

Standards for

Hematopoietic Progenitor Cell and Cellular Product Services

THIRD EDITION

aa AMERICAN
BB ASSOCIATION
OF BLOOD BANKS

**Standards for Hematopoietic
Progenitor Cell and Cellular
Product Services**

3rd edition

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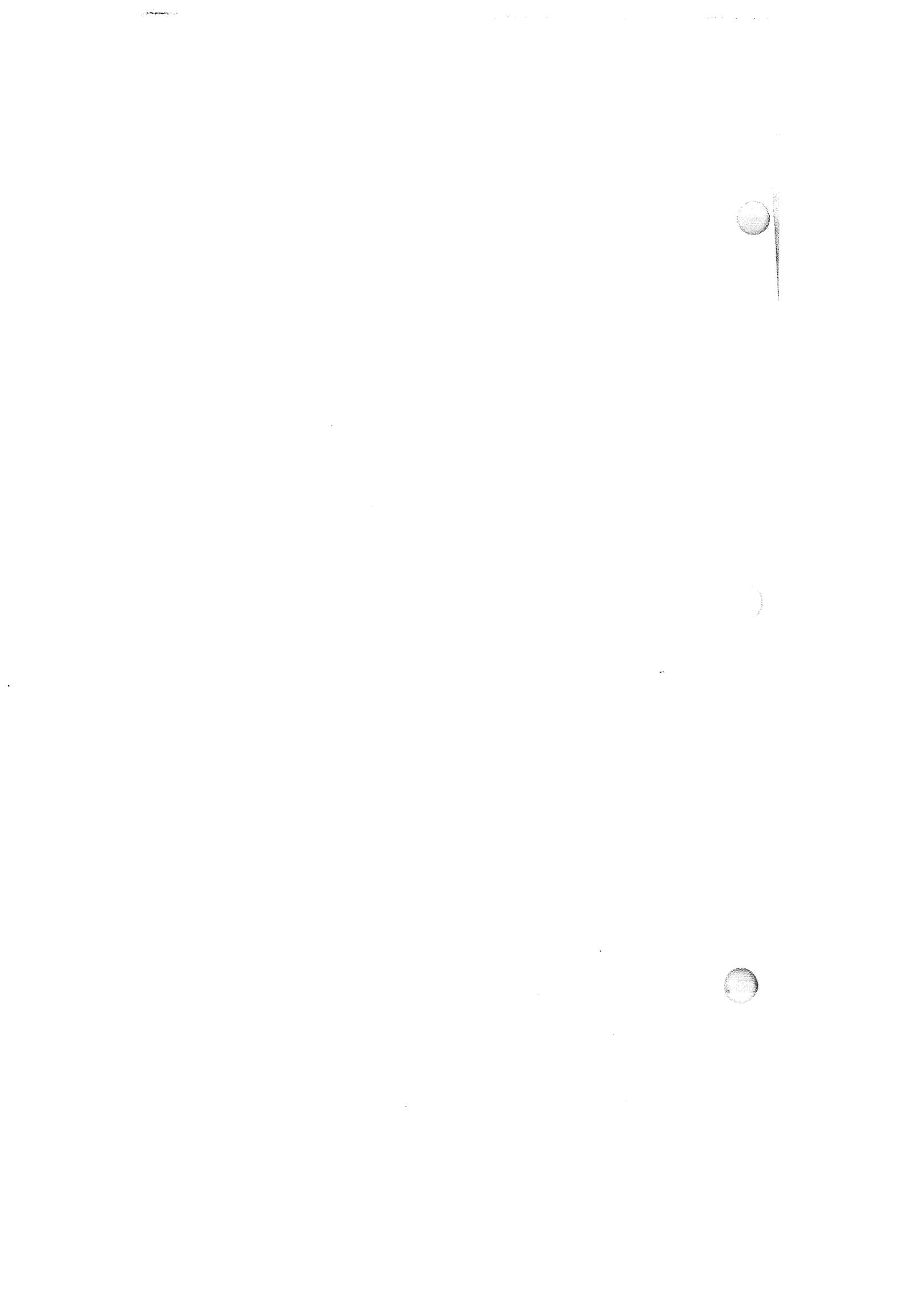
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PREFACE

These *Standards for Hematopoietic Progenitor Cell and Cellular Product Services* have been prepared by the Hematopoietic Progenitor Cell and Cellular Product Services Standards Program Unit (HPC SPU), the Quality Management Subcommittee (QMS), and the Standards Program Committee (SPC) of the American Association of Blood Banks (AABB) to maintain and enhance the quality and safety of services provided by hematopoietic progenitor cell (HPC) and cellular product services and to provide a basis for the accreditation program of the Association. The effective date of this 3rd edition, for purposes of the activities of the AABB, is May 1, 2002.

This 3rd edition of *Standards for Hematopoietic Progenitor Cell and Cellular Product Services (HPC and Cellular Product Standards)* has been broadened in its name and in its scope. With the addition of cellular products, these standards now encompass a larger portion of a new and expanding field.

