critical calculations.
7) Transfer of source material, biotherapy products, media, or reagents between containers.
8) Sampling of source material, biotherapy products, media, reagents, or other materials used in product manipulation.
9) Acceptable control limits for temperature, humidity, and gases such as oxygen and carbon dioxide, if applicable.
10) Labeling.
11) Disposition of processing and/or manufacturing by-products.

^ FDA Guidance for Industry: Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (December 2011)
* 21 CFR 211.111

5.4.2 Aseptic Methods

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

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

Standards 5.3.5, 5.12 and 10.1 apply.

21 CFR 1271.150.

✎C **5.4.2.1** The effectiveness of such measures shall be monitored and reviewed at defined intervals. Chapter 7, Deviations, Nonconformances, and Adverse Events, applies.

✎C **5.4.3 Operational Controls**

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

1) Movement and storage of materials (including waste) and equipment within workspaces.
2) Physical and/or temporal segregation of equipment and materials.
3) Physical and/or temporal segregation for processing different biotherapy products or biotherapy product lots.
4) Physical and/or temporal segregation of biotherapy products determined to be nonconforming or where donor eligibility has not been determined or the donor is ineligible.
5) Use and storage of materials that may adversely affect the quality of the biotherapy product.
6) Cleaning and setup of spaces and equipment between manufacturing runs.
7) Labeling processes.
8) Clerical identification checks at critical steps.

Chapter 7, Deviations, Nonconformances, and Adverse Events, applies.

5.4.4 Irradiation and Leukocyte Reduction

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

5.4.4.1 Methods shall be in place to prevent unintentional irradiation or leukocyte reduction (eg, filtration) of biotherapy products. Reference Standard 5.6.2A, Requirements for Labeling of Biotherapy Products, applies.

5.5 Product Identification and Traceability

The facility shall maintain the chain of identity and chain of custody for identification and traceability of each biotherapy product and all related samples and by-products from their initial source, through all processing and testing steps, to their final disposition. Policies, processes, and procedures shall also allow the identification and traceability of each biotherapy product and all related samples from their final disposition, through all processing and/or testing steps, back to their source.

C **5.5.1 Traceability and Unique Identification**

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

5.5.1.1 Unique Identification of Intermediate Facility

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

5.5.1.2 Special Requirements for Pooled Biotherapy Products or Combined Products

Where pooling or combining of biotherapy products is permissible, there shall be a procedure to ensure traceability of all biotherapy products in a pool, and the quantitative contribution of each product to the final biotherapy product.* Standard 1.4 applies.

*21 CFR 1271.220(b).

5.5.1.3 Sample Traceability

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

5.6 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 biotherapy product label templates.

C 2) Verification that the label stock meets facility-defined specifications.

C 3) The qualification, review, and approval of labels before use. Standard 6.1.2 applies.

4) The controls in place to ensure proper biotherapy product identification.

C 5) The control of label inventory and templates, including discard. Chapter 6, Documents and Records, applies.

Standards 1.1.2 and 5.10.10 apply.

*21 CFR 1271.10(a)(2).
FDA Guidance: Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue Based Products: Minimal Manipulation and Homologous Use (July 21, 2020).

C **5.6.1** Biotherapy products shall be labeled in conformance with the current versions of ISBT 128 or Eurocode labeling. Standard 5.5 applies.

5.6.1.1 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.

‡www.iccbba.org/standard-terminology/

5.6.1.2 Apheresis and marrow cellular starting materials shall be labeled with ISBT 128 or Eurocode labels at the time of procurement.

5.6.1.3 If the information required for a complete ISBT 128 label is not available at the time of procurement, products shall be labeled with the proper name and a unique alpha numeric identifier, at a minimum.

5.6.1.4 Biotherapy products shall be labeled with ISBT 128 or Eurocode labels at the completion of processing.

5.6.1.4.1 For biotherapy products that are procured but do not require further processing/manufacture, an ISBT 128 or Eurocode compliant label shall be applied before distribution or administration.

5.6.1.5 The facility shall have policies to address emerging labeling standards and ensure action is taken, as applicable.

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

5.6.1.7 Special Labeling Requirements of Investigational Products
Investigational products shall be labeled with ISBT 128, Eurocode labels or a label approved by the FDA or relevant Competent Authority.

5.6.1.7.1 If an ISBT 128 or Eurocode label has not been approved by the FDA or relevant Competent Authority, the label shall include the following at a minimum:
1) For procurement facilities:
-Product name
-Unique alpha or numeric product identifier
-Product type
-Two unique donor identifiers

-Chain of identity identifier, if applicable
-Date and time of procurement
2) For processing facilities, additionally:
-Processing facility identifier
-Product expiration date and time, if applicable.

5.6.2 All containers of source materials, in-process biotherapy products, and final products shall be labeled in accordance with Reference Standards 5.6.2A, Requirements for Labeling of Biotherapy Products, and 5.6.2B, Requirements for Labeling Shipping Containers.

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

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

C **5.6.3 Labeling**

Labeling information shall be verified for accuracy and completeness.

5.6.3.1 The procurement facility shall verify labeling immediately after procurement.

5.6.3.2 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.

5.6.3.3 The administering facility shall verify labeling before administration of the biotherapy product.

5.6.3.4 When labeling a licensed biotherapy product, the information contained on the label shall be consistent with the distributor's accompanying information.

5.6.3.4.1 If a label cannot display all required product attributes, an additional label with the remaining information shall be attached. Reference Standard 5.6.2A, Requirements for Labeling of Products applies.

5.6.4 Investigational biotherapy products for use or approved for use by the FDA or relevant Component Authority shall be labeled according to protocol, and all elements required shall be included in the accompanying records or be readily available. Reference Standard 5.6.2A, Requirements for Labeling of Biotherapy Products, applies.

✎C5.7 Transport and Shipping

The facility shall limit deterioration, prevent damage, ensure timely delivery, and protect the quality of the materials and biotherapy products during transport and shipping while maintaining chain of custody and chain of identity.*

*21 CFR 1271.265.

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

✎C **5.7.2** Shipping or transport containers shall be qualified at defined intervals to ensure that they maintain temperatures within the acceptable range for the expected duration of transport or shipping.

✎F **5.7.3** 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 **5.7.3.1** When cryopreserved products are shipped, the temperature of the shipping container shall be continuously monitored.

5.7.4 The facility shall label shipping containers and biotherapy products in a manner designed to allow positive identification and to inform the carrier of the appropriate handling. Reference Standards 5.6.2A, Requirements for Labeling of Biotherapy Products, and 5.6.2B, Requirements for Labeling Shipping Containers, apply.

5.7.5 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. Standard 4.3.5 and Reference Standard 5.7.5A, Labeling and Packaging Requirements upon Shipping of Biotherapy Products, apply.

✎C **5.7.6** Facilities shall maintain records of product origin, custody, transfer, identity, integrity, and acceptability.

✎C5.8 Inspection and Testing of Cellular Starting Materials and Final Biotherapy Products

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

✎C **5.8.1 Receipt of Incoming Cellular Starting Materials**

At the time of receipt, incoming cellular starting materials shall be inspected, sampled, and/or tested, as appropriate, to determine their acceptability. Standards 5.6.1, 5.6.3, and 5.7.6 apply. Records of the following shall be maintained:

1) Name of the supplier(s)/procurement facility.
2) Donation identification number.
3) Product description code, type of collection, and division code.

4) Product name and attributes.
5) Unique donor identifier, if applicable.
6) Unique, traceable, chain-of-identity identifier, if applicable.
7) Date and time of receipt.
8) Date and time of procurement and/or manufacture.
9) Date of expiration, if applicable.
10) Results of inspection upon receipt, if applicable, including:
    a) Product appearance.
    b) Appropriate labeling.
    c) Integrity of the container(s).
    d) Presence or absence of visible evidence of contamination and tampering.
    e) Acceptable temperature range.
11) Identity of the person receiving and/or inspecting the product.
12) Indication of acceptance, quarantine, or rejection.
13) Disposition.
14) Certificate of analysis, summary of records, or manufacturer's insert or equivalent, if applicable.
15) Identification of the intended recipient, if applicable.

5.8.1.1 Identification of Cellular Starting Materials upon Receipt

The facility shall require verification of the chain of identity of cellular starting materials.

5.8.1.2 Cellular starting materials shall be quarantined upon receipt and their disposition determined by a qualified individual when any of the following occur:

1) There is a delay in inspection, labeling, sampling, or testing procedures for determination of acceptability.
2) The cellular starting materials are judged as not meeting acceptance criteria.
3) The cellular starting materials require further sampling, labeling, processing, or testing before disposition.
4) The cellular starting materials are determined to be nonconforming, or donor eligibility has not been determined, or the donor is ineligible.

C **5.8.2 In-Process and Final Product Inspection and Testing**

In-process testing and monitoring shall be defined. The facility shall:

1) Inspect and test the biotherapy 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 5.20.3.
3) Report to the customer(s) identified in the disposition agreement any patient-specific biotherapy products that are lost, damaged, or otherwise unsuitable for use. Standard 7.0 applies.

5.9 Storage and Preservation

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

✎*C* **5.9.1** Storage areas shall have the capacity and design to ensure that proper temperature, humidity, and light*, as applicable, are maintained.

*21 CFR 211.142(b)

✎*C* **5.9.1.1** If biotherapy products are stored in an open storage area, the ambient temperature and humidity shall be recorded at facility defined intervals based on the product's stability profile(s) and a risk assessment. Standard 1.4 applies.

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

✎*C* **5.9.3** Storage devices containing biotherapy products and critical materials shall have a system to continuously monitor, and also record at defined intervals, the temperature and/or liquid nitrogen levels. Standard 5.7 applies.

5.9.3.1 The temperature and/or liquid nitrogen levels of freezers where biotherapy products are immersed in liquid nitrogen or stored in vapor phase shall be recorded at manufacturer defined intervals, or if not provided, at facility defined intervals based on the biotherapy product's stability profile(s) and a risk assessment. Standard 1.4.2 applies.

5.9.3.2 The temperature of refrigerators and freezers where biotherapy products are stored shall be recorded at manufacturer defined intervals, or if not provided, at facility defined intervals based on the product's stability profile(s) and a risk assessment. Standard 1.4.2 applies.

✎*C* **5.9.4** Storage devices containing cellular starting materials, intermediate products, and final biotherapy 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.

<u>Procurement Activities</u>

✎*F* **5.10 Donor Evaluation**

Donor evaluation shall be performed and informed consent obtained, in accordance with Reference Standards 4.5A, Donor Informed Consent or Authorization; 5.10A, General

Requirements for Cellular Starting Material and Biotherapy Donors; 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.10C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.10D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Material Donors; and 5.10E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors.

5.10.1 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 starting material or biotherapy product. This evaluation shall be conducted by a qualified health-care professional and shall include, based on examination, clinical history, and relevant medical record(s):

5.10.1.1 The ability to tolerate the collection procedure.

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

5.10.1.3 If applicable, risk for hemoglobinopathy.

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

5.10.1.4 If applicable, pregnancy evaluation.

5.10.1.5 If applicable, the administering facility shall ensure that HLA typing is performed on the donor and verify that the HLA type meets specified HLA requirements. Reference Standards 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.15B, Processing Tests for HPC, Cord Blood Products or Gestational Materials; 5.15C, Processing Tests for Biotherapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood or Gestational Materials, apply.

5.10.1.5.1 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.

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

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

5.10.1.7 The facility shall define criteria for evaluating pediatric donors.

5.10.2 Donor Eligibility

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

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

5.10.2.1.1 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 of relevant communicable disease.
2) Testing.

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

F **5.10.2.2 Cadaveric Donor Eligibility**

The evaluation of the donor's eligibility required by Reference Standard 5.10A, General Requirements for Cellular Starting Material Donors, shall be performed by interviewing a family member or other knowledgeable person.

F **5.10.2.3 Collection of Samples for Infectious Disease Testing**

Samples associated with the products listed below shall be collected within the following time frames, unless FDA or relevant Competent Authority regulations are more stringent:
1) HPC, Cord Blood: Obtain maternal sample within 7 days before or after collection.
2) HPC, Marrow and HPC, Apheresis: Collect from the donor within 30 days before procurement.
3) All other biotherapy products: Collect from the donor within 7 days before or after procurement.

F **5.10.2.4** Donor testing shall be performed in conformance with Reference Standards 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.10C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.10D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Material Donors; and 5.10E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors.

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

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

21 CFR 1271.80.

5.10.2.5.1 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.

5.10.2.6 All donor infectious disease testing shall be performed using assays in accordance with the manufacturer's written instructions that have been approved for donor screening by the FDA or relevant Competent Authority, if such assays are available. Standard 4.3.5 applies.

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

5.10.2.8 The following tests shall be performed:
1) Hepatitis B virus (HBsAg; anti-HBc; HBV DNA).
2) Hepatitis C virus (anti-HCV; HCV RNA).
3) Human immunodeficiency virus (anti-HIV-1/2; HIV-1 RNA).
4) Human T-cell lymphotropic virus, type I and II (anti-HTLV-I/II), for viable leukocyte-rich products only.
5) Antibody to cytomegalovirus for viable leukocyte-rich products only.
6) A serologic test for syphilis.*
7) West Nile virus (WNV RNA).

Reference Standards 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.10C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.10D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Material Donors; and 5.10E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors, apply.

*FDA 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).

5.10.2.8.1 For facilities not subject to US laws and regulations, HBV DNA testing is acceptable in place of anti-HBc testing. Standards 1.4, 5.10.7, and Reference Standard 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors apply.

5.10.2.8.2 Facilities not subject to US laws and regulations shall conform to the following alternatives if testing of donors for West Nile virus is not required by their Competent Authority:
1) Facilities shall determine all donors to be ineligible for a minimum of 28 days if they have traveled to WNV-endemic areas as determined by the Competent Authority (eg, WHO, CDC, or ECDC surveillance maps).
2) Facilities shall determine all donors to be ineligible for a minimum of 120 days if they have tested positive for or have a history of WNV.¶

Standards 1.4, 5.10.7, and Reference Standard 5.10B apply.

¶FDA Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (August 2007)

5.10.2.8.3 Facilities not subject to US laws and regulations, and where testing for *T. cruzi* is not required by the facility's Competent Authority, shall determine all donors to be ineligible if any of the following apply:
1) Donors have tested positive for *T. cruzi.*
2) Donors have a history of *T. cruzi* infection.
3) Donors have a health history or environmental risk factors for *T. cruzi* that would be identified by the donor screening process.

Standards 1.4, 5.10.7, and Reference Standard 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors apply.

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

5.10.2.10 The facility shall ensure relevant infectious diseases and emerging infectious diseases are addressed, and action taken in regard to the donor screening and testing process.†

†FDA Guidance for Industry: Recommendations to Reduce the Risk of Transmission of Disease Agents Associated with Sepsis by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (January 2025)

5.10.3 Samples for Testing Donations after Brain or Cardiac Death

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

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

F **5.10.4 Evaluation of Cellular Starting Materials and Biotherapy Products**
Before shipment or transport of cellular starting materials and biotherapy products, the receiving facility shall review the donor screening and infectious disease testing records for compliance with applicable local and FDA or relevant Competent Authority regulations of the receiving facility, to ensure the product meets specified requirements.

F **5.10.5** A final determination of donor eligibility for allogeneic donors shall be made and shall include the following information:
1) A statement that the donor has been determined to be eligible or ineligible, noting the name and address of the facility that made the donor eligibility determination. Standards 5.10.1.5.1 and 5.10.8 apply.
2) A statement that the infectious disease testing was performed by a laboratory that has been certified to perform such testing on human samples under CLIA regulations or that has met equivalent requirements as determined by the CMS. For facilities located outside of the United States, the use of a laboratory authorized as a testing center by the FDA or relevant Competent Authority is permissible.
3) For a product from an ineligible donor, a statement noting the reason(s) for the determination of ineligibility.

5.10.6 Indeterminate or Reactive Results on Donor Screening and Testing

5.10.6.1 The facility shall establish policies, processes, and procedures for notification of indeterminate or reactive infectious disease test results. Standard 7.2.4 applies.

F **5.10.6.2** Indeterminate or reactive 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.

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

5.10.6.2.2 For cadaveric donors, all infectious disease test results shall be reported to the procurement facility. The procurement facility shall report positive test results to appropriate authorities as mandated by law or regulation, and test results shall be made

available to the donor's legal next of kin when the test result(s) could affect the health of others.

F **5.10.6.3** Indeterminate or reactive 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 biotherapy product shall be communicated to the recipient's physician and to the recipient before distribution of the biotherapy product for clinical use. Reference Standards 4.5A, Donor Informed Consent or Authorization, and 4.7A, Patient Informed Consent, apply.

C **5.10.6.4** Records of donors determined ineligible after procurement of the product shall be maintained.

5.10.6.4.1 Records of cord blood or gestational material donors shall include the gestational parent and, if applicable, the genetic parent.

F **5.10.7 Products from Ineligible Donors**

The biohazard label shall be attached to any allogeneic product for which there are incomplete donor screening or indeterminate or reactive testing results. All allogeneic products from ineligible donors shall be provided only under urgent medical need and according to local and/or FDA or relevant Competent Authority regulations. The product shall be labeled with the phrase "WARNING: Advise patient of communicable disease risks." Reference Standard 5.6.2A, Requirements for Labeling of Biotherapy Products, applies.

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

F **5.10.8 Donors with Incomplete Eligibility Determinations**

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

5.10.8.1 If testing is not performed in conformance with Standard 5.10.2.8 or if testing does not meet the requirements of the manufacturer of the test kit, the donor eligibility determination shall be incomplete.

5.10.8.1.1 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.

5.10.8.2 When the donor eligibility determination is incomplete, the facility shall complete the eligibility determination during or after use of the product, if

possible, or indicate in the associated records the reason that the eligibility determination could not be completed. The results of the determination of donor eligibility shall be communicated to the recipient's physician.

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

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

5.10.9 Labeling for Autologous Products

Autologous units shall be labeled with the phrase "For autologous use only" and, if testing or screening is not completed or performed, shall be labeled with the statement "Not evaluated for infectious substances." Standard 5.6 and Reference Standard 5.7.5A, Labeling and Packaging Requirements upon Shipping of Biotherapy Products, apply.

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

5.11 Medical Management and Emergency Care of Donors

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

C **5.11.2** 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.

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

C **5.11.3.1** Allogeneic and autologous donors shall be evaluated for the risk of hemoglobinopathy before the administration of a mobilizing agent.

5.11.4 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 anesthesia provider. Pain management for postprocedure care shall be available, if necessary.

5.11.5 The procurement facility shall protect the health and safety of the donor. Criteria for discontinuation of procurement due to medical complications shall be specified.

5.11.5.1 Cord blood or gestational material procurement procedures shall ensure the safety of the gestational parent and the neonate.

5.12 Procurement

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

F **5.12.1 Medical Order for Procurement**

The procuring facility shall obtain a medical order before the procurement procedure for all cellular starting materials. The medical order shall include procurement goals. Standard 5.13 applies.

5.12.1.1 Cellular starting materials collected via a noninvasive procedure and before identification of an intended recipient do not require a medical order before procurement. Standard 5.22 applies.

5.12.2 Verification of Medical Suitability

5.12.2.1 Before procurement, the procurement facility shall verify that the determination of medical suitability has been completed. Standard 5.2.1 and Reference Standards 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.10C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.10D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Material Donors (#I); and 5.10E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors, apply.

F **5.12.2.2** 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 5.10A, General Requirements for Biotherapy Product Donors; 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; and 5.10C, Clinical Evaluation and Laboratory Testing of Autologous Donors.

C **5.12.2.3** For marrow donors or donors of cells collected by apheresis, facilities shall:
1) Define criteria to evaluate the results of a complete blood count before each procurement.
2) Define time frames for obtaining a complete blood count before the initial

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

F **5.12.2.4** On each day of procurement, a qualified 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 Standards 4.5A, Donor Informed Consent or Authorization, and 5.10A, General Requirements for Biotherapy Product Donors, apply.

5.12.3 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 5.10.8 applies.

F **5.12.4 Donor Identity**

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

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

F **5.12.5 Procurement Records**

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

Standards 5.6.1, 7.2.5, and 7.3 apply.

F **5.12.6 Review of Procurement Records**

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

5.12.7 Procurement Record Availability

Each facility performing procurement shall provide access to biotherapy product

procurement record(s) to the facility receiving the product while maintaining the chain of custody. Chapter 4, Suppliers and Customers, applies.

5.12.7.1 Records shall include:

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

***F*5.13 Procurement Goals**

Procurement goals shall be defined.

5.13.1 Unrealized Goals

If expected goals are not met, Chapter 7, Deviations, Nonconformances, and Adverse Events, applies as appropriate.

5.13.1.1 If expected goals are not met, the intended recipient's physician, the processing facility, and other relevant parties shall be notified. Standard 7.1.3.1 applies.

5.14 Packaging

As soon as possible after procurement, each organ, tissue component, or biotherapy product shall be packaged in an individually labeled container suitable for the specific product. Reference Standard 5.6.2A, Requirements for Labeling of Biotherapy Products, applies.

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

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

5.14.1.2 For ex-utero cord blood or gestational material collections, the procurement facility shall verify the label on the collection container against the donor identification.

Processing Activities

5.15 Testing

Products shall be tested during processing in conformance with Reference Standards 5.15A, Processing Tests for HPC, Apheresis and HPC, Marrow; 5.15B, Processing Tests for HPC, Cord Blood Products or Gestational Materials; and 5.15C, Processing Tests for Biotherapy 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 biotherapy product:
1) Incoming cells, tissues, and organs.

2) Intermediate products, if applicable.
3) Final products.

✎F **5.15.1 Medical Order for Processing, Preservation, or Storage**

The facility performing processing, preservation, or storage shall obtain a medical order from a health-care provider, if applicable. The medical order shall contain information that uniquely identifies the donor and the recipient. Specific instruction for processing and preservation shall be provided in the order as appropriate.

5.15.1.1 Facilities that process, preserve, or store products collected via a noninvasive procedure and before identification of an intended recipient are not required to obtain a medical order before processing, preservation, or storage. Standard 4.2.3.1 applies.

✎F **5.15.2 Processing Record**

A complete processing record shall include:
1) Donation identification number.
2) Product description code, type of collection, and division code.
3) Product name and attributes.
4) Unique donor and/or patient identifier, if available.
5) Unique, traceable, chain-of-identity identifier, if applicable.
6) Date and time of procurement.
7) Name and address of processing facility.
8) All details of critical processing, preservation, and storage steps.* Records shall include:
   a) Date and time (if applicable) of critical steps.
   b) Names of persons responsible for each step.
   c) Names, manufacturers, lot numbers, and expiration dates of all critical materials used in processing, preservation, and storage.
   d) Quantities of reagents used.
   e) Identifiers of equipment used.
9) Documentation of product distribution or final disposition.
10) Final review as defined by the facility's policies, processes, and procedures.

*5.17.3 applies

✎C **5.15.3 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 or cellular starting material [eg, recovery of specific cell populations, cell viability, cell identification and potency assays, function(s), purity, as appropriate, and sterility]. Reference Standards 5.15A, Processing Tests for HPC, Apheresis and HPC, Marrow; 5.15B, Processing Tests for HPC, Cord Blood Products or Gestational Materials; and 5.15C, Processing Tests for Biotherapy Products

Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood or Gestational Materials, apply.

F **5.15.4 Managing Red Cell Antigen Incompatibility**

The processing facility shall manage red cell antigen incompatibility between the donor and the recipient, as applicable.

5.15.5 Processing Records

Each facility or the facilities performing processing, preservation, or storage shall provide a copy of the product processing record concerning the safety, purity, and potency of the product or cellular starting material involved, or a summary of the product processing record to the facility(ies) receiving the product, while maintaining chain of custody and chain of identity. Chapter 4, Suppliers and Customers, applies.

C **5.16 Storage of Noncryopreserved Biotherapy Products or Cellular Starting Materials**

The facility shall establish, for each type of product or cellular starting material, the storage specifications and defined storage conditions, including temperature range and length of storage to maintain facility-defined critical characteristics, including viability, to ensure integrity and suitability for use.

5.16.1 Management of Stored Noncryopreserved Inventory

5.16.1.1 Biotherapy products shall be maintained under defined conditions, including temperature range, between donation and final disposition.

5.16.1.2 Aliquot(s) of biotherapy products shall be maintained under defined conditions, including temperature range.

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

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

5.17 Cryopreservation of Biotherapy Products

Biotherapy products shall be cryopreserved using a controlled-rate freezing procedure or equivalent procedure validated to maintain critical characteristics, including viability. The temperature of the product(s) and/or freezing process shall be monitored.

5.17.1 Management of Cryopreserved Stored Inventory

5.17.1.1 An aliquot of cryopreserved biotherapy products shall be retained and stored under conditions equivalent to those of the biotherapy products. The use and disposition of aliquot(s) shall be defined by the facility.

5.17.1.2 An inventory control system shall be defined and validated to ensure that any given biotherapy product, aliquot, and reference sample can be located while in storage.

5.17.2 Special Requirements for Cord Blood

5.17.2.1 Cord blood products shall have at least two integrally attached segments cryopreserved with the product for further testing. Standard 5.5.1.3 and Reference Standard 5.15B, Processing Tests for HPC, Cord Blood Products or Gestational Materials (#5), apply.

C **5.17.2.1.1** 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.

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

F **5.17.3 Records for Cryopreserved Products**

Cryopreservation records shall include, as applicable:

1) Donation identification number.
2) Product description code, type of collection, and division code.
3) Product name and attributes.
4) Unique donor and/or patient identifier, if available.
5) Unique, traceable, chain-of-identity identifier, if applicable.
6) Date and time of procurement.
7) Concentration or quantitation of the relevant cell type(s). Reference Standards 5.15A, Processing Tests for HPC, Apheresis and HPC, Marrow; 5.15B, Processing Tests for HPC, Cord Blood Products or Gestational Materials; and 5.15C, Processing Tests for Biotherapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood or Gestational Materials, apply.
8) Cell viability. Reference Standards 5.15A, Processing Tests for HPC, Apheresis, and HPC, Marrow; 5.15B, Processing Tests for HPC, Cord Blood Products or Gestational Materials; and 5.15C, Processing Tests for Biotherapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood Products or Gestational Materials, apply.
9) Name and volume or concentration of the cryoprotective agent(s).
10) Date and time of cryopreservation.
11) Temperature record during cryopreservation.
12) Endpoint temperature after cryopreservation.
13) Storage location of the cryopreserved product and any related test aliquots.

Chapter 4, Suppliers and Customers, applies.

✎*C*5.18 **Expiration Dates and Stability of Products**

5.18.1 The facility shall define and validate expiration dates for each biotherapy product type based on facility-defined critical characteristics. Reference Standard 5.6.2A, Requirements for Labeling of Biotherapy Products (#13), applies.

5.18.2 Stability and expiration dating programs shall be based on the storage conditions for the final product.

5.18.2.1 For each critical quality characteristic, statistical criteria for sample size and test intervals shall be established to demonstrate stability.*

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5.18.3 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.

5.18.3.1 The stability program shall include product container integrity, viable cell recovery, and an assessment of potency and purity of the relevant cell population(s).

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

5.18.4.1 If facilities reassign product expiration dates based on documented stability program data, the facility shall relabel products with new expiration dates. Reference Standard 5.6.2A, Requirements for Labeling of Biotherapy Products, applies.

✎*F*5.19 **Discard and Disposal**

The facility shall have policies, processes, and procedures for 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 4.1 applies.

5.20 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 5.22.1, 5.26.2, 7.1.3, and 7.2.6.2 apply.

5.20.1 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.

5.20.2 Before a product is made available for distribution, the records relevant to Standards 5.20.2.1 and 5.20.2.2 shall be reviewed. The responsibility for completion and review of these records shall be defined in an agreement between the applicable parties. Standard 4.2.3.2 applies.

5.20.2.1 Donation Criteria

Review of donation criteria shall confirm that:

1) Donor informed consent was obtained.

2) Donor eligibility determination was performed, when applicable. Standards 5.10 and 7.2 apply.

3) The donor met other applicable selection criteria.

4) The procurement order was obtained.

5.20.2.2 Product Processing Review

Review of the final biotherapy product processing record shall confirm that:

1) Processing order was obtained, if applicable.

2) Facility-defined specified requirements were achieved.

3) Records of processing, cryopreservation, and storage are complete and contain appropriate initials and/or signatures, and critical calculations have been verified.

4) Appropriate, in-date, critical reagents and materials were used and lot numbers recorded in a manner that ensures traceability.

5) Appropriate equipment was used and identification numbers recorded in a manner that ensures traceability.

6) The accuracy and completeness of the product labeling was verified.

7) All pending infectious disease testing, if applicable, was completed.

5.20.2.3 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.

5.20.3 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 7.2.6.2.

5.21 Distribution

F **5.21.1** Upon request for distribution, the following items shall be reviewed:

1) Documentation that the product was requested. Standards 4.2.3.1 and 4.2.5 apply.

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) including.

-Recipient's name and unique identifier(s).

-Donation identification number.

-Product description code, type of collection, and division code.
-Product name and attributes.
-Unique donor identifier, if available.
- Chain of identity identifier, if applicable
- Chain of custody, if applicable
3) Product condition by visual inspection, including container closure and integrity.
4) 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 **5.21.2** The processing facility shall document the following at the time of distribution:
1) Identity of person(s) verifying that the product is intended for the recipient.
2) Identity of the person distributing the product.
3) Identity of the person to whom the product was distributed.
4) Date(s) and time(s) of distribution.

5.21.3 Instructions shall be made available for the handling, storage, and preparation of products for administration. Standard 4.3.5 applies.

5.21.4 At distribution of allogeneic products, the following information shall accompany the product or be readily available wherever the product is located to maintain the chain of custody:
1) A statement that the donor has been determined to be eligible or ineligible, or donor eligibility determination is incomplete, noting the name and address of the facility that made the donor eligibility determination. Standard 5.10.5 applies.
2) A statement that the infectious disease testing was performed by a laboratory that has been certified to perform such testing on human samples under current CLIA regulations or that has met equivalent requirements as determined by the CMS. For testing facilities located outside of the United States, the use of a non- US laboratory as a testing center is permissible if authorized by the FDA or relevant Competent Authority as an approved laboratory for infectious disease testing in that country.
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.
6) A statement that the product was stored under the applicable environmental conditions as outlined in the instructions. Standard 7.2.6.2 applies.