The Food and Drug Administration published a proposed rule on January 8, 2001, titled "Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products." The good tissue practice (GTP) requirements were considered in the development of these *HPC and Cellular Product Standards*. The HPC SPU incorporated requirements derived from the GTP document that were considered to reflect a desirable standard of care.

While many aspects of the *HPC and Cellular Product Standards* have not been changed, the HPC SPU wishes to inform readers of the following key revisions in the certain specific chapters.

Section 3—Agreement Review. Standard 3.7, Tracing and Tracking, is new and it requires that facilities be able to trace and track the cellular product from the point of collection until that of administration. While the requirement for traceability of the product is not new, the requirement for an agreement to ensure traceability is. Also, a new Reference Standard 3R-A, Informed Consent for Cellular Collection Procedure, has been added. Reference Standard 3R-A is consistent with the

Standards for Cord Blood Services, 1st edition, and articulates the process of informed consent for donor or the donor's legally authorized representative.

Section 9—Process Control. Due to the fact that Section 9 contains a majority of the technical and operational requirements, there are many new and revised standards in this section. Standard 9.2, Equipment, has been added, with the purpose of providing clarity to the selection of equipment used in collection or processing. Standard 9.2.2 has been added and addresses the need to ensure the cleanliness of and scheduled preventive maintenance for all critical equipment. While this was implied in previous editions, the HPC SPU felt it would be best to specifically include it in this edition. The control of the inspection, measuring, and testing equipment is addressed in Section 11. With this new edition, changes have been made to the reference standards, particularly the consolidation of both related and unrelated allogeneic donor qualification requirements into a single Reference Standard, 9R-B. Also new to both Reference Standards 9R-A and 9R-B is the deletion of the requirement that all donor-patients of childbearing potential be tested for pregnancy within 72 hours prior to initiation of hematopoietic growth factor administration, or myeloablative therapy. The standard now merely states that a pregnancy assessment must be performed without prescribing a timeframe. Finally, Reference Standard 9R-C, Processing Tests, has been updated with the addition of four new tests to be performed on each cellular product. These tests include a relevant cell count, antigen expression analysis appropriate for the cellular product, test(s) for cell viability, and test(s) for product sterility.

Section 11—Control of Equipment. While this section did not undergo many changes content-wise, the format has changed to better articulate the meaning and scope of the requirements in this section. The change of format for this section runs in accordance with the creation of Standards 9.2, 9.2.1, 9.2.2, and 9.2.3. As stated above, the purpose of Section 9 is to define the criteria by which an HPC facility selects and qualifies its equipment, whereas Section 11 is designed to ensure validation and calibration of equipment within the facility. This section also ad-

dresses the control and use of equipment used for inspection, measuring, and testing of specific equipment. Standard 11.2.1, Equipment Malfunction, has been added. The standard requires that records of all malfunctions and any associated corrective actions be maintained, in conformance with Section 16, Control of Records.

Section 13—Deviations and Nonconforming Products and Services. Standard 13.1.2, Review and Disposition of Nonconforming Materials and Products, has been significantly revised since the last edition. The standard now requires that all nonconformances deemed to affect quality be reported to the recipient's physician, as well as any facility that may have received the nonconforming cellular product. Also, all records of such nonconforming activities, including the actions taken or the acceptance for use, have to be maintained in accordance with Section 16, Control of Records. A new Standard, 13.4.2, concerning adverse events, has been added. Administering facilities must have a process for the notification of the collection or processing service when an adverse event relating to any kind of product failure occurs.

Section 16—Control of Records. The majority of changes to this section reflect the changes in language throughout the rest of the *HPC and Cellular Product Standards*. Reference Standard 16R-A has been changed to allow for records to be retained for 10 years after the transplantation or final disposition of the HPC or cellular product. The previous retention time had been indefinite. This has been changed in accordance with the GTP requirements, which only require a maximum record retention of 10 years after transplantation or disposition of the product for retention.

This is a very visible and rapidly changing field of medicine. As the use of cellular therapies becomes more prominent in hospitals and clinics around the country, standards to provide a quality framework for collecting and processing of cellular products are needed to keep pace with the developments of these highly innovative treatments. The committee has broadened the focus of these *HPC and Cellular Product Standards* to include general requirements for cells from many sources, instead of focusing solely on peripheral blood progenitor cells.

Preface

From a personal point of view, I want to express my deep appreciation to the program unit members and liaisons for their expertise, diligence, and commitment to producing standards for this emerging field.

N. Rebecca Haley, MD
Chair, Hematopoietic Progenitor Cell Standards Program Unit

INTRODUCTION

The Standards Program Committee (SPC) is an umbrella committee whose primary role is to oversee the creation, development, and revision of all AABB standards to ensure harmonization and consistency in AABB's standard-setting activities. The SPC consists of the chair, the Quality Management Subcommittee (QMS), and specialty program units, such as the Hematopoietic Progenitor Cell Standards Program Unit (HPC SPU). The QMS ensures that all quality management concepts incorporate a consistent message. The standards program units are responsible for creating technical standards based on a review of current scientific and medical data, when available. The subcommittees and program units work together to ensure that the format and content of the *HPC and Cellular Product Standards*, particularly as it relates to quality management concepts, is consistent with the goals of the AABB.