5.21.5 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.

*F*5.22 Return of Biotherapy Products

The facility shall have a policy for the return of biotherapy products that includes:

1) The reason for the return of the biotherapy product.

2) Inspection of the product for the following elements that can affect product quality, including, but not limited to:

a) Maintenance of appropriate storage and transportation conditions.

b) Integrity of the product container closure.

c) Traceability and chain of custody of the biotherapy product.

d) Product expiration date and time.

3) Determination of the acceptability and disposition of the biotherapy product, such as redistribution, storage, further manufacturing, or discard.

4) Notification and consultation with the patient's physician or other relevant parties, as applicable.

*F*5.23 Redistribution of Returned Biotherapy Products

The facility shall have a policy for the redistribution of biotherapy products that includes:

1) Criteria for redistribution eligibility.

2) An approval process, including authorization from the laboratory director in consultation with the patient's physician or other relevant parties, as applicable.

3) Maintenance of traceability and chain of custody.

4) Product preparation for redistribution, including label verification.

Standards 5.21.1 and 5.21.2 apply.

Clinical Activities

5.24 Clinical Program

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

5.24.1 The facility shall define clinical indications and ensure that recipient evaluation criteria are met and continue to be met before treatment. This evaluation shall be conducted by a qualified health-care professional and approved by a physician.

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

*F*5.25 Clinical Care of the Recipient

The facility shall address 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 biotherapy-associated complications.

Standard 2.2 applies.

5.25.1 Medical Orders

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

5.25.1.1 Medical therapy(ies) shall be ordered by a qualified physician or an authorized healthcare professional.

F **5.25.1.2** Orders for biotherapy product administration shall uniquely identify the recipient, type of biotherapy product ordered, and the dose. The order shall be obtained before the product is distributed for administration. Specific instructions for administration shall be provided.

F **5.26 Preparation of the Recipient for Administration of Biotherapy Products**

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

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

Standard 5.26.1 applies.

5.27 Receipt of Biotherapy Products

The clinical facility shall have procedures for the receipt and preparation of products while maintaining the chain of identity and chain of custody. Standards 5.5, 5.6, 5.8, and 5.20 apply.

F **5.27.1** The clinical facility shall review and verify the following items at the time of final biotherapy product receipt:

1) Recipient's name and unique identifier(s).
2) Donation identification number.
3) Product description code, type of collection, and division code.
4) Product name and attributes.
5) Product condition by visual inspection, including container closure and integrity. Standard 4.1 applies.
6) Summary of donor eligibility determination.

Standards 5.22.2 and 5.22.3 apply.

5.28 Storage at Administering Facility

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

F 5.29 Administration

Immediately before the administration of the final biotherapy 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 biotherapy 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 biotherapy 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) Infusion toxicities and adverse reactions resulting from biotherapy 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 biotherapy products.
6) Treatment of, or prophylaxis for, infectious disease.
7) Use of blood products.
8) Management of graft-vs-host-disease for allogeneic products.
9) Complications of immune effector biotherapy.

F 5.29.3 There shall be procedures for recording adverse events and processes for the communication of such events from the clinical program to the issuing facility and/or registry while maintaining chain of identity. Standards 4.3.2 and 4.3.3 and Chapter 7, Deviations, Nonconformances, and Adverse Events, apply.

5.29.3.1 Responsibility for treating recipient adverse events shall be defined. Standard 7.3.4 applies.

F 5.29.4 Administration Records

Records of administration shall include:

1) Patient's name and unique identifier(s).
2) Donation identification number.
3) Product description code, type of collection, and division code.
4) Product name and attributes.
5) Medical 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) Date and time of expiration, if applicable.

10) Chain of identity identifier, if applicable.
11) All administration information, including the patient's vital signs and the time of all recorded events.
11) Whether any adverse events occurred, including a reference to the appropriate documentation of adverse event forms.
12) Records of notification if an adverse event occurred.
13) Critical steps related to product administration shall be entered into the permanent medical record by the ordering or administering qualified health-care professional according to facility-defined protocol. An anesthesiology record (if anesthesia is required) shall become part of the permanent medical record.

F **5.29.5 Patient Records**

Patient records shall include the following:
1) Patient's name and unique identifier(s).
2) Order for administration.
3) Donation identification number.
4) Product description code, type of collection, and division code.
5) Product name and attributes.
6) Medical and surgical history and physical examination.
7) If applicable, interpretation of tests for infectious disease markers.
8) Signed informed consent for administration of the biotherapy product.
9) Unique biotherapy product identifier(s).
10) If applicable, interpretation of ABO and other red cell antigen and Rh typing 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.
11) Documentation of HLA typing results, if indicated.
12) Other relevant testing records.

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

5.30 Postadministration Monitoring

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

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

Reference Standard 5.6.2A—Requirements for Labeling of Biotherapy Products
*(For labeling of regulated investigational products or licensed products, Standards 5.6.2.1 and 5.6.2.2 apply.)**

Item No.	Element	Completion of Procurement[1]	In-Process Label[1]	Completion of Processing	Distribution [2]
1	Donation identification number (Unique alpha and/or numeric identifier of the product)[3]	P	P	P	P
2	Name of the product	P	P	P	P
3	Product attributes[4]	A[5] or P	R	A[5] or P	P[6]
4	Product code[3] • Product description code • Collection type code • Division code	P	N/A	P	P
5	Unique donor identifier or name[7]	A or P	N/A	A[5] or P	A[5] or P
6	Date of procurement	R	N/A	R	R
7	Unique, traceable, chain-of-identity identifier	P	P	P	P
8	Time of completion of procurement (time zone, if applicable)[8]	R	N/A	R	R
9	Name of procurement facility/donor registry	R	N/A	R	R
10	Approximate product volume or weight (if applicable)	R	N/A	R	R
11	Names/volumes of anticoagulants and other additives (if applicable)	R	N/A	A[5] or P	A[5] or P
12	Recipient name and/or identifier (if known)[9]	R	R	R	A[5] or P
13	Expiration date and time (if applicable)	N/A	N/A	A[10] or P	A or P
14	ABO and Rh of the donor (if applicable)	N/A	N/A	R	R
15	CMV status of the donor (if applicable)	N/A	N/A	N/A	R
16	Red cell compatibility (if applicable)	N/A	N/A	N/A	R

17	Recommended storage temperature (in degrees Celsius)	R	N/A	A or P	A or P
18	Name and address of the facility that determines the product has met release criteria and makes the product available for distribution	N/A	N/A	N/A	R
19	Biohazard label (if applicable; see Reference Standard 5.6.2B, Requirements for Labeling Shipping Containers)	A or P	A[5] or P	A[5] or P	A[5] or P
20	Phrase: "Do Not Irradiate" (if applicable)	N/A	R	A[5] or P	A[5] or P
21	Phrase: "Do Not Use Leukoreduction Filters" (if applicable)	N/A	N/A	A[5] or P	A[5] or P
22	Phrase: "NOT EVALUATED FOR INFECTIOUS SUBSTANCES" and the statement "WARNING: Advise Patient of Communicable Disease Risks" (if applicable)	A or P	A[5] or P	A[5] or P	A[5] or P
23	Phrases: "WARNING: Reactive Test Results for [name of disease agent or disease]" and "WARNING: Advise Patient of Communicable Disease Risks" (if applicable)	A or P	A[5] or P	A[5] or P	A[5] or P
24	Phrase: "For Autologous Use Only" (if applicable)	A or P	A[5] or P	A[5] or P	A[5] or P

25	Phrase: “For Use by Intended Recipient Only” (if applicable)	N/A	A[5] or P	A[5] or P	A[5] or P
26	Phrase: “Properly Identify Intended Recipient and Product”	N/A	A[5] or P	A[5] or P	A[5] or P
27	Phrase: “CAUTION: New Drug – Limited by Federal (or United States) Law to Investigational Use” (if applicable)	N/A	N/A	N/A	A[5] or P
28	Phrase: “For Nonclinical Use Only” (if applicable)	N/A	R	A[5] or P	A[5] or P

[*] When more than one element is indicated, either option is suitable.
[1]The in-process label may be used during processing and before distribution.
[2]The final labeling information for distribution shall be on or included with the container before the product is distributed.
[3]Standard 5.6.1 applies.
[4]Additional characteristics that uniquely define a biotherapy 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 Eurocode labeling requirements, as applicable.
[5]If attaching the applicable warnings and statements to the container is physically impossible, then the label element(s) must accompany the human cells, tissues, and cellular and tissue-based products.
[6]If label size precludes displaying all product attributes, the label shall refer to accompanying documentation for details.
[7]In cases where donor anonymity must be preserved, such as with products from unrelated-donor registries, this information is not required.
[8]Time zone: only applicable if the procurement facility is different from the processing facility.
[9]Ensure maintenance of the chain of identity.
[10]If expiration date is not affixed to cryopreserved products at the end of processing, then records of stability studies shall be available to demonstrate expiration date at release of the cryopreserved product.

A = attached; CMV = cytomegalovirus; N/A = not applicable; P = permanently affixed; R = accompanying records.

Reference Standard 5.6.2B—Requirements for Labeling Shipping Containers

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

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

Reference Standard 5.7.5A—Labeling and Packaging Requirements upon Shipping of Biotherapy 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 5.8.1).

[1]21 CFR 1271.55(a), 21 CFR 1271.55(b), 21 CFR 1271.60(d)(2), 21 CFR 1271.65(b)(2), 21 CFR 1271.90(c), 21 CFR 1271.370(c), and 21 CFR 1271.265 (b).
[2]Includes, but is not limited to, a written description of the product.

Reference Standard 5.10A—General Requirements for Biotherapy Product and Cellular Starting Material Donors[1]

I. Donor Advocacy and Translation Services

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

II. Donor Education

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

B. Educational materials shall include the following elements:
   1) General explanation of the indications for and results of biotherapy.
   2) General description of the donation process, donation alternatives, and the risks of donation.
   3) For marrow donors:
      a) Information about the 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 biotherapy product.
      a) For cord blood or gestational material 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 biotherapy product. Reference Standard 5.10A, #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 5.10.6.2 applies.

3) The facility shall evaluate donor eligibility and medical suitability according to defined risk-based clinical and laboratory testing criteria.
4) Donor eligibility and medical suitability determination shall be performed and approved in a manner and time frame 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. Products 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 determination could not be completed.
    b) Communicate results of the determination of donor eligibility to the 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 eligibility and suitability shall be performed before the recipient receives myeloablative marrow conditioning therapy or is otherwise prepared for receipt of the donation.
    b) Interim health assessments, including psychosocial evaluation as appropriate, shall be performed by a qualified 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 qualified health-care professional at the procurement site shall confirm that the donor's medical status permits procurement and document that the donor's health status is acceptable for donation.
2) Autologous Donors
A medical suitability assessment specific to the donation procedure shall be performed by a qualified health-care professional and approved by a physician before the scheduled procurement.
3) Mothers of Cord Blood or Gestational Material Donors
    a) Personal, family medical, and genetic histories of the family of the prospective cord blood or gestational material 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 gestational parent.
c) In the case of a gestational surrogate, the gestational mother's medical history shall be obtained and documented in addition to that of the biologic parents. A genetic history of the gestational mother need not be obtained.

4) Cadaveric Donors
a) The evaluation of donor eligibility shall be performed by interviewing a family member or other knowledgeable person.
b) When organs, tissues, or cells 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.
c) Organs, tissues, or cells procured from cadaveric donors shall be within 24 hours after death if the body is cooled or refrigerated within 12 hours of death, or 15 hours after death if the body was not cooled or refrigerated.

[1]FDA Guidance: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (August 8, 2007).
21 CFR 1271.

Reference Standard 5.10B—Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors

	Required (Yes/No)[1]
I. Clinical Evaluation to Protect the Safety of the Donor	
Physical examination and health history	Yes
Hemoglobinopathy risk[2]	Yes
Anesthesia risk, if applicable	Yes
Vascular access	Yes
Pregnancy in female donors	Yes
II. Clinical Evaluation to Protect the Safety of the Recipient[3]	
Donor screening for clinical and physical evidence of risk for, or symptoms of, relevant communicable disease[4]	Yes
Hemoglobinopathy risk[2]	Yes
Risk of any acquired condition, such as malignancy, or any inherited condition that could be transferred to the recipient by the transplant	Yes
Risk of transmission of infectious agents to others by product collection, processing, storage, or handling, including those associated with xenotransplantation	Yes
Evaluation for recent immunization and vaccination history	Yes
History and behavioral risk for exposure to the following infectious agents or diseases[3]:	
HIV	Yes
HBV	Yes
HCV	Yes
HTLV (viable, leukocyte-rich products only)	Yes
Syphilis	Yes
WNV[5]	Yes
Vaccinia (smallpox vaccine)	Yes
Human TSEs	Yes
Malaria (travel or residence in malaria-endemic areas)[6]	Yes
Trypanosoma cruzi (Chagas disease)[6]	Yes
Mycobacterium tuberculosis (Mtb)[8]	Yes
Sepsis[7]	Yes
III. Laboratory Testing for Allogeneic Donors[3,8]	
HIV-1/2	Yes
HBV	Yes
HCV	Yes

Syphilis	Yes
HTLV-I/II (viable, leukocyte-rich products only)	Yes
CMV (viable, leukocyte-rich products only)	Yes
WNV[5]	Yes
Trypanosoma cruzi (Chagas disease)[6]	No
HLA type, if applicable[9,10]	Yes
ABO/Rh, if applicable[9]	Yes
CBC, if applicable	Yes

[1]These *Biotherapies Standards* are minimum requirements and are not meant to preempt any local or FDA or relevant Competent Authority regulations that may be more stringent. Standard 5.10.2.6 applies.
[2]Applies only to donors whose hemoglobinopathy will put the donor or recipient at risk.
[3]Relevant medical records as described in 21 CFR 1271.3(s).
[4]The relevant communicable disease agents or diseases are described in 21 CFR 1271.3(r)(1)(i)(ii) and 1271.3(r)(2).
[5]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 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).
[6]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 identified health history risks and the test results for these diseases affect eligibility determination.
[7]FDA Guidance for Industry: Recommendations to Reduce the Risk of Transmission of Disease Agents Associated with Sepsis by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (January 2025).
[8]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).
[9]Testing shall be performed whenever this information is necessary for the selection and/or clinical use of a biotherapy product.
[10]*HLA-A, HLA-B, HLA-C,* and *HLA-DRB1* loci shall be determined. All typing used for the final selection of the donor shall use DNA-based technologies.

CBC = complete blood count; CMV = cytomegalovirus (anti-CMV, IgG and IgM); HBV = hepatitis B virus; HCV = hepatitis C virus; HIV-1/2 = human immunodeficiency virus, types 1 and 2; HTLV-I/II = human T-cell lymphotropic virus, types I and II; TSEs = transmissible spongiform encephalopathies; WNV = West Nile virus.