This 3rd edition of *Standards for Hematopoietic Progenitor Cell and Cellular Product Services*, developed by the HPC SPU, is based on input from a variety of sources, including member comments, a public member on the program unit, and recognized experts in progenitor cell and cellular product collection and processing. These standards have been developed on the basis of good medical practice and, when available, scientific data.

These standards outline the elements that must be covered in a comprehensive quality plan to provide the necessary requirements for operating an accredited hematopoietic progenitor cell and cellular product service. This includes the establishment and maintenance of a quality system and additional technical policies, processes, and procedures to address requirements such as those for the qualification and training of personnel, the management of agreement reviews, proper document and record control, and design review (including, for example, a responsible change control mechanism). The goal of the standards is to ensure quality in the care of the patient or donor and the proper control of safeguards necessary for the provision of HPCs and cellular products that can be used with confidence by the recipient's physician.

For the purposes of this publication, an HPC and cellular product service qualifies donors and collects, processes, stores, and distributes HPCs and cellular products for medical procedures such as marrow transplantation and cellular therapy for disease. While the requirements address the interface between the collecting/processing and transplanting facilities, they do not specifically address the transplantation of HPCs or cellular products. There is an appropriate overlap of concern for patient protection in this interface; however, the transplanting facility should have additional policies, processes, and procedures to address the safety of the patient and to ensure the appropriate use of the HPC or cellular product.

The *HPC and Cellular Product Standards* represents accepted minimum requirements that may be exceeded in practice. Many organizations working in special situations can, and should, be more rigorous in their internal requirements. Urgent medical conditions may warrant abbreviations of practices required by these *HPC and Cellular Product Standards*; records of the need to do so must be maintained.

The majority of the *HPC and Cellular Product Standards* is in compliance with existing applicable federal laws and requirements. However, no assurances can be given that compliance with these standards will result in compliance with all applicable laws and regulations (federal, state, or local). HPC services must take all steps necessary to ensure compliance with all applicable laws and regulations.

Alternative methods or approaches that deviate from these standards require written approval of a variance or exemption by the HPC SPU. Requests for a variance or exemption should be submitted to the HPC SPU through the AABB National Office with supporting data. The program unit will review the request and report its decision to the submitting laboratory. If a laboratory disagrees with the decision, it may appeal the decision to the Standards Review Committee.

Investigative studies may necessitate deviation from these standards. Such studies must be performed under the direction of qualified individuals with consideration for the therapeutic requirements of the patient and the safety of the patient, donor, and facility personnel. When possible, such modifications should not supplant or eliminate the requirements of

these *HPC and Cellular Product Standards*. Scientific studies that modify or replace these requirements must be approved by the appropriate Institutional Review Board for the Protection of Human Subjects.

The guiding principle of this document is to be consistent with available scientific information. The program unit endeavored to make the requirements simple, clear, practical, and helpful, rather than restrictive. The use of these *HPC and Cellular Product Standards* should aid in developing and maintaining processes and procedures that will provide safe and effective transplantation, as well as a safe work environment for laboratory personnel.

“Notes” and “Reference Standards” have been retained for this edition. Notes are meant to be explanatory, giving the setting or scope in which the standard’s requirements are considered. On the other hand, reference standards are very specific technical standards, often in a chart format, that address “how” a requirement is to be met. All requirements—whether in paragraph, list, or chart format—are of equal importance. From a practical point of view, it is anticipated that from edition to edition of these *HPC and Cellular Product Standards*, the reference standards will be revised most often, while the more general standards will change with less frequency. Throughout the text, the reader is referred to the end of each section, where the reference standards are located. For example, 9R-B refers to Section 9, Process Control, and is the second reference standard in this section.

A glossary is also included, with terms defined to reflect usage in the context of the *HPC and Cellular Product Standards*, rather than general usage. Terms listed in the glossary are underscored when first used in the text. As stated in the glossary, the word “shall” is used to indicate a mandatory requirement and describes the single acceptable activity or method; all standards are requirements, and failures to meet a specified requirement constitutes a nonconformance under the accreditation program of the AABB.



1. MANAGEMENT RESPONSIBILITY

1.1 **Quality Policy**

The hematopoietic progenitor cell and cellular product service's (hereinafter, "HPC and cellular product service") executive management shall define and document the HPC and cellular product service's policy for achieving and maintaining quality in donor selection, collection, processing, storage, distribution, and administration and/or the provision of services (hereinafter, "the collection, processing, storage, distribution, and administration of HPCs and cellular products and the provision of related services"). The quality policy shall describe the HPC and cellular product service's objectives for quality and its commitments to quality. The HPC and cellular product service's executive management shall ensure that this quality policy is understood, implemented, and maintained at all levels of the organization.

1.2 **Organization**

1.2.1 **Responsibility and Authority**

The HPC and cellular product service shall define and document the responsibility, authority, and relationship of personnel who perform, verify, or manage work covered by these *Standards for Hematopoietic Progenitor Cell and Cellular Product Services (HPC and Cellular Product Standards)*, particularly for personnel who:

- 1) Ensure that the collection, processing, storage, distribution, and administration of HPCs and cellular products and services conform to specified requirements (see Section 2.1, General).
- 2) Identify, and maintain records of, any problems related to the quality system, the collection, processing, storage, distribution, and administration of HPCs and cellular products and services.

1. Management Responsibility

- 3) Initiate, recommend, or implement corrective action to these problems.
- 4) Verify the implementation and assess the effectiveness of corrective action.
- 5) Control further collection, processing, storage, distribution, or administration of HPCs and cellular products and the provision of services until the problem has been corrected.
- 6) Maintain, monitor, and control the adequacy of facilities and environmental conditions.

1.2.2 Resources

The HPC and cellular product service shall identify resource requirements and provide adequate resources to perform, verify, and manage any activity covered by these *HPC and Cellular Product Standards*.

1.2.3 Management Representative

The HPC and cellular product service's executive management shall appoint a member of management who, irrespective of other responsibilities, shall have defined authority for ensuring that the HPC and cellular product service establishes, implements, and maintains a quality system that meets the requirements of these *HPC and Cellular Product Standards*. This individual shall report to executive management on the performance of the quality system. This report shall be the basis for management review and improvement of the quality system.

1.2.4 Management Review

The HPC and cellular product service's executive management shall review the quality system at defined intervals that ensure the system meets the requirements of these *HPC and Cellular Product Standards*. Records of these reviews shall be maintained in conformance with Section 16, Control of Records.

1.2.5 Management Responsibility and Qualifications

1.2.5.1 Executive Management

The HPC and cellular product service shall define executive management. Executive management shall have responsibility and authority for the HPC and cellular product service's operations and the authority to establish or make changes to the HPC and cellular product service's quality policy and quality system.

1.2.5.2 Medical Director

The HPC and cellular product service shall have a medical director(s) who is a licensed physician and qualified by training or experience in performing or supervising the procurement, processing, and storage of HPCs and cellular products. The medical director(s) shall have responsibility and authority for all medical aspects of the HPC and cellular product service that are related to the provision of HPCs and cellular products and related services.

1.2.5.3 Laboratory Director

The HPC and cellular product service shall have a laboratory director with a relevant doctoral degree who is qualified by training and/or experience. The laboratory director shall be responsible for all technical aspects of the HPC and cellular product service that are related to the provision of HPCs and cellular products and related services.

1.2.5.4 Job Qualifications

The HPC and cellular product service shall identify appropriate qualifications for each job position that affects quality.

2. QUALITY SYSTEM

2.1 **General**

The HPC and cellular product service shall establish, document, and maintain a quality system to ensure that the collection, processing, storage, distribution, and administration of HPCs and cellular products and services conform to specified requirements. The HPC and cellular product service shall prepare a quality manual that incorporates or references the requirements of these *HPC and Cellular Product Standards*, incorporates or references detailed HPC and cellular product service processes and procedures, and outlines the structure of the documentation used in the quality system.

2.2 **Quality System Policies, Processes, and Procedures**

The HPC and cellular product service shall develop, document, and effectively implement policies, processes, and procedures for the quality system to ensure that the requirements of these *HPC and Cellular Product Standards* are satisfied.

2.3 **Quality Planning for New or Changed Products or Services**

The HPC and cellular product service shall define and document how the requirements of these *HPC and Cellular Product Standards* will be ensured for each new or changed product or service. The documentation shall be in a format that suits the nature of the change and the HPC and cellular product service's operations.

2.4 **Annual Review of Policies, Processes, and Procedures**

Annual review of each policy, process, and procedure of the HPC and cellular product service shall be performed by the laboratory director and/or medical director. Records of these reviews shall be maintained in conformance with Section 16, Control of Records.

3. AGREEMENT REVIEW

3.1 General

The HPC and cellular product service shall establish and maintain policies, processes, and procedures for reviewing agreements to provide products and services to the HPC and cellular product service's customers.

[Note 1: For issues relating to the acquisition of materials or services by an HPC and cellular product service, see Section 6, Obtaining Materials (Including HPCs and Cellular Products) and Services.]

3.2 Review

Before acceptance of a verbal or written agreement, the agreement shall be reviewed by the HPC and cellular product service to ensure that:

- 1) The customer's requirements are adequately defined.
- 2) Any differences between the agreement requirements and the products or services offered under the agreement are resolved.
- 3) The HPC and cellular product service has the capability to meet the agreement requirements.

3.3 Changes to Agreements

The HPC and cellular product service shall define how changes to agreements are made and communicated to affected HPC and cellular product service personnel.