Reference Standard 5.10C—Clinical Evaluation and Laboratory Testing of Autologous Donors

	Required (Yes/No)[1]
I. Clinical Evaluation to Protect the Safety of the Donor/Recipient	
Physical examination and health history	Yes
Hemoglobinopathy risk[2]	Yes
Anesthesia risk, if applicable	Yes
Vascular access	Yes
Pregnancy in female donors	Yes
Sepsis	Yes
II. Laboratory Testing	
ABO/Rh, if applicable[3]	Yes
CBC, if applicable	Yes

[1]These *Biotherapies Standards* are minimum requirements and are not meant to preempt any local or FDA or relevant Competent Authority regulations that may be more stringent. Standard 5.10.2.6 applies.
[2]Applies only to donors whose hemoglobinopathy will put the donor or recipient at risk.
[3]Testing shall be performed whenever this information is necessary for the selection and/or clinical use of a biotherapy product.

CBC = complete blood count.

Reference Standard 5.10D—Clinical Evaluation and Laboratory Testing of Cord Blood or Gestational Material Donors

	Required (Yes/No)[1]
I. Clinical Evaluation to Protect the Safety of the Donor	
Physical examination and health history	Yes
II. Clinical Evaluation to Protect the Safety of the Recipient[2,3]	
Donor screening for clinical and physical evidence of risk for, or symptoms of, relevant communicable disease[4]	Yes
Risk of any condition, such as malignancy or any inherited condition that could be transferred to the recipient by the transplant	Yes
Risk of transmission of infectious agents to others by product collection, processing, storage, or handling, including those associated with xenotransplantation	Yes
Evaluation for recent immunization and vaccination history	Yes
History and behavioral risk for exposure to the following infectious agents or diseases[2, 3, 4]:	
HIV	Yes
HBV	Yes
HCV	Yes
HTLV (viable, leukocyte-rich products only)	Yes
Syphilis	Yes
WNV[5]	Yes
Vaccinia (smallpox vaccine)	Yes
Human TSEs	Yes
Malaria (travel or residence in malaria-endemic areas)[6]	Yes
Trypanosoma cruzi (Chagas disease)[6]	Yes
Mycobacterium tuberculosis (Mtb)	Yes
Sepsis[7]	Yes
III. Laboratory Testing for Allogeneic Donors[3,8]	
HIV-1/2	Yes
HBV	Yes
HCV	Yes
Syphilis	Yes
HTLV-I/II (viable, leukocyte-rich products only)	Yes
CMV (viable, leukocyte-rich products only)	Yes
WNV[5]	Yes
Trypanosoma cruzi (Chagas disease)[6]	No

[1]These *Biotherapies Standards* are minimum requirements and are not meant to preempt any local or FDA or relevant Competent Authority regulations that may be more stringent. Standard 5.10.2.6 applies.
[2]Relevant medical records as described in 21 CFR 1271.3(s).
[3]Required for cord blood or gestational materials with the potential for allogeneic use.
[4]The relevant communicable disease agents or diseases are described in 21 CFR 1271.3(r)(1)(i)(ii) and 1271.3(r)(2).
[5]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 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).
[6]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 identified health history risks and the test results for these diseases affect eligibility determination.
[7]FDA Guidance for Industry: Recommendations to Reduce the Risk of Transmission of Disease Agents Associated with Sepsis by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (January 2025).
[8]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).

CBC = complete blood count; CMV = cytomegalovirus (anti-CMV, IgG, and IgM); HBV = hepatitis B virus; HCV = hepatitis C virus; HIV-1/2 = human immunodeficiency virus, types 1 and 2; HTLV-I/II = human T-cell lymphotropic virus, types I and II; TSEs = transmissible spongiform encephalopathies; WNV = West Nile virus.

Reference Standard 5.10E—Clinical Evaluation and Laboratory Testing of Cadaveric Donors

	Required (Yes/No)[1]
I. Clinical Evaluation to Protect the Safety of the Recipient[2]	
Donor screening for clinical and physical evidence of risk for, or symptoms of, relevant communicable disease[3]	Yes
Risk of any condition, such as malignancy or any inherited condition that could be transferred to the recipient by the transplant	Yes
Risk of transmission of infectious agents to others by product collection, processing, storage, or handling, including those associated with xenotransplantation	Yes
Evaluation for recent immunization and vaccination history	Yes
Coroner and/or autopsy report (if available)	Yes
History and behavioral risk for exposure to the following infectious agents or diseases[1, 3]:	
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
Mycobacterium tuberculosis (Mtb)	Yes
Sepsis[6]	Yes
II. Laboratory Testing for Donors[7]	
HIV-1/2	Yes
HBV	Yes
HCV	Yes
Syphilis	Yes
HTLV-I/II (viable, leukocyte-rich products only)	Yes
CMV (viable, leukocyte-rich products only)	Yes
WNV[4]	No
Trypanosoma cruzi (Chagas disease)[5]	No
HLA type, if applicable[8]	Yes
ABO/Rh, if applicable[8]	Yes

[1]These *Biotherapies Standards* are minimum requirements and are not meant to preempt any local or FDA or relevant Competent Authority regulations that may be more stringent. Standard 5.10.2.6 applies.

[2]Relevant medical records as described in 21 CFR 1271.3(s).
[3]The relevant communicable disease agents or diseases are described in 21 CFR 1271.3(r)(1)(i)(ii) and 1271.3(r)(2), and physical assessment is described in 1271.3(o). Standard 5.10.2.5 applies.
[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 FDA Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (August 2007).
[5]As of this date, the FDA does not consider these risk factors to render donors ineligible; facility policies must define how identified health history risks and the test results for these diseases affect eligibility determination.
[6]FDA Guidance for Industry: Recommendations to Reduce the Risk of Transmission of Disease Agents Associated with Sepsis by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (January 2025).
[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 biotherapy or tissue product.

CBC = complete blood count; CMV = cytomegalovirus (anti-CMV, IgG and IgM); HBV = hepatitis B virus; HCV = hepatitis C virus; HIV-1/2 = human immunodeficiency virus, types 1 and 2; HTLV-I/II = human T-cell lymphotropic virus, types I and II; TSEs = transmissible spongiform encephalopathies; WNV = West Nile virus.

Reference Standard 5.15A—Processing Tests for HPC, Apheresis and HPC, Marrow

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

1) Cell characterization specific to the biotherapy product. This includes:
   a) Total nucleated cell count.
   b) Total nucleated cells and/or CD45 viability.
   c) CD34 cell count.
   d) CD34 cell viability.
   e) Nucleated red cell count or corrected total nucleated cell count.

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

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

Reference Standard 5.15B—Processing Tests for HPC, Cord Blood

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

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

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

*FDA Guidance for Industry: Biologics License Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System (March 2014)

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

   If results affect the donor's health as determined by the appropriate medical director, notification of the positive culture results shall be given to the following:
   a) The gestational parent or gestational surrogate's physician; or if a physician is not identified, notify the gestational parent or gestational surrogate.
   b) The recipient's physician.

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

5) The following tests shall be performed before distribution:
   a) Confirmatory HLA testing on a sample obtained from an integrally attached segment for autologous and allogeneic cord blood products.
   b) If used for hematopoietic reconstitution, hemoglobinopathy testing of allogeneic cord blood units on a sample obtained from the product or from the donor.
   c) Viable CD34 assay after cryopreservation from an integrally attached segment on products that will be used for hematopoietic reconstitution.
   d) Other tests as required by the applicable registry.

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

Reference Standard 5.15C—Processing Tests for Biotherapy Products Other than HPC, Apheresis; HPC, Marrow; and HPC, Cord Blood

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

1) If the final product contains Red Blood Cells (RBCs), testing for ABO group and Rh type shall be performed before cryopreservation.

2) Testing specific to the biotherapy product shall include:
   a) For T cells, CD3+ cell count.
   b) For islets, islet equivalents (IEQ).
   c) Relevant cell viability, if applicable.
   d) For other biotherapy products, the relevant cell count shall be defined by the facility and appropriate product characterization criteria and measurements be defined, if applicable.

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

4) Characterization of cell identity specific to the biotherapy product, if applicable.

5) Other assays:
   a) Functional assay(s) specific to the biotherapy product shall be performed, as applicable.
   b) Relevant purity and potency assay(s) shall be defined by the facility.

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

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

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

Excerpt of Reference Standard 6.2.9A Relevant to Process Control

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/Management Issues	Unit/Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
5.1.1	Validation of new or changed processes and procedures	X	X	X	C	10
5.1.2	Quality control records and review of quality control results	X	X	X	C	10
5.1.8	Identification and traceability of products	N/A	N/A	X	C	10
5.1.9.1	Supplier and/or consignee processes for traceability, tracking, and recall of products	X	X	X	C	10
5.1.9.1.1	Facility policy for the use/distribution of a biotherapy product provided by a supplier and/or received by a consignee that lacks a complete chain of custody	X	X	X	F	10
5.1.10	Participation in an external proficiency testing program	X	X	X	C	10
5.1.10.3	Proficiency testing results reviewed by the medical or	X	X	X	C	10

	laboratory director					
5.1.11	Investigational New Drug (IND) application or equivalent review	X	X	X	C	10
5.2	Outcome data	X	X	X	F	10
5.2.4.1	Notification by patient-care service to issuing or processing facility of adverse events	N/A	N/A	X	F	10
5.3	Qualification of all materials used in the procurement, processing, and/or administration of biotherapy products	X	X	X	C	10
5.3.2.1	Quarantine of critical materials	X	X	X	C	10
5.3.2.2	Complete records of the inspection of incoming materials that come into contact with the biotherapy product or that directly affect the quality of the product	N/A	N/A	X	C	10
5.3.2.3	Identification of materials used on an emergency basis	N/A	N/A	X	C	10
5.3.4	Inspection of in-house reagents	N/A	N/A	X	C	10
5.3.5	Validation and monitoring of equipment, materials, and methods used in cleaning and sterilization of	X	X	X	C	10

	non-single-use materials					
5.3.6	Use and identification of critical materials that come into contact with the patient or biotherapy product	X	X	X	F	10
5.3.6.1	Package inserts, certificates of analysis, or any manufacturer's documentation, including recall or defect notices, advisories, etc, for all critical materials used	X	X	X	C	10
5.4.2.1	Monitoring and review of the effectiveness of aseptic methods	N/A	N/A	X	C	10
5.4.3	Operational controls to prevent mix up and contamination	X	X	X	C	10
5.5.1	Unique identification and traceability of biotherapy products and samples from source to final disposition	N/A	N/A	X	C	10
5.6, #2, 3, 5	Labeling controls	N/A	N/A	X	C	10
5.6.1	ISBT 128 implementation	N/A	N/A	X	C	10
5.6.3	Verification of product packaging and labeling	N/A	N/A	X	C	10
5.7	Transport of products	N/A	N/A	X	C	10

5.7.2	Qualification of shipping containers and periodic requalification	X	X	X	C	10
5.7.3	Monitoring of temperature for noncryopreserved products	N/A	N/A	X	F	10
5.7.3.1	Continuous monitoring of temperature for cryopreserved products	N/A	N/A	X	F	10
5.7.6	Product acceptance and shipper temperature upon receipt	N/A	N/A	X	C	10
5.8	Inspection and testing activities	X	X	X	C	10
5.8.1	Inspection of incoming cells, tissues, and organs	N/A	N/A	X	C	10
5.8.2	Inspection and testing of products during processing	N/A	N/A	X	C	10
5.9.1	Storage area temperature and humidity	X	X	X	C	10
5.9.1.1	If biotherapy products are stored in an open storage area, the ambient temperature recorded at least every 4 hours	X	X	X	C	10
5.9.3, 5.9.4	Monitoring of temperature and/or liquid nitrogen levels in storage devices and documentation of alarm activation	X	X	X	C	10

5.10	Determination of donor eligibility and verification that procurement criteria (eg, informed consent) have been met	N/A	X	N/A	F	10
5.10.2.2	Cadaveric donor eligibility	N/A	X	N/A	F	10
5.10.2.3	Infectious disease testing of donors	N/A	X	N/A	F	10
5.10.2.4	Donor testing performed	N/A	X	N/A	F	10
5.10.4	Review of donor screening and infectious disease testing record before international shipment or transport	N/A	X	N/A	F	10
5.10.5	Final determination of donor eligibility	N/A	X	N/A	F	10
5.10.6.2	Communication of abnormal results on medical history screening or testing that may affect the donor's health	N/A	X	N/A	F	10
5.10.6.3	Communication of abnormal results on medical history screening or testing that may affect the recipient's health or the therapeutic value of the biotherapy product	N/A	X	N/A	F	10
5.10.6.4	Ineligible donors	N/A	X	N/A	C	10
5.10.7	Products from ineligible donors	N/A	X	N/A	F	10

5.10.8	Incomplete donor eligibility determination for donors not screened or tested	N/A	X	N/A	F	10
5.10.8.2	Physician notification of incomplete donor eligibility	N/A	X	N/A	C	10
5.11.2	Central venous access device placement by qualified individual or physician	N/A	X	N/A	C	10
5.11.3.1	Evaluation of allogeneic and autologous donors for the risk of hemoglobinopathy before the administration of a mobilizing agent	N/A	X	N/A	C	10
5.12.1	Medical orders for procurement	X	X	X	F	10
5.12.2.2, 5.12.2.4	Final approval and documentation by the donor's physician (or by a health-care professional, if appropriate) that the donor is able to proceed with donation in conformance with Reference Standard 5.10A, General Requirements for Biotherapy Product Donors	N/A	X	N/A	F	10
5.12.2.3	For donors of mobilized cells (apheresis), a	N/A	X	N/A	F	10

	complete blood count obtained within 24 hours before each procurement procedure; for marrow donors, a complete blood count obtained before procurement					
5.12.4	Confirmation of donor identity, at the time of procurement, by two identifiers	N/A	X	N/A	F	10
5.12.5	Identification numbers and expiration dates of lot numbers of all disposables and additives used in procurement	N/A	X	N/A	F	10
5.12.5, 5.12.6	Complete procurement record; review of procurement record	N/A	X	N/A	F	10
5.13	Definition of procurement goals	N/A	N/A	X	F	10
5.15.1	Medical orders for processing, preservation, or storage	X	X	X	F	10
5.15.2	Complete processing record; verification that acceptable values or ranges for defined critical characteristics for each product were obtained	N/A	N/A	X	F	10

5.15.3	Determination of acceptable values or ranges	N/A	N/A	X	C	10
5.15.4	Procedures used to manage red cell antigen incompatibility	N/A	N/A	X	F	10
5.16	Product-specific specifications and acceptable storage conditions of noncryopreserved products	N/A	N/A	X	C	10
5.17.2.1.1	Segment identification by two individuals	N/A	N/A	X	C	10
5.17.3	Complete cryopreservation records	N/A	N/A	X	F	10
5.18	Stability program for each type of biotherapy product and expiration dates	X	X	X	C	10
5.19	Disposition of products consistent with informed consent and laws and regulations	X	X	X	F	10
5.20.2, 5.20.2.3	Review of donation criteria, final processing criteria, and final product-specified requirements	N/A	N/A	X	F	10
5.21.1	Request for distribution	N/A	N/A	X	C	10
5.21.1	Product distribution	N/A	N/A	X	F	10
5.21.2, 5.26	Review of criteria for receipt	N/A	N/A	X	F	10
5.22	Product return	N/A	N/A	X	F	10
5.23	Product redistribution	N/A	N/A	X	F	10

5.25	Clinical care of the recipient	N/A	N/A	X	F	10
5.25.1.2	Medical orders for administration	X	X	X	F	10
5.26	Preparation of the recipient for administration of the biotherapy product	N/A	N/A	X	F	10
5.29	Confirmation of identity of the product and the intended recipient, using at least two identifiers	N/A	N/A	X	F	10
5.29.3	Identification of adverse events occurring during the infusion of final biotherapy products and communication to the issuing facility	N/A	N/A	X	F	10
5.29.4, 5.29.5	Complete administration record and patient records	N/A	N/A	X	F	10

[1]Applicable federal, state, or local law may exceed this period.

QSE 6 – Documents and Records

Key Concepts

This QSE focuses on the need to maintain all documents and records in a manner that ensures their confidentiality, traceability, completeness, uniformity, and ability to be located and retrieved in a time deemed adequate. This QSE also includes the need to ensure data integrity and that all data can be backed up and retrieved.

Key Terms

Backup: Digital data and/or physical storage containing copies of relevant data.

Confidentiality: The protection of private, sensitive, or trusted information resources from unauthorized access or disclosure.

Data Integrity: The accuracy, completeness, and consistency of information resources.

Document (noun): Written or electronically generated information and work instructions. Examples of documents include quality manuals, procedures, or forms.

Document (verb): To capture information through writing or electronic media.

Label: An inscription affixed or attached to a product for identification.

Labeling: Information that is required or selected to accompany a product, which may include content, identification, description of processes, storage requirements, expiration date, cautionary statements, or indications for use.

Master List of Documents: A reference list, record, or repository of an organization's policies, processes, procedures, forms, and labels related to the Standards, including information for document control.

Record (noun): Information captured in writing or through electronically generated media 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 and documented.

Record (verb): To capture information for use in records through writing or electronic media.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Records of activities performed.
- Record system.
- Master list of documents.
- An electronic record system, if applicable.
- Uniform storage media and ability to track newer technologies to older ones as needed.
- Evidence of document and record review.
- Evidence of standardized formats for all documents and records.
- Record retention periods.

- Record traceability.
- Data backup plans.
- Record change process.
- Obsolescence of records and disposition.
- Record destruction.

6. Documents and Records

6.0 Documents and Records

The organization shall ensure that documents and records are created, stored, and archived in accordance with record retention policies.

6.1 Document Control

The organization shall control all documents that relate to the requirements of these Biotherapies Standards. Documents shall be protected from unauthorized access and accidental or unauthorized modification, deletion, or destruction.

6.1.1 Format

Documents shall be in standardized formats. Additional policies, processes, and procedures (such as those in an operator's manual or published in the AABB Technical Manual, and AABB Biotherapies Manual) may be incorporated by reference.

✎C 6.1.2 Document Review, Approval, and Distribution

The document control process shall ensure that documents:

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 Biotherapies Standards are performed.
5) Are not used when deemed invalid or obsolete.
6) Are identified as archived or obsolete when appropriate.

✎C 6.1.3 Document Changes

Changes to documents shall be reviewed and approved by an authorized individual.

6.1.3.1 The organization shall track changes to documents.

✎C 6.1.4 Master List of Documents

The organization shall maintain complete lists of all active policies, processes, procedures, labels, forms, and other documents that relate to the requirements of these Biotherapies Standards.

✎C 6.1.5 Review of Policies, Processes, and Procedures

Review of each policy, process, and procedure shall be performed by an authorized individual at a minimum of every 2 years.

✎C 6.1.6 Document Retention

The organization shall determine which documents shall be archived, destroyed, or made obsolete.

6.1.7 Document Storage

Documents shall be stored in a manner that preserves integrity and legibility; protects from

accidental or unauthorized access, loss, destruction, or modification; and ensures accessibility and retrievability.

6.1.8 Document Retrieval

The organization shall ensure that documents are retrievable in a timely manner.

6.1.9 The organization shall use only current and valid documents. Applicable documents shall be available at all locations where activities essential to meeting the requirements of these Biotherapies Standards are performed.

6.2 Record Control

The organization shall maintain a system for identification, collection, indexing, accessing, filing, storage, maintenance, and disposition of original records.

6.2.1 Records

Records shall be complete, retrievable in a period appropriate to the circumstances, and protected from accidental or unauthorized destruction or modification.

6.2.2 Record Traceability

The records system shall ensure traceability of:

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 organization where the activity was performed.

6.2.3 Information to Be Retained

Records shall demonstrate that a material, product, or service conforms to specified requirements and that the quality system is operating effectively.

6.2.3.1 Records from suppliers shall be an element of this information.

6.2.4 Legibility

All records shall be legible and indelible.

C 6.2.5 Record Change

The organization shall establish 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.

6.2.5.1 Changes to records (including electronic records) shall be verified for accuracy and completeness.

6.2.5.2 Modifications or changes that can affect the safety of the recipient or quality of the biotherapy product shall be approved by the authorized individual. Chain of identity shall be maintained.

6.2.5.3 The 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.

6.2.6.1 The record shall identify the work performed, the individual performing the activity, the date and if applicable, time it was performed.

✎C **6.2.7 Copies**

Before destruction of 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 organization shall ensure the confidentiality of records.

6.2.9 Retention

Records required by these Biotherapies Standards shall be retained for a period indicated in the record retention table at the end of each chapter.

6.2.9.1 These records shall be retained at least 10 years following either their creation (*C*) or the final disposition (*F*) of the biotherapy product with which they are associated. Applicable FDA, relevant Competent Authority, or local law may exceed this period.

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

✎C **6.2.10 Record Review**

Records shall be reviewed for accuracy, completeness, and compliance with applicable standards, laws, and regulations.

6.2.11 Storage of Records

Records shall be stored to:

1) Preserve record legibility and integrity for the entire retention period.

2) Protect from accidental or unauthorized access, loss, deterioration, damage, destruction, mix-up, or modification.

3) Permit ready identification.

4) Allow retrieval in a defined time frame.

6.2.12 Destruction of Records

Destruction of records shall be conducted in a manner that protects the confidential content of the records.

C6.3 Electronic Records

The organization shall support the management of information systems.

6.3.1 Access to Data and Information

Access to data and information shall be controlled.

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.

C **6.3.1.1.1** Electronic records shall include the date and identity of the person making a change.

6.3.1.2 The facility shall define and identify which individuals are authorized to create, modify, maintain, or transmit records in a controlled and approved manner in conformance with the FDA or relevant Competent Authority requirements.

6.3.2 Data Integrity

Data integrity shall ensure that data are retrievable and usable.*

*FDA Guidance for Industry: Data Integrity and Compliance with Drug cGMP Questions and Answers (December 2018).

6.3.2.1 Data shall be accurately, reliably, and securely sent from the point of entry to final destination.

6.3.2.2 Data shall be retrievable for the entire retention period.

6.3.2.2.1 The organization shall archive records or data from media and platforms no longer in use.

6.3.2.3 There shall be a process in place for routine backup of all critical data.

6.3.3 Storage Media

Data storage media shall be protected from damage or unintended access and destruction.

6.3.4 Backup Data

The organization shall back up all critical data.

6.3.4.1 Backup data shall be stored in a secure offsite location.

6.3.4.2 Backup data shall be protected from unauthorized access, loss, or modification.

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

Excerpt of Reference Standard 6.2.9A Relevant to Documents and Records

Standard	Record to be Maintained	Quality System Records	Donor Eligibility/Management Issues	Unit/Recipient	Retention After Creation or Final Disposition of Related Product	Minimum Retention Time (Years)[1]
6.1.2	Document control, including review and approval of all documents before use	X	X	X	C	10
6.1.3	Review and approval of changes to documents	X	X	X	C	10
6.1.4	List of all active policies, processes, procedures, labels, and forms	X	X	X	C	10
6.1.5	Biennial review of each policy, process, or procedure	X	X	X	C	10
6.1.6	Documents that are archived, destroyed, or made obsolete	X	X	X	C	10
6.2.5	Record change	X	X	X	C	10
6.2.7	Verification that copies of records contain the original content and are legible, complete, and accessible before the original records are destroyed	X	X	X	C	10
6.2.10	Review of records for accuracy,	X	X	X	C	10

	completeness, and compliance with applicable standards, laws, and regulations					
6.3	Electronic records	X	X	X	C	10
6.3.1.1.1	Date and identity of person making change(s) to electronic records	X	X	X	C	10

[1]Applicable federal, state, or local law may exceed this period.

Reference Standard 6.2.9A—Retention of Records

Standard	Record to be Maintained	Quality System Records	Donor Eligibility/Management Issues	Unit/Recipient	Retention After Creation or Final Disposition of Related Product	Minimum Retention Time (Years)[1]
1.1.3	Procurement medical director management or review of 10 cell procurement procedures	X	X	X	C	10
1.1.4	Laboratory medical director and laboratory director management or review of 10 cell product processing procedures	X	X	X	C	10
1.1.5	Relevant continuing education of the clinical program director	X	X	X	C	10
1.2.1.1.1, 1.2.1.1.2	Quarterly reports by quality representative to executive management	X	X	X	C	10
1.2.2	Management review of effectiveness of the quality system	X	X	X	C	10
1.2.2.1	Executive management review of the quality system and related reports	X	X	X	C	10

1.2.2.1.1	Yearly review of the quality system	X	X	X	C	10
1.3	Policies, processes, and procedures	X	X	X	C	10
1.3.1.1	Procurement medical director review and approval of all medical policies, processes, and procedures	X	X	X	C	10
1.3.1.2	Laboratory medical director review and approval of all medical policies, processes, and procedures	X	X	X	C	10
1.3.1.3	Laboratory director review and approval of all technical policies, processes, and procedures	X	X	X	C	10
1.3.1.4	Clinical program director review and approval of all clinical policies, processes, and procedures	X	X	X	C	10
1.3.2	Exceptions to policies, processes, and procedures	X	X	X	C	10
1.4	Risk assessment	X	X	X	C	10
1.6.1	Emergency operation plan tested at defined intervals	X	X	X	C	2 years, or two organizational testing intervals (whichever is longer)
2.1.1	Job descriptions	X	X	X	C	10

2.1.2	Qualification of personnel performing critical tasks	X	X	X	C	10
2.1.3	Training records of personnel	X	X	X	C	10
2.1.3.1	Identification of qualifications required for trainers	X	X	X	C	10
2.1.4	Evaluations of competence	X	X	X	C	10
2.1.4.1	Corrective action when competence has not been demonstrated	X	X	X	C	10
2.1.5	Personnel records of each employee	X	X	X	C	10
2.1.6, 2.1.6.1	Continuing education requirements	X	X	X	C	10
3.2	Equipment qualification	X	X	X	F	10 years after retirement of the equipment
3.4	Unique identification of equipment	X	X	X	F	10
3.5.1	Equipment calibration activities	X	X	X	F	10
3.5.2	Equipment found to be out of calibration	X	X	X	F	10
3.5.3	Equipment monitoring, maintenance, calibration, and repair	X	X	X	F	10
3.6	Implementation and modification of software, hardware, or databases	X	X	X	F	2 years after retirement of system
3.6.1	Testing of alternative systems	X	X	X	F	10

3.7	Monitoring or technology infrastructure	X	X	X	F	10
3.7.1	Artificial intelligence oversight	X	X	X	F	10
4.1	Evaluation and participation in selection of suppliers	X	X	X	C	10
4.1.3	Review of agreements before acceptance and at facility-defined intervals	X	X	X	C	10
4.2	Agreements	X	X	X	C	10
4.2.1	Agreement review	X	X	X	C	10
4.2.3	Agreements concerning activities involving more than one organization	X	X	X	C	10
4.2.4	Agreement changes communicated to affected parties	X	X	X	C	10
4.2.5.1	Agreements for the timing and responsibility of medical orders	X	X	X	F	10
4.3	Inspection of incoming critical materials	X	X	X	C	10
4.3.1	Agreements between departments or facilities regarding the transfer of products	X	X	X	F	10
4.3.2	Agreements for the collection, trans-port, receipt, handling, and administration of	X	X	X	F	10

	the biotherapy product, reporting adverse events, and obtaining outcome data					
4.3.3	Agreement between processing/issuing facility and the administering facility or registry for creation and retention of records; agreements for each facility to access relevant records	X	X	X	C	10
4.3.4	Conditions for product storage and dis-position	X	X	X	C	10
4.3.6	Shipment of biotherapy products	N/A	N/A	X	F	10
4.4	Claims in educational and promotional materials	X	X	X	F	10
4.5	Donor informed consent	X	X	X	F	10
4.6	Authorization for cadaveric donors	X	X	X	F	10
4.7	Patient informed consent	X	X	X	F	10
4.8.1, 4.8.2	Evaluation, qualification, and selection of suppliers of materials, services, and products	X	X	X	F	10
4.8.3	Monitoring of suppliers (including reporting to management of a	X	X	X	F	10

	supplier's failures to meet specified requirements)					
4.8.4	Notification of shipping facility and manufacturer (if applicable) when materials are received in an unacceptable condition	X	X	X	C	10
5.1.1	Validation of new or changed processes and procedures	X	X	X	C	10
5.1.2	Quality control records and review of quality control results	X	X	X	C	10
5.1.8	Identification and traceability of products	N/A	N/A	X	C	10
5.1.9.1	Supplier and/or consignee processes for traceability, tracking, and recall of products	X	X	X	C	10
5.1.9.1.1	Facility policy for the use/distribution of a biotherapy product provided by a supplier and/or received by a consignee that lacks a complete chain of custody	X	X	X	F	10
5.1.10	Participation in an external proficiency testing program	X	X	X	C	10
5.1.10.3	Proficiency testing results reviewed by the medical or	X	X	X	C	10

	laboratory director					
5.2	Outcome data	X	X	X	F	10
5.2.4.1	Notification by patient-care service to issuing or processing facility of adverse events	N/A	N/A	X	F	10
5.3	Qualification of all materials used in the procurement, processing, and/or administration of biotherapy products	X	X	X	C	10
5.3.2.1	Quarantine of critical materials	X	X	X	C	10
5.3.2.2	Complete records of the inspection of incoming materials that come into contact with the biotherapy product or that directly affect the quality of the product	N/A	N/A	X	C	10
5.3.2.3	Identification of materials used on an emergency basis	N/A	N/A	X	C	10
5.3.4	Inspection of in-house reagents	N/A	N/A	X	C	10
5.3.5	Validation and monitoring of equipment, materials, and methods used in cleaning and sterilization of non-single-use materials	X	X	X	C	10
5.3.6	Use and identification of	X	X	X	F	10

	critical materials that come into contact with the patient or biotherapy product					
5.3.6.1	Package inserts, certificates of analysis, or any manufacturer's documentation, including recall or defect notices, advisories, etc, for all critical materials used	X	X	X	C	10
5.4.2.1	Monitoring and review of the effectiveness of aseptic methods	N/A	N/A	X	C	10
5.4.3	Operational controls to prevent mix up and contamination	X	X	X	C	10
5.5.1	Unique identification and traceability of biotherapy products and samples from source to final disposition	N/A	N/A	X	C	10
5.6, #2, 3, 5	Labeling controls	N/A	N/A	X	C	10
5.6.1	ISBT 128 implementation	N/A	N/A	X	C	10
5.6.3	Verification of product packaging and labeling	N/A	N/A	X	C	10
5.7	Transport of products	N/A	N/A	X	C	10
5.7.2	Qualification of shipping containers and periodic requalification	X	X	X	C	10