3.4 Records

Records of agreements, reviews of, and changes to agreements, shall be maintained in conformance with Section 16, Control of Records.

3. Agreement Review

3.5 Agreements Relating to HPCs and Cellular Products

3.5.1 **Agreements to Collect Data Regarding Transplantation or Cellular Therapy**

The collecting HPC and cellular product service shall ensure that an agreement is made with the administering HPC and cellular product service to collect and provide engraftment data, and/or outcomes of transplantation or cellular therapy and information on adverse events suspected to be linked to the administered product. Reference Standard 16R-B applies.

3.5.2 **Disposition Agreements**

Prior to collection, there shall be agreement with the donor (or donor's legally authorized representative), the intended recipient (if one has been identified), the transplanting physician (if any), and the storage HPC and cellular product service about the conditions of storage and the indications for discard of the HPCs and cellular products. Prior to discard, the HPC and cellular product service shall make a good-faith effort to notify either the intended recipient, the intended recipient's physician, or the transplant physician.

- 3.5.2.1** If the conditions for discard are not described in the original agreement(s), the storage HPC and cellular product service shall communicate with the intended recipient's physician to evaluate the continuing need for storage of the HPCs and cellular products. Prior to discard, the HPC and cellular product service shall make a good-faith effort to notify either the intended recipient, the intended recipient's physician, or the transplant physician.

3.5.2.2 Documentation of death or of no further need for HPCs and cellular products shall be made prior to discard.

3.5.3 Physician Orders

Any medical therapy to be provided by the HPC and cellular product service shall be ordered by the patient's physician. Orders shall contain sufficient information for positive identification of the patient.

3.5.4 Informed Consent

Prior to collection, the HPC and cellular product service shall obtain informed consent of the donor or the donor's legally authorized representative in conformance with AABB Reference Standard 3R-A and applicable law. Informed consent records shall be maintained in conformance with Section 16, Control of Records.

3.5.4.1 The HPC and cellular product service shall ensure that informed consent of the allogeneic donor is obtained prior to myeloablative therapy of the recipient.

3.6 Claims

Any claims or promotional material shall be based on data and validated processes. Information and educational materials provided to potential donors and recipients shall be supported.

3.7 Tracing and Tracking

The HPC and cellular product service shall ensure that the receiving facility has agreed to participate in HPC and cellular product tracing and tracking.

3. Agreement Review

Reference Standard 3R-A. Informed Consent for Cellular Collection Procedure

The informed consent process shall include an explanation in understandable terms to the donor or the donor's legally authorized representative of any applicable risks, discomforts, benefits, and alternatives, and shall include the following elements:

- A. Description of participation and invitation to become a donor, including:
 - 1. Cellular collection procedure, including a general explanation of the indications for and results of cellular collection.
 - 2. Sample collection and storage for possible future testing.
 - 3. Testing for infectious diseases and genetic disorders, or other conditions as indicated.
 - 4. Notification of abnormal test results.
 - 5. Review of medical history.
 - 6. Possible dispositions of the cellular donation.
 - 7. Discussion of confidentiality.
 - 8. Ownership.
- B. The donor or the donor's legally authorized representative shall acknowledge in writing that he or she has understood the risks and benefits of cellular donation and that he or she has been given the opportunity to ask questions and had those questions answered satisfactorily.
- C. The informed consent process shall be in conformance with all applicable law.
- D. Informed consent requirements and regulations that apply to donors who are minors shall be met.
- E. The donor or the donor's legally authorized representative shall have the opportunity to deny or withdraw consent to the collection procedures without affecting their access to medical care.

4. DESIGN CONTROL

4.1 **General**

The HPC and cellular product service shall establish and maintain policies, processes, and procedures to control and verify the design of new or changed HPCs and cellular products or services to ensure that the design goals and specified requirements are met.

4.2 **Design Goals**

The HPC and cellular product service shall identify, document, and review design goals and requirements. Incomplete, ambiguous, or conflicting requirements shall be resolved with those responsible for creating the requirements.

4.3 **Design and Development Planning**

The HPC and cellular product therapy service shall identify how design output will meet design goals. The appropriate organizational and technical groups, including groups responsible for software or hardware processes, shall be identified and consulted during the planning process.

4.4 **Design Output**

Design output shall:

- 1) Be documented in a manner that permits verification of the output against design goals and requirements.
- 2) Meet the design goals.
- 3) Contain or make reference to acceptance criteria.
- 4) Meet the characteristics of the design that are critical to the safety and efficacy of a new or modified product or service.

Records shall be maintained in conformance with Section 16, Control of Records.

4. Design Control

4.5 **Design Review**

Where applicable, reviews of the design output shall be planned and conducted at appropriate stages of design. Records shall be maintained in conformance with Section 16, Control of Records.

4.6 **Design Verification**

Design verification shall be performed to ensure that the design output meets the design goals. Records shall be maintained in conformance with Section 16, Control of Records.

4.7 **Design Validation**

Design validation shall be performed to ensure that the product or service consistently conforms to defined requirements. Records shall be maintained in conformance with Section 16, Control of Records.

4.8 **Design Changes**

All design changes shall be identified, documented, reviewed, and approved by appropriate personnel before their implementation. Records shall be maintained in conformance with Section 16, Control of Records.

4.9 **Design Approvals**

Research performed under a research protocol that involves administration of HPCs and cellular products shall be performed only after approval of the protocol by an Institutional Review Board (IRB) and, where applicable, under an Investigational New Drug (IND) application or Investigational Device Exemption (IDE). Records of approvals shall be maintained in conformance with Section 16, Control of Records.

4.9.1 **Research Results**

Records of research results pertaining to expected and unexpected clinical effects shall be maintained in conformance with Section 16, Control of Records.

5. DOCUMENT CONTROL

5.1 General

The HPC and cellular product service shall establish and maintain policies, processes, and procedures to control all documents that relate to the requirements of these *HPC and Cellular Product Standards*.

5.2 Document Approval and Distribution

The HPC and cellular product service shall review and approve all documents prior to issuance. The document control process shall ensure that:

- 1) Documents are identified with the current revision status.
- 2) Appropriate documents are available at all locations where operations covered by these HPC Standards are performed.
- 3) Invalid or obsolete documents are not used.
- 4) Any archived obsolete documents are suitably identified as such.

5.3 Document Changes

Changes to documents shall be reviewed and approved in the same manner as the original review and approval, unless a different process or procedure is specifically established. Individuals authorized to review and approve changes shall have access to all background information necessary to conduct the review and approval.

5.4 List of Documents

The HPC and cellular product service shall maintain a master list of all documents that relate to the requirements of these *HPC and Cellular Product Standards*.

5. Document Control

5.5 **Format**

Policies, processes, and procedures established by the HPC and cellular product service shall be in a standardized format. Additional policies, processes, and procedures, such as those in an operator's manual, may be incorporated by reference.

5.6 **Document Retention**

The HPC and cellular product service shall determine which, if any, documents shall be archived or made obsolete. Copies of archived policies, processes, and procedures shall be retained. Standard 16.4, Record Retention, applies.

6. OBTAINING MATERIALS (INCLUDING HPCS AND CELLULAR PRODUCTS) AND SERVICES

6.1 General

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

[Note 2: Purchased, donated, or otherwise acquired materials include but are not limited to, HPCs and cellular products, HPCs and cellular products intended for further processing, containers, test kits, and reagents. Services include activities required to maintain HPC and cellular product service equipment and instruments.]

6.2 Evaluation of Suppliers

The HPC and cellular product service shall:

- 1) Evaluate and select any supplier of a material or service that is intended for incorporation into HPCs and cellular products or services, or that affects the quality of the HPCs and cellular products or services, on the basis of the supplier's ability to meet specified requirements.
- 2) Define the type and extent of control required over the supplier. The type and extent of control shall depend upon the type of material or service, the impact of the material or service on the quality of the final product or final service, and the previous performance of the supplier.
- 3) Maintain records of acceptable suppliers in conformance with Section 16, Control of Records.
- 4) Report to management personnel with contracting authority when a supplier fails to meet specified requirements.

6. Obtaining Materials and Services

6.3 Purchasing Information

Purchasing documents shall contain information that clearly describes the material or service ordered. The HPC and cellular product service shall review and approve purchasing documents for adequacy of the specified requirements prior to release.

[Note 3: This section only applies to HPC and cellular product services that have the authority to review and/or approve purchasing documents.]

6.4 Verification of Obtained Materials

6.4.1 Certificate of Analysis

The HPC and cellular product service shall request a certificate of analysis from the supplier for material that comes into contact with the HPC or cellular product.

6.4.2 Test Kits

FDA-licensed, -approved, or -cleared test kits shall be used. Test kits shall be used in accordance with the manufacturer's directions.

6.5 Records

Records required by Reference Standard 6R-A shall be created for obtained materials and maintained in conformance with Section 16, Control of Records.

Reference Standard 6R-A. Records of Obtained Materials

The following information regarding obtained materials shall be recorded:

1. Type of materials.
2. Manufacturer or source.
3. Lot number or unique identifier.
4. Date of receipt.
5. Expiration date.

7. CONTROL OF PATIENT-SPECIFIC (AUTOLOGOUS OR RELATED ALLOGENEIC) PRODUCTS

7.1 General

The HPC and cellular product service shall establish and maintain policies, processes, and procedures to control 1) the qualification of donor-patients and related allogeneic donors; 2) testing of patient-specific products for infectious diseases, and 3) disposition of patient-specific products.

- 7.1.1 The HPC and cellular product service shall report to the recipient's physician any products that are lost, damaged, or otherwise unsuitable for administration. Records shall be maintained in conformance with Section 16, Control of Records.

[Note 4: For the remainder of the process control requirements related to collection, processing, storage, distribution, and administration of patient-specific HPCs and cellular products and services, see Section 9, Process Control. For allogeneic donor qualification, see Reference Standard 9R-B.]