5.7.3	Monitoring of temperature for non-cryopreserved products	N/A	N/A	X	F	10
5.7.3.1	Continuous monitoring of temperature for cryopreserved products	N/A	N/A	X	F	10
5.7.6	Product acceptance and shipper temperature upon receipt	N/A	N/A	X	C	10
5.8	Inspection and testing activities	X	X	C	C	10
5.8.1	Inspection of incoming cells, tissues, and organs	N/A	N/A	X	C	10
5.8.2	Inspection and testing of products during processing	N/A	N/A	X	C	10
5.9.1	Storage area temperature and humidity	X	X	X	C	10
5.9.1.1	If biotherapy products are stored in an open storage area, the ambient temperature recorded at least every 4 hours	X	X	X	C	10
5.9.3, 5.9.4	Monitoring of temperature and/or liquid nitrogen levels in storage devices and documentation of alarm activation	X	X	X	C	10
5.10, 5.10.2.2	Determination of donor eligibility and verification that procurement	N/A	X	N/A	F	10

	criteria (eg, informed consent) have been met, in conformance with Reference Standards 4.5A, Donor Informed Consent or Authorization, Reference Standards 5.10B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.10C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.10D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Materials Donors; and 5.10E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors.					
5.10.2.2	Cadaveric donor eligibility	N/A	X	N/A	F	10
5.10.2.3	Infectious disease testing of donors	N/A	X	N/A	F	10
5.10.2.4	Donor testing performed in conformance with Reference Standards 5.10B, Clinical	N/A	X	N/A	F	10

	Evaluation and Laboratory Testing of Living Allogeneic Donors; 5.10C, Clinical Evaluation and Laboratory Testing of Autologous Donors; 5.10D, Clinical Evaluation and Laboratory Testing of Mothers of Cord Blood or Gestational Materials Donors; and 5.10E, Clinical Evaluation and Laboratory Testing of Cadaveric Donors.					
5.10.4	Review of donor screening and infectious disease testing record before international shipment or transport	N/A	X	N/A	F	10
5.10.5	Final determination of donor eligibility	N/A	X	N/A	F	10
5.10.6.2	Communication of abnormal results on medical history screening or testing that may affect the donor's health	N/A	X	N/A	F	10
5.10.6.3	Communication of abnormal results on	N/A	X	N/A	F	10

	medical history screening or testing that may affect the recipient's health or the therapeutic value of the biotherapy product					
5.10.6.4	Ineligible donors	N/A	X	N/A	C	10
5.10.7	Products from ineligible donors	N/A	X	N/A	F	10
5.10.8	Incomplete donor eligibility determination for donors not screened or tested	N/A	X	N/A	F	10
5.10.8.2	Physician notification of incomplete donor eligibility	N/A	X	N/A	C	10
5.11.2	Central venous access device placement by qualified individual or physician	N/A	X	N/A	C	10
5.11.3.1	Evaluation of allogeneic and autologous donors for the risk of hemoglobinopathy before the administration of a mobilizing agent	N/A	X	N/A	C	10
5.12.1	Medical orders for procurement	X	X	X	F	10
5.12.2.2, 5.12.2.4	Final approval and documentation by the donor's physician (or by a health-care professional, if appropriate) that the donor is able	N/A	X	N/A	F	10

	to proceed with donation in conformance with Reference Standard 5.10A, General Requirements for Biotherapy Product Donors					
5.12.2.3	For donors of mobilized cells (apheresis), a complete blood count obtained within 24 hours before each procurement procedure; for marrow donors, a complete blood count obtained before procurement	N/A	X	N/A	F	10
5.12.4	Confirmation of donor identity, at the time of procurement, by two identifiers	N/A	X	N/A	F	10
5.12.5	Identification numbers and expiration dates of lot numbers of all disposables and additives used in procurement	N/A	X	N/A	F	10
5.12.5, 5.12.6	Complete procurement record; review of procurement record	N/A	X	N/A	F	10
5.13	Definition of procurement goals	N/A	N/A	X	F	10
5.15.1	Medical orders for processing, preservation, or storage	X	X	X	F	10

5.15.2	Complete processing record; verification that acceptable values or ranges for defined critical characteristics for each product were obtained	N/A	N/A	X	F	10
5.15.3	Determination of acceptable values or ranges	N/A	N/A	X	C	10
5.15.4	Procedures used to manage red cell antigen incompatibility	N/A	N/A	X	F	10
5.16	Product-specific specifications and acceptable storage conditions of noncryopreserved products	N/A	N/A	X	C	10
5.17.2.1.1	Segment identification by two individuals	N/A	N/A	X	C	10
5.17.3	Complete cryopreservation records	N/A	N/A	X	F	10
5.18	Stability program for each type of biotherapy product and expiration dates	X	X	X	C	10
5.19	Disposition of products consistent with informed consent and laws and regulations	X	X	X	F	10
5.20.2, 5.20.2.3	Review of donation criteria, final processing criteria, and final product-specified requirements	N/A	N/A	X	F	10

5.21.1	Request for distribution	N/A	N/A	X	C	10
5.21.1	Product distribution	N/A	N/A	X	F	10
5.21.2, 5.26	Review of criteria for receipt	N/A	N/A	X	F	10
5.22	Product return	N/A	N/A	X	F	10
5.23	Product redistribution	N/A	N/A	X	F	10
5.25	Clinical care of the recipient	N/A	N/A	X	F	10
5.25.1.2	Medical orders for administration	X	X	X	F	10
5.26	Preparation of the recipient for administration of the biotherapy product	N/A	N/A	X	F	10
5.29	Confirmation of identity of the product and the intended recipient, using at least two identifiers	N/A	N/A	X	F	10
5.29.3	Identification of adverse events occurring during the infusion of final biotherapy products and communication to the issuing facility	N/A	N/A	X	F	10
5.29.4, 5.29.5	Complete administration record and patient records	N/A	N/A	X	F	10
6.1.2	Document control, including review and approval of all documents before use	X	X	X	C	10
6.1.3	Review and approval of	X	X	X	C	10

	changes to documents					
6.1.4	List of all active policies, processes, procedures, labels, and forms	X	X	X	C	10
6.1.5	Biennial review of each policy, process, or procedure	X	X	X	C	10
6.1.6	Documents that are archived, destroyed, or made obsolete	X	X	X	C	10
6.2.5	Record change	X	X	X	C	10
6.2.7	Verification that copies of records contain the original content and are legible, complete, and accessible before the original records are destroyed	X	X	X	C	10
6.2.10	Review of records for accuracy, completeness, and compliance with applicable standards, laws, and regulations	X	X	X	C	10
6.3	Electronic records	X	X	X	C	10
6.3.1.1.1	Date and identity of person making change(s) to electronic records	X	X	X	C	10
7.1	Deviations	X	X	X	F	10
7.2	Nonconforming products or services	X	X	X	F	10
7.2.4	Nature of nonconformances discovered after release and	X	X	X	F	10

	subsequent actions taken, including acceptance for use					
7.2.4.1	Disposition of the nonconforming product or service	X	X	X	F	10
7.2.5.3	Impact of nonconforming products on purity, potency, safety or efficacy of the product.	X	X	X	F	10
7.2.6.2	Authorized release of nonconforming products	X	X	X	F	10
7.3.3	Detection, reporting, and evaluation of procurement-related donor adverse events	X	X	X	F	10
7.3.4	Detection, reporting, evaluation, and treatment of administration-related recipient adverse events	X	X	X	F	10
7.3.5	Evaluation reported adverse events.	X	X	X	F	10
7.3.6.1	Evaluation and reporting of communicable diseases	X	X	X	F	10
8.1	Internal assessments	X	X	X	C	10
8.2	External assessments	X	X	X	C	10
8.3	Management of assessment results	X	X	X	C	10
8.5	Monitoring of clinical activities	X	X	X	C	10

9.0	Implementation of changes to policies, processes, and procedures resulting from corrective and preventive action	X	X	X	C	10
9.1	Corrective action	X	X	X	F	10
9.2	Preventive action	X	X	X	F	10
10.1.3.1.1	Alarm investigation	X	X	X	C	10
10.1.4, #3	Cleaning or sanitation processes	X	X	X	C	10
10.1.4.1	Environmental monitoring	X	X	X	C	10
10.2	Monitoring of biological, chemical, and radiation safety	X	X	X	C	10
10.3	Appropriate discard of products	X	X	X	C	10

[1]Applicable federal, state, or local law may exceed this period.

QSE 7 – Deviations, Nonconformances, and Adverse Events

Key Concepts

This QSE focuses on the need to ensure capture of, management of, and response to deviations, nonconformances, or adverse events. This also includes the need to maintain records of resolution.

Key Terms

Adverse Event: A complication. Adverse events may occur in relation to organization-defined activities.

Conformance: Fulfillment of requirements. Requirements may be defined by customers, practice standards, regulatory agencies, or law.

Deviation: A departure from policies, processes, procedures, applicable regulations, standards, or specifications.

Disaster: An event (internal, local, or national) that can affect the safety and availability of the organization's products or the safety of individuals.

Near-Miss Event: An unexpected occurrence that did not adversely affect the outcome but could have resulted in a serious adverse event.

Nonconformance: Failure to meet requirements.

Root Cause(s): The underlying cause(s) of an event or nonconformance that, if eliminated, would prevent recurrence.

Traceability: The ability to follow the history of a product or service from source to final distribution or disposition using records.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Records and evaluation of deviations, nonconformances, and adverse events.
- Notification to customer(s) following investigation, if appropriate.
- Records of evidence that measures were taken to ensure deviations, nonconformances, and adverse events do not recur.
- Planned deviation records, if any.
- Records of deviation reporting to appropriate parties [eg, Food and Drug Administration (FDA)].

7.0 Deviations, Nonconformances, and Adverse Events

The organization shall capture, assess, investigate, and monitor failures to meet specified requirements. The responsibility for review and authority for the disposition of nonconformances shall be defined. These events shall be reported in accordance with specified requirements and to outside agencies as required.

✎F7.1 Deviations

The organization shall capture, assess, investigate, and report events that deviate from accepted policies, processes, or procedures. The assessment shall ensure timely and appropriate clinical management of the recipient, if applicable.

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 Nonconformances

Upon discovery, nonconforming products or services shall be evaluated and their disposition determined.

7.2.1 Nonconforming products or services shall be quarantined and/or destroyed.

7.2.2 The unintended distribution or use of products or services that do not conform to specified requirements shall be prevented.

7.2.3 The organization shall:
1) Identify, quarantine, retrieve, recall, and determine the disposition of nonconforming products or services.
2) Identify and manage nonconforming products or services.

✎*F* **7.2.4 Released Nonconforming Products or Services**

Products or services that are determined after release not to conform to specified requirements shall be evaluated to determine the effect of the nonconformance on the quality and/or safety of the product or service.

✎*F* **7.2.4.1** Records shall include the disposition of the nonconforming product or service, the rationale, and the name(s) of the individual(s) responsible for the decision.

7.2.4.1.1 The records shall include a description of nonconformances and any subsequent actions taken.

7.2.5 Product Review, Investigation, and Look-Back

The facility shall identify and manage nonconforming products and the initiation of an investigation, including look-back as applicable, as soon as possible.

7.2.5.1 Customer Notification

The facility shall report to the customer:
1) Any biotherapy products lost, damaged, or otherwise unsuitable for use.
2) Released products or delivered services that are determined to be nonconforming, as soon as possible.

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

*21 CFR 1271.350.

F **7.2.5.3** Customers shall be notified when the nonconforming products can impact the safety, purity, potency, or efficacy of the product.

7.2.6 Review and Disposition of Nonconforming Products and Services

Authority for determining disposition of nonconforming products and review of nonconforming services shall be defined.

7.2.6.1 A nonconforming material or product shall be managed in one of the following ways:
1) Modified to meet the specified requirements.
2) Accepted by the customer, after disclosure of the nonconformance.
3) Relabeled, in conformance with applicable requirements.
4) Destroyed.

F **7.2.6.2 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 relevant medical director and other relevant facility-defined personnel, including a quality representative. Standard 5.20.1 applies.

7.2.6.2.1 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 5.23.1 applies.

7.2.7 Microbially Contaminated Products

The facility shall address the management of biotherapy 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 the recipient's physician.
6) Recipient follow-up and outcome analysis.
7) Reporting to regulatory agencies, if appropriate.

Standard 7.2.6.2 applies.

7.3 Adverse Events

The organization shall detect, monitor, evaluate, manage, and report adverse events related to safety and quality.

7.3.1 Records of adverse events and the related investigations, evaluations, and notifications shall be maintained.

7.3.2 Investigation results and analysis shall be communicated among all facilities involved, if applicable.

✎F **7.3.3** The procurement facility shall have a process to detect, monitor, evaluate, manage, and report donor adverse events.

✎F **7.3.4** The processing facility shall have a process to evaluate reported adverse events.

✎F **7.3.5** The clinical facility shall have a process to detect, monitor, evaluate, manage, and report recipient adverse events related to the biotherapy. Standard 5.28 applies.

7.3.6 Communicable Diseases

✎F **7.3.6.1 Reporting of Communicable Diseases**

The administering facility shall have a defined process to evaluate and report communicable disease transmission by biotherapy products. The process shall include the following (Standard 5.10.2.8 applies):

7.3.6.1.1 Prompt investigation of each event by the appropriate medical director or designee.

7.3.6.1.2 If transmission is confirmed or not ruled out, the identity of the implicated biotherapy product(s) shall be reported to the procurement facility, supplier, or manufacturer.

7.4 Reporting

Reporting of deviations, nonconforming products, and adverse events shall be in accordance with the facility's policies, these *Biotherapies Standards*, and applicable laws and regulations.*

*21 CFR 1271.350.

7.4.1 When more than one facility is responsible for the reporting of deviations, nonconforming products, and adverse events, the responsibility to share results of any subsequent investigation(s) shall be defined by agreement.

Excerpt of Reference Standard 6.2.9A Relevant to Deviations, Nonconformances, and Adverse Events

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/Management Issues	Unit/Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
7.1	Deviations	X	X	X	F	10
7.2	Nonconforming products or services	X	X	X	F	10
7.2.4	Nature of nonconformances discovered after release and subsequent actions taken, including acceptance for use	X	X	X	F	10
7.2.4.1	Disposition of the nonconforming product or service	X	X	X	F	10
7.2.5.3	Impact of nonconforming products on purity, potency, safety, or efficacy of the product	X	X	X	F	10
7.2.6.2	Authorized release of nonconforming products	X	X	X	F	10
7.3.3	Detection, reporting, and evaluation of procurement-related donor adverse events	X	X	X	F	10

7.3.4	Evaluation of reported adverse events	X	X	X	F	10
7.3.5	Detection, reporting, evaluation, and treatment of administration-related recipient adverse events	X	X	X	F	10
7.3.6.1	Evaluation and reporting of communicable diseases	X	X	X	F	10

[1]Applicable federal, state, or local law may exceed this period.

QSE 8 – Internal and External Assessments

Key Concepts

This QSE addresses the organization's internal quality assessment functions as well as processes to support external assessments by accreditors, health authorities, and regulators. This chapter also describes the need for the organization to engage in ongoing quality monitoring and utilization review.

Key Terms

Adverse Event: A complication. Adverse events may occur in relation to organization-defined activities.

Assessment: A systematic examination to determine whether actual activities comply with planned activities, are implemented effectively, and achieve objectives. Types of assessments include external assessments, internal assessments, peer review, and self-assessments.

Competent Authority: The agency responsible under its national law for regulations applicable to the organization.

Conformance: Fulfillment of requirements. Requirements may be defined by customers, practice standards, regulatory agencies, or law.

Corrective Action: Actions taken to address the root cause(s) of an existing nonconformance or other undesirable situation in order to reduce or eliminate recurrence.

Deviation: A departure from policies, processes, procedures, applicable regulations, standards, or specifications.

Nonconformance: Failure to meet requirements.

Preventive Action: An action taken to reduce or eliminate the potential for unexpected deviations, nonconformances, or other undesirable situations.

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.

Root Cause(s): The underlying cause(s) of an event or nonconformance that, if eliminated, would prevent recurrence.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Records of internal assessments scheduled and conducted.
- Records of evidence that deficiencies discovered during assessments and inspections have been addressed, including changes to quality or operational functions.
- Records of external assessments being conducted.

- Quality indicator data collection and review.

8. Internal and External Assessments

8.0 Internal and External Assessments

The organization shall conduct assessments of operations and quality systems.

✎C8.1 Internal Assessments

The organization shall conduct internal assessments. Internal assessments shall be performed by personnel independent of those having direct responsibility for the activity being assessed.

✎C8.2 External Assessments

The organization shall participate in an external assessment program applicable to the activities performed in the organization.

✎C8.3 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.
3) Communicated to the appropriate staff.
4) Reported to executive management.

8.3.1 When corrective action is taken, it shall be developed, implemented, and evaluated in accordance with Chapter 9, Process Improvement.

8.4 Quality Monitoring

The organization shall collect and evaluate quality indicator data on a scheduled basis, including adverse events.

8.4.1 The organization shall provide data generated to the personnel who have responsibility for the quality indicator data collected.

✎C8.5 Monitoring Clinical Activities

Facilities performing clinical activities shall have a program that addresses, evaluates, and monitors patient care practices for all biotherapies. 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) Conformance with peer-reviewed recommendations.
9) Adherence to research protocols or investigator's brochures, if applicable.
10) Critical process points for conformance with policies, processes, procedures, and protocols.

Excerpt of Reference Standard 6.2.9A Relevant to Internal and External Assessments

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/Management Issues	Unit/Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
8.1	Internal assessments	X	X	X	C	10
8.2	External assessments	X	X	X	C	10
8.3	Management of assessment results	X	X	X	C	10
8.5	Monitoring of clinical activities	X	X	X	C	10

[1]Applicable federal, state, or local law may exceed this period.

QSE 9 – Process Improvement

Key Concepts

This QSE focuses on the use of corrective and preventive actions to drive process improvement. It describes measures to ensure that the root causes of nonconformances are effectively addressed.

Key Terms

Adverse Event: A complication. Adverse events may occur in relation to organization-defined activities.

Assessment: A systematic examination to determine whether actual activities comply with planned activities, are implemented effectively, and achieve objectives. Types of assessments include external assessments, internal assessments, peer review, and self-assessments.

Corrective Action: Actions taken to address the root cause(s) of an existing nonconformance or other undesirable situation in order to reduce or eliminate recurrence.

Deviation: A departure from policies, processes, procedures, applicable regulations, standards, or specifications.

Near-Miss Event: An unexpected occurrence that did not adversely affect the outcome but could have resulted in a serious adverse event.

Nonconformance: Failure to meet requirements.

Preventive Action: An action taken to reduce or eliminate the potential for unexpected deviations, nonconformances, or other undesirable situations.

Root Cause(s): The underlying cause(s) of an event or nonconformance that, if eliminated, would prevent recurrence.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Records of collected data analysis and corrective action taken when near-misses, deviations, or adverse events are discovered.
- Tracking of relevant data that affect the organization's current and future operations.
- Records indicating that corrective and preventive action was taken.
- Records indicating that corrective and preventive action taken was effective and is being monitored.
- Documentation that process improvement data are included in executive management review.

9. Process Improvement

C9.0 Process Improvement

The organization shall collect data, perform analysis, and follow up on issues requiring corrective and preventive action, including near-miss events.

F9.1 Corrective Action

The organization shall have a process for corrective action that includes:

1) Description of the event.

2) Investigation of the root cause(s) of nonconformances relating to the product or service, the process, and the quality system.

3) Determination of the corrective action needed to eliminate the cause of nonconformances, as applicable.

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

9.1.1 Investigation and corrective action shall include consideration of deviations, nonconformances, and complaints. Chapter 7, Deviations, Nonconformances, and Adverse Events, applies.

F9.2 Preventive Action

The organization shall have a process for preventive action that includes:

1) Analysis of appropriate sources of information 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.

4) Risk assessment and mitigation strategies at defined intervals.

Standard 1.4 applies.

9.3 Performance Improvement

The organization shall track and identify trends in information related to its operational and quality system performance to identify opportunities for improvement.

9.3.1 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.

Excerpt of Reference Standard 6.2.9A Relevant to Process Improvement

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/Management Issues	Unit/Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
9.0	Implementation of changes to policies, processes, and procedures resulting from corrective and preventive action	X	X	X	C	10
9.1	Corrective action	X	X	X	F	10
9.2	Preventive action	X	X	X	F	10

[1]Applicable federal, state, or local law may exceed this period.

QSE 10 – Facilities and Safety

Key Concepts

This QSE addresses the safety and adequacy of areas where the work required by these Biotherapies Standards is performed. This includes occupational safety, biohazardous material disposal, environmental monitoring, and compliance with applicable local and national regulations.

Key Terms

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.

Executive Management: The highest-level personnel within an organization, including employees, clinical leaders, and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or a group of individuals.

Organization: An institution, or part thereof, that has its own functions and executive management.

Examples of Objective Evidence

- Policies, processes, and procedures related to this chapter.
- Safe environmental conditions for all individuals in the organization.
- Local, state, and national regulations being followed.
- Proper discard of hazardous and potentially hazardous materials.
- Personal protective equipment (PPE) is available and in use.

10. Facilities and Safety

10.0 Facilities and Safety

The organization shall ensure safe environmental conditions. The work area shall be suitable for the activities performed. Safety programs shall meet local, state, and national regulations.

10.1 Safe Environment

The organization shall minimize and respond to environmentally related risks to the health and safety of all individuals and products or services. Suitable quarters, environment, and equipment shall be available to maintain safe operations.

10.1.1 Policies, processes, and procedures shall identify and take appropriate intervention to limit exposure to hazards present in the facility including, but not limited to:
1)Biological,
2) Chemical, and,
3) Radiation safety, if applicable.

10.1.1.1 The facility shall maintain a system for monitoring exposures and for minimizing potential exposure to hazards.

10.1.2 Biohazardous materials shall be handled and discarded in a manner that minimizes the potential for human exposure to infectious agents.

10.1.3 Where liquid nitrogen is present, specific hazards shall be addressed.

10.1.3.1 The facility shall have a system in place to monitor oxygen levels and an alarm system set to activate under conditions that will allow action to be taken.

C **10.1.3.1.1** Alarm activation shall require personnel to investigate and document the condition activating the alarm and to take immediate corrective action as necessary.

10.1.4 Environmental Controls
The facility shall design, approve, and implement an environmental control system that:
1) Optimizes donor, recipient, and employee safety.
2) Ensures product integrity and safety.
C 3) Monitors cleaning or sanitation processes to minimize and mitigate contamination or accidental exposure to infectious disease agents.

C **10.1.4.1** The degree of environmental monitoring and controls shall be specific to the biotherapy product manipulation performed.

10.1.5 The clinical facility shall have either on-site or ready access to services, resources, and personnel to manage anticipated adverse events and provide emergency medical care.

C10.2 Biological, Chemical, and Radiation Safety

The organization shall monitor adherence to biological, chemical, and radiation safety standards and regulations.

C10.3 Handling and Discarding of Biological Materials

Biological materials shall be handled and discarded in a manner that minimizes the potential for human exposure to infectious agents.

10.4 General Operational Controls

Access to facilities used for procurement, processing, preservation, and storage shall be limited to authorized individuals.

Excerpt of Reference Standard 6.2.9A Relevant to Facilities and Safety

Standard	Record to Be Maintained	Quality System Records	Donor Eligibility/Management Issues	Unit/Recipient	Retention after Creation (C) or Final Disposition (F) of Related Product	Minimum Retention Time (in years)[1]
10.1.3.1.1	Alarm investigation	X	X	X	C	10
10.1.4, #3	Cleaning or sanitation processes	X	X	X	C	10
10.1.4.1	Environmental monitoring	X	X	X	C	10
10.2	Monitoring of biological, chemical, and radiation safety	X	X	X	C	10
10.3	Appropriate discard of products	X	X	X	C	10

[1]Applicable federal, state, or local law may exceed this period.

GLOSSARY

Active Labor: A period characterized by regular painful uterine contractions, a substantial degree of cervical effacement, and more rapid cervical dilatation from 5 cm until full dilatation for first and subsequent labors.

Administration: With respect to biotherapy products, the act of delivering the product into a recipient, including, but not limited to, infusion, transplantation, implantation, or injection.

Adverse Event: A complication. Adverse events may occur in relation to organization-defined activities.

Advocacy: A service whereby an impartial individual or a team who has/have working knowledge of biotherapy and whose interest is centered on the well-being of the subject speaks on the subject's behalf. The subject could be a donor or recipient. The service helps the subject understand the process, procedures, and the potential risks or benefits.

Agreement: A contract, order, or understanding between two or more parties, such as between an organization and one of its customers.

Agreement Review: Systematic activities carried out before finalizing the agreement to ensure that requirements are adequately defined, free from ambiguity, documented, and achievable.

Allogeneic Donor: An individual from whom biotherapy 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 examination to determine whether actual activities comply with planned activities, are implemented effectively, and achieve objectives. Types of assessments include external assessments, internal assessments, peer review, and self-assessments.

Attributes: Additional characteristics that uniquely define a biotherapy 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: An individual who acts as their own biotherapy product(s) donor.

Backup: Digital data and/or physical storage containing copies of relevant data.

Bacteremia: Systemic inflammatory response due to an infectious agent and accompanied by characteristic clinical and laboratory findings.

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

Biologic Agent: A substance that is made from a living organism or its products and is used in the prevention, diagnosis, or treatment of diseases.

Biotherapies: For the purposes of these Standards, biotherapies are products derived from cells or tissues that may be unmanipulated, manipulated, or manufactured and are intended for therapeutic use in accordance with applicable requirements of the appropriate Competent Authority. These Standards may also apply to cellular starting materials, intermediate products, and materials intended for nonclinical research that support the development of these therapies.

By-Products: Portions of the original biotherapy product (eg, cells, tissues or organs) retained for further use.

Cadaveric Donor: A deceased donor from whom biotherapy products (eg, cells, tissues, or organs) or organs are procured.

Calibrate: To set or align measurement equipment against a known standard.

Cellular Starting Material (CSM): Initial or raw biological material from cells, tissue, or organs that may be further manipulated through various techniques such as processing, selection, expansion, gene editing, and other combinations of engineering for therapeutic benefit.

Certified by Centers for Medicare and Medicaid Services (CMS): Having met the requirements of the Clinical Laboratory Improvement Amendments of 1988 through inspection by the CMS, a deemed organization, or an exempt state agency.

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

Chain of Identity (COI): The permanent and transparent association of a biotherapy's unique identifiers from procurement of cells, tissues or organs throughout the full product(s) lifecycle, including posttreatment monitoring.

Change Control: A structured method of revising a policy, process, or procedure, including hardware or software design, transition planning, and revisions to all related documents.

Characterization: A process by which the molecular, physical, and/or functional attribute(s) of cells, tissues, or organs are defined.

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 Biotherapy Products: Products that come from two or more different sources.

Competence: An individual's demonstrated ability to apply knowledge and skills needed to perform their job tasks and responsibilities.

Competent Authority: The agency responsible under its national law for regulations applicable to the organization.

Completion of Processing: The point in processing at which no further actions are required to be taken in connection with a biotherapy product before it is placed into storage.

Compliance: See Conformance.

Compliance (Biotherapy Standards): The act of adhering to regulatory requirements.

Confidentiality: The protection of private, sensitive, or trusted information resources from unauthorized access or disclosure.

Conformance: Fulfillment of requirements. Requirements may be defined by customers, practice standards, regulatory agencies, or law.

Consenter(s): Individual(s) whose consent is obtained for the procurement of biotherapy products. For cord blood or gestational material procurement, this may include, but is not limited to, the neonatal donor's gestational parent, genetic parent, gestational surrogate, 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 biological matter.

Continuing Education: Ongoing adult learning and training after initial qualification/education has been granted. Relevant continuing education consists of educational activities related to the activities performed at the facility that serve to enhance professional development related to the job functions by maintaining, developing, or increasing, the knowledge and skills of an individual.

Continuing Medical Education: Ongoing adult learning and training after completion of medical training. Continuing medical education is received from an accredited organization with the goal of maintaining competency or increasing the knowledge, skills, and professional abilities that a physician uses to provide services in the relevant field of work.

Continuous Monitoring: Uninterrupted 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: 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 blood that is collected.

Corrective Action: Actions taken to address the root cause(s) of an existing nonconformance or other undesirable situation in order to reduce or eliminate recurrence.

Critical Equipment/Materials/Tasks: A piece of equipment, material, service, or task that can affect the quality of the organization's products or services.

Cryopreservation: The process of freezing and storage of biotherapy products at low temperature in the presence of a cryoprotectant to preserve their key critical characteristics.

Cryoprotectant: A solution or additive that, when combined with living cells, provides protection from damage otherwise induced by the freezing and/or thaw 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 recipient of a product or service. A customer may be internal (eg, another organizational unit within the same organization) or external (eg, a patient, client, donor, or another organization).

Data Integrity: The accuracy, completeness, and consistency of information.

Designee: An individual with appropriate experience or expertise who is given the authority to assume a specific responsibility and who is not the primary individual responsible by job description.

Deviation: A departure from policies, processes, procedures, applicable regulations, standards, or specifications.

Disaster: An event (internal, local, or national) that can affect the safety and availability of the organization's products or the safety of individuals.

Disposition: For biotherapy products, the status or control of a biotherapy product in a given facility. For records, disposition occurs at the end of their retention period.

Distribution: The transportation or shipment of a biotherapy product or its precursor that meets facility defined release criteria, or urgent medical need as applicable.

Distributing Facility: The facility that distributes the biotherapy product or its precursor for further manufacturing, storage, or clinical use.