7.2 Control of Patient-Specific (Autologous or Related Allogeneic) Products

7.2.1 Qualification of Donor-Patients and Related Allogeneic Donors

The HPC and cellular product service shall qualify donor-patients and related allogeneic donors in conformance with Reference Standard 9R-A and 9R-B.

7.2.2 Testing of Donors for Infectious Diseases

The HPC and cellular product service shall perform tests on the donor intended to prevent disease transmission in conformance with Reference Standard 10R-A.

7. Control of Patient-Specific Products

7.2.2.1 The acceptability of related allogeneic donors with positive infectious disease test results shall be determined prior to initiation of myeloablative therapy of the intended recipient. Standard 9.4.1 applies.

7.2.3 Disposition of Patient-Specific Products
The HPC and cellular product service shall define the length of storage and terms of disposal of patient-specific HPCs and cellular products. Standard 3.5.2 applies.

8. PRODUCT AND SAMPLE IDENTIFICATION AND TRACEABILITY

8.1 General

The HPC and cellular product service shall establish and maintain policies, processes, and procedures that ensure the identification and traceability of each cellular product and associated samples from donor source, through all processing steps, to final disposition.

8.2 Product and Sample Identification

A numeric or alphanumeric system shall be used that will make it possible to trace any product or sample from source to final disposition, and to recheck records applying to the specific product, including investigation of reported adverse reactions. This unique identification shall not be obscured, altered, or removed.

8.2.1 Unique identifiers shall not be obscured, altered, or removed except to replace them with other unique identifiers.

8.2.2 Unique Product and Sample Identification

The HPC and cellular product service shall affix a unique numeric or alphanumeric identifier to each product.

8.2.2.1 Unique Identification of HPC and Cellular Product Service

A unique local identifier assigned by the HPC and cellular product service shall be included in the unique identifier for the product or be affixed to the container.

8.2.2.2 If an intermediary facility assigns or affixes a local, unique numeric or alphanumeric identification to the product, the label shall be affixed to the product, and shall identify the facility assigning the identification.

8. Product and Sample Identification and Traceability

8.2.2.3 If replaced with another unique identifier, the HPC and cellular product service shall make it possible to link the current unique identifier to the previous unique identifier.

8.2.3 Limit of Two Unique Identifications

No more than two sets of unique numeric or alphanumeric identifications from separate facilities shall be affixed to a product container. No more than two sets of unique numeric or alphanumeric identifications from separate facilities shall be visible on a finished product, ideally that of the originating facility and that of the final facility. It may be necessary to remove or obliterate identifications assigned by intermediate facilities.

8.3 Traceability

Each HPC and cellular product shall be labeled in conformance with the Reference Standard 8R-A. At a minimum, the label shall contain the elements required on the original collection container label. Traceability of products shall be ensured through conformance with all labeling requirements.

8.3.1 Labeling for Storage, Issue, or Transport

When HPCs and cellular products are stored, issued, or transported to another department within the HPC and cellular product service or another HPC and cellular product service, containers shall include the complete set of labeling elements included in the Reference Standard 8R-A or shall have an attached tag that contains the complete set of labeling elements. If shipped or issued, the labeling information required by Reference Standard 8R-B shall accompany the unit. Records shall be maintained in conformance with Section 16, Control of Records.

8.3.1.1 The outer shipping container shall be labeled "Medical specimen" and "Do not X-ray."

8. Product and Sample Identification and Traceability

8.3.2 Circular of Information

A Circular of Information for HPCs and cellular products shall be made available to all appropriate individuals.

8.4 Process or Procedure Steps

There shall be a means to identify individuals performing each critical step from donor selection to final disposition of HPCs and cellular products. Records shall be maintained in conformance with Section 16, Control of Records.

Reference Standard 8R-A. Requirements for HPC and Cellular Product Labels and Labeling

Element	Original Collection Container Label ¹	Collection Labeling Information ²	Processing Labeling Information ³	Final Label on Product Container ⁴
Name of product	X	X	X	X
Date of collection	X	X		X
Time of collection		X, if applicable		
Unique alpha and/or numeric identifier	X	X	X	X
Name of collection service/donor registry		X		X
Approximate product volume		X		X
Names/volumes of anticoagulants and other additives		X		X
For patient-specific product, name or identifier of intended recipient	X, if applicable	X, if applicable		X, if applicable
Phrase: "Do Not Irradiate"	X, if applicable			X, if applicable
Expiration date/time*	X, if applicable [†]	X, if applicable [†]	X, if applicable [†]	
Biohazard label (see 10R-B)				X, if applicable
Phrase: "Donor Untested" (see 10R-B)				X, if applicable
Do Not Use Leukoreduction Filters				X, if applicable

*If a product is needed after the stated expiration date, documentation of viability and physician approval must be included in the patient record.

[†]Labels on products that will not be cryopreserved shall include expiration date and time.

¹The original Collection Container Label shall be on the container before the HPCs and cellular products are collected.