Document (noun): Written or electronically generated information and work instructions. Examples of documents include quality manuals, procedures, or forms.

Document (verb): To capture information through writing or electronic media.

Donation Identification Number (DIN): A 13-character code that identifies products from a single donation event that allows each event to be uniquely identified. The DIN contains three elements: the five-character alphanumeric facility identification number (FIN), the two digit year the DIN was assigned, and the six digit sequence number.

Donor: A living or deceased person who is the source of a biotherapy 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 biotherapy facility to potential donors, patients, and others, including, but not limited to, therapeutic benefit claims on the facility's website, in 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, and benefits of the donation, as well as alternatives to the donation of the product.

Eligibility: With respect to donors, the evaluation for risk factors for 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 Donor). Alternatively, the determination may be incomplete (eg, screening is incomplete or donor testing is not performed in a time frame specified by the test kit manufacturer's instructions).

Emergency Management: Strategies and specific activities designed to manage situations in which there is a significant disruption to organization operations or a significantly increased demand for the organization's products or services.

Engraftment: The reconstitution of recipient hematopoiesis with white cells, RBCs, 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 identification of 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.

Establish: To perform all of the activities required to plan, validate, and implement a system or process.

Exception: An action or condition that is not part of normal operations.

Executive Management: The highest-level personnel within an organization, including employees, clinical leaders, and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or a group of individuals.

Facility: A location or operational area within an organization. The part of the organization that is assessed by the AABB and receives AABB accreditation for its specific activities.

Final Biotherapy Product: A biotherapy product that is ready for distribution.

Final Disposition: The terminal status of the product after which no further action can be taken (eg, discard or infusion).

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 biotherapy product that can be qualitatively or quantitatively evaluated (eg, by in-vitro or in-vivo assays).

Genetic Parent: The person who is the source of the ovum.

Gestational Materials: Any tissue procured at or near the time of birth (eg, umbilical cord tissue, placental tissue, amniotic fluid).

Gestational Parent: The person carrying the fetus to term.

Gestational Surrogate: The person who carries the fertilized ovum of another person.

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 biotherapy).

Handling: The various operations involved in the preparation, processing, and movement of materials and products. This includes actions such as receiving, transporting, shipping, unpacking, sorting, and preparing items for manufacturing or further distribution.

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).

Human Subject Research: Refers to any study, investigation, or experiment that involves the collection, use, analysis, or dissemination of data obtained from living individuals.

Identity: A set of factors that distinguishes one product from another. For biotherapy products, identity is often stated in terms of specific positive and negative markers expressed by the cells.

In-House Reagents: See Reagent.

In-Process Label: A label used to identify a biotherapy product at any intermediate processing step when a full label cannot be used due to space or size limitations.

In Vitro: Biological or chemical processes that are performed outside a living organism.

In Vivo: Biological or chemical processes that are performed inside a living organism.

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 international) consisting of medical professionals and nonmedical members. The group is responsible for ensuring the protection of the rights, safety, and well-being of human subjects involved in a trial and to provide public assurance of that protection by reviewing and approving and/or providing professional opinion on a trial protocol, including the suitability of investigator(s), facilities, and the methods and materials used in recruiting participants and obtaining and documenting informed consent of the trial subjects. The legal status, composition, function, operations, and regulatory requirements pertaining to independent ethics committees may differ between countries, but the independent ethics committee should promote good clinical practice.

Ineligible Donor: A designation applied to a donor whose product may be at risk of transmitting an infectious disease as detected by donor testing and/or donor screening.

Information System Life-Cycle Requirements: The stages and time span from initial planning of an information system software program to its retirement; that is, from concept, to software development, to business changes, to revisions, to retirement.

Inner Shipping Container: A box, container, or bag that holds a labeled product during shipping inside an outer shipping container.

Inspect: To measure, examine, or test one or more characteristics of a product or service and compare results with specific requirements.

Installation Qualification: Verification that the correct equipment is received and that it is installed according to specifications and the manufacturer's recommendations in an environment suitable for its operation and use.

Intermediate Facility: Any facility other than the procurement facility and administering facility that manipulates or performs any activity covered by these Biotherapies Standards.

Investigator's Brochure: A compilation of clinical and nonclinical data about the investigational biotherapy product(s) used in research of human subjects. It describes the product's formulation and effects, including information related to 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 biotherapy product consisting of partially purified pancreatic islets of Langerhans. Insulin-producing beta cells within such islets make up the functional component of the product.

Key Quality Functions: Essential job functions that affect the services provided by the organization.

Label: An inscription affixed or attached to a product for identification.

Label (Accompanying): Product information that 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 the product, which may include content, identification, description of processes, storage requirements, expiration date, cautionary statements, 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 biotherapy service.

Laboratory Medical Director: A qualified licensed physician who has overall responsibility and authority for all medical aspects of the biotherapy service.

Legal Custodian: A person legally responsible for the donor until the donor's age of majority.

Leukocyte-Rich Products: Leukocyte-rich products are products that contain a high number of leukocytes/white blood cells. They are defined at the time of collection/procurement, even if later processing might remove leukocytes.

Look-Back: The process of reviewing and, if necessary, removing from inventory any product that is potentially infectious or nonconforming.

Maintain: To keep in the current state; to preserve or retain; to keep in a state of validity.

Manufacture: All steps in the preparation and testing of a biotherapy product, from donor evaluation to making the product available for distribution.

Master List of Documents: A reference list, record, or repository of an organization's policies, processes, procedures, forms, and labels related to the Biotherapies Standards, including information for document control.

Material: A supply item used in a process or procedure.

Medical Suitability: Refers to the health status of an individual to donate or receive a product.

Medical Therapy: The direct provision of a medical intervention ordered by a physician (eg, harvest of hematopoietic progenitor cells by apheresis for reinfusion to the autologous donor/patient, administration of a pharmaceutical agent to a patient, or administration of a biotherapy product).

Myeloablative Therapy: Treatment of a patient with an agent (eg, chemotherapy or gamma irradiation) that causes irreversible marrow aplasia.

Near-Miss Event: An unexpected occurrence that did not adversely affect the outcome but could have resulted in a serious adverse event.

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.

Offsite Location: A location that is not within the same contiguous building as the facility's primary site of activity, physical storage facility, or electronically supported storage medium that provides reliable redundancy of data.

Operational Qualification: Verification that equipment will function according to the operational specifications provided by the manufacturer.

Operational Systems: Processes, resources, and activities that work together to result in a product or service.

Organization: An institution, or a location or operational area within that organization; the entity assessed by the AABB and receiving AABB accreditation for specific activities.

Outer Shipping Container: A container made of material adequate to withstand leakage of contents, impact shocks, pressure changes, temperature changes, puncture, and other conditions incident to ordinary handling.

Output: The product, information, or service that results from performing a process or procedure.

Parties: Entities or individuals who have entered into an agreement.

Patient: An individual undergoing medical care. The individual may also be a research subject.

Patient-Specific Product: A product collected and/or prepared exclusively for a particular autologous or allogeneic recipient.

Performance Qualification: Verification that equipment performs consistently as expected for its intended use in the organization's environment, using the organization's procedures and supplies.

Policy: A set of basic principles or guidelines that direct or restrict the organization's plans, actions, and decisions.

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

Preparative Regimen: Any regimen of immunosuppressive and/or myelosuppressive chemotherapeutic agents and/or radiation therapy that is given to prepare the recipient before the administration of a biotherapy product.

Preventive Action: An action taken to reduce or eliminate the potential for unexpected deviations, nonconformances, or other undesirable situations.

Procedure: A defined series of tasks and instructions that specify how an activity is to be performed.

Process: A set of related activities that transform inputs into outputs.

Process Control: Activities designed to ensure that processes are stable and consistently operate within acceptable limits of variation in order to produce predictable output that meets specifications.

Processing: Any activity performed on a biotherapy product, other than recovery, donor screening, donor testing, storage, labeling, packaging, or distribution. Such processing activities include testing for microorganisms, preparation, sterilization, steps to inactivate or remove adventitious agents, preservation for storage, and removal from storage.

Processing Facility: The facility involved in receipt of the product from the procurement facility. The processing facility may perform further manufacturing, testing, and/or distribution of the product.

Procurement: The act of obtaining a biotherapy product(s) or cellular starting material from a donor by facility-approved methods, including, but not limited to, apheresis, marrow harvest, cord blood or gestational material collection, or organ or tissue harvesting from a donor.

Procurement-Associated Intervention: Any event intended to assist with the procurement of a biotherapy 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 biotherapy products or a facility that ensures, through agreements, that one or more of these activities is/are performed in conformance with these Biotherapies Standards.

Procurement Goal: The desired outcome of the procurement process.

Product: A tangible output from a process.

Product Code: An eight-character ISBT 128 code that comprises the five-character product description code, the one-character collection type code, and the two-character division code.

Proficiency Testing: The structured external evaluation of laboratory methods that assesses the performance of the test system.

Protected Health Information (PHI): Individually identifiable health information that can be linked to a particular person that is related to the physical or mental health status, type of health-care provided, or

payment for the health-care provided. Common identifiers of health information include names, social security numbers, addresses, and birth dates. PHI can be in electronic, oral, or written format.

Purity: Dominance of a targeted cellular population defined by specific cell markers and with minimal to no contamination of cells negative for the same markers.

Qualification (equipment or suppliers): A documented process of verifying that equipment and/or systems are properly installed, function as intended, and are fit for their designated use.

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 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 US FDA or relevant Competent Authority.

Quality: Characteristics of a product or service that bear on its ability to fulfill customer expectations. The measurable or verifiable aspects of a product or service that can be used to determine if requirements have been met.

Quality Control: Testing routinely performed on materials 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 executive 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 Management System: The organizational structure, responsibilities, policies, processes, procedures, and resources established by executive management to achieve quality.

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.

Quarantine: Storage of biotherapy products, reagents, or materials, in order to prevent improper release and/or cross contamination, either in a physically separate area clearly identified for such use, or by identification of a product through the use of other procedures, including automated designation, for the same purpose.

Reagent: A substance used to perform an analytical or manufacturing procedure. A substance used (as in detecting or measuring a component or preparing a product) because of its biological or chemical activity. Reagents can be either purchased ready for use or prepared within the facility (in-house).

Receiving Facility: A facility receiving products or services.

Recipient: The patient receiving a biotherapy product.

Record (noun): Information captured in writing or through electronically generated media 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 and documented.

Record (verb): To capture information for use in records through writing or electronic media.

Reference Sample: A sample collected from a donor or product that is retained and used for future testing to establish identity, compatibility, or quality of the product.

Reference Standard: Specified requirements defined by the AABB. Reference standards define how or within what parameters an activity shall be performed and are more detailed than quality system requirements.

Registry: An organization that maintains a database of biotherapy donors or products and coordinates the acquisition of biotherapy products for transplantation or implantation.

Regulation: Rules promulgated by federal, national, state, or local authorities to implement laws enacted by legislative bodies.

Regulatory Enforcement Action: Measures taken by a Competent Authority that include, but are not limited to, progressive measures (eg, suspension or termination of operations, information notices requiring specific documentation or data, fines incurred) or action based on critical triggers (eg, pattern of recurrent, unresolved issues, deficiencies in risk management systems).

Release: Removal of a product from quarantine or in-process status for the purpose of distribution.

Risk: The threat of quantifiable damage or any other negative occurrence that is caused by external or internal vulnerabilities and that may be avoided through preemptive action.

Root Cause(s): The underlying cause(s) of an event or nonconformance that, if eliminated, would prevent recurrence.

Service (noun): An intangible output of a process.

Service (verb): An action that leads to the creation of a product or a result that can affect donors, patients, and/or recipients.

Shall: A term used to indicate a requirement.

Shipping: The physical act of transferring a biotherapy product within or between facilities. During shipping, the product is not under 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: Any requirements in these Biotherapies Standards, including, but not limited to, FDA requirements; requirements of a facility's internal policies, processes, and procedures; manufacturers' instructions; customer agreements; practice standards; and requirements of accrediting organizations such as the 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 biotherapy 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.

Stakeholder: An individual, group, or organization that has an interest or concern in activities performed by a facility accredited by AABB, or as defined through an agreement of two or more parties.

Standard: A set of specified requirements upon which an organization 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: Being free of living microorganisms.

Storage: The state of being kept in a place while not being used or transferred, shipped, or transported.

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

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

Summary of Records: A condensed version of the required testing and screening records that contains the identity of the testing laboratory, the listing and interpretation of all required infectious disease tests, a listing of the documents reviewed as part of the relevant medical records, and the name of the person or establishment determining the suitability of the human tissue for transplantation.

Supplier: An entity that provides a material, product, or service.

Supplier Qualification: Evaluation of a potential supplier to assess its ability to consistently deliver products or services that meet specified requirements.

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 forms a functional unit and, in the context of biotherapy, is intended for transplantation or implantation.

Total Nucleated Cell (TNC) Count: The total number of nucleated cells in a volume of a biotherapy product. Nucleated cells include white blood cell (WBC) populations such as neutrophils, monocytes, lymphocytes, eosinophils, and basophils, and nucleated red blood cells (NRBCs). The TNC count is

calculated by the following formula: TNC = (WBCs + NRBCs) × volume. The contribution of NRBCs, if any, should be separately noted.

Traceability: The ability to follow the history of a product or service from source to final distribution or disposition using records.

Transfer: The act of relocating a final biotherapy product or its intermediate in-process precursors.

Transport: The physical act of transferring a biotherapy product within or between facilities. During transport, the product remains under the control of trained personnel at the originating or receiving facility.

Unanticipated Event: Unplanned occurrences that can cause serious injury or harm, or death, to an individual resulting from a deviation(s).

Urgent Medical Need: No comparable biotherapy product is available and the recipient is likely to suffer death or serious illness without receiving the biotherapy product.

Validation: Establishing evidence that a process, executed by users in their environment, will consistently meet predetermined specifications.

Verification: Confirmation by examination and provision of objective evidence that specified requirements have been met.

Viability: The measurement of living cells.

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.

QUICK REFERENCE

Abbreviations Used

CBC	Complete blood count
CFR	Code of Federal Regulations (United States)
CJD	Creutzfeldt-Jakob disease
CLIA	Clinical Laboratory Improvement Amendments of 1988
CMS	Centers for Medicare and Medicaid Services
CMV	Cytomegalovirus
EBMT	European Group for Blood and Marrow Transplantation
FACT	Foundation for the Accreditation of Cellular Therapy
FDA	Food and Drug Administration
HBc	Hepatitis B core antigen
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCT/Ps	Human cells, tissues, and cellular and tissue-based products
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HIV-1-Ag	Human immunodeficiency virus (type 1) antigen
HPC	Hematopoietic progenitor cells
HPC(A)	HPC, Apheresis
HPC(CB)	HPC, Cord Blood
HPC(M)	HPC, Marrow
HTLV	Human T-cell lymphotropic virus
IDE	Investigational device exemption
IND	Investigational new drug
IRB	Institutional Review Board
ISBT	International Society of Blood Transfusion
ISCT	International Society for Cellular Therapy
JACIE	Joint Accreditation Committee—ISCT and EBMT
NRBCs	Nucleated red blood cells
TC	Therapeutic cells
TSE	Transmissible spongiform encephalopathy
WNV	West Nile virus