²Collection labeling information shall be included on/with the HPCs and cellular products before they are removed from the donor's immediate presence. If these elements will not fit on container label, they may be included in the container package.

³Processing labeling information shall be included on the label during processing steps.

⁴The final label on product container shall be on the container before the HPCs and cellular products are stored, issued, or transported. If elements cannot fit on the attached label, they shall be attached to the container.

8. Product and Sample Identification and Traceability

Reference Standard 8R-B. Labeling Requirements Upon Shipping or Issuing HPC and Cellular Products

1. Summary of processing records, infectious disease testing results, and testing records, including name, address, and emergency contact information for releasing facility.
2. Warning label(s) for potentially toxic or volatile packing materials, including dry ice or liquid nitrogen.
3. Expiration time of systems or materials used for temperature control.
4. Instructions for receiving and opening container.
5. Name, address, and phone number of contact person at receiving facility.
6. Circular of Information and product information*.
7. Notification of biohazardous materials (see Reference Standard 10R-B).
8. Phrase: "Donor Untested," if applicable.
9. Methods of manipulation.
10. Expiration date/time, if applicable.
11. Phrase: "For autologous use only," if applicable.
12. Phrase: "Rx only".

*Includes but is not limited to: Investigator's brochure, or written description of product

9. PROCESS CONTROL

9.1 General

The HPC and cellular product service shall identify, plan, and validate the policies, processes, and procedures that affect the quality of products and services. These processes and procedures include the collection, processing, storage, distribution, and administration of HPCs and cellular products and the provision of related services. The HPC and cellular product service shall ensure that these policies, processes, and procedures are carried out under controlled conditions. Controlled conditions shall include:

- 1) Use of policies, processes, and procedures for the collection, processing, storage, distribution, and administration of HPCs and cellular products and services.
- 2) Use of suitable equipment and a suitable working environment.
- 3) Compliance with policies, processes, and procedures, and external standards.
- 4) Monitoring and control of suitable process parameters and product characteristics.
- 5) Approval of processes and equipment.
- 6) Criteria for acceptable results.
- 7) Control of equipment.

9.1.1 Use of Materials and Supplies

All materials, solutions, and reagents that come into contact with HPCs and cellular products during collection, processing, storage, distribution, or administration shall be sterile and of appropriate grade for intended use and shall, whenever possible, be approved for human use by the Food and Drug Administration (FDA).

- 9.1.1.1 Materials, solutions, and reagents that are not FDA-approved for human use may be used 1) if approved by the HPC and cellular product service's IRB, or

9. Process Control

with IND or IDE acceptance; or 2) if established in the scientific literature through IRB-approved trials to be acceptable for the specified purpose.

9.1.1.2 Materials, solutions, and reagents that can be expected to have an adverse effect on the HPC or cellular product shall be removed or limited to an amount that does not affect the product viability or function.

9.1.1.3 If the HPC container is not FDA-cleared, it shall have a port that can be entered aseptically.

9.1.2 Proficiency Testing Program

The HPC and cellular product service shall participate in a Center for Medicare and Medicaid Services (CMS, formerly HCFA)-approved proficiency testing program, if available, for each analyte tested by the laboratory. (Section 19.2, Application of Statistical Techniques, applies.) If there is no external CMS-approved proficiency testing program, there shall be a process for determining accuracy and reliability of test results. Section 10, Inspection and Testing, applies. Records shall be maintained in conformance with Section 16, Control of Records.

9.1.3 Quality Control

The HPC and cellular product service shall establish and maintain a process for quality control that is sufficiently comprehensive to ensure that reagents and equipment function as required.

9.1.4 Use of Aseptic Methods

The HPC and cellular product service shall use aseptic methods that provide maximum assurance of a sterile product.

9.1.5 Blood Component Support

The HPC and cellular product service shall have access to adequate blood component support.

9.1.6 Validation of Policies, Processes, and Procedures

The HPC and cellular product service shall validate all policies, processes, and procedures prior to use. Records shall be maintained in conformance with Section 16, Control of Records.

9.1.7 Facility

9.1.7.1 Security

The HPC and cellular product service shall ensure that access to the facility is limited to authorized personnel.

9.1.7.2 Environmental Conditions

The HPC and cellular product service shall ensure that the cleanliness and adequacy of facilities and environmental conditions is maintained, monitored, and controlled.

9.2 Equipment

The HPC and cellular product service shall have a process to define the selection criteria for collection, processing, and storage equipment.

9.2.1 All equipment shall be qualified for its intended use. Only FDA-cleared devices, if available, or devices and equipment validated by the HPC and cellular product service shall be used.

9.2.2 The HPC and cellular product service shall ensure that the handling, cleanliness, and storage of equipment is such that it remains fit for use; preventive maintenance and cleaning shall be done in accordance with a defined schedule.

- 9.2.3** The record system shall allow tracking and tracing of HPCs and cellular products to the equipment used in their collection, processing, and storage.

9.3 Computer Systems

The HPC and cellular product service shall have a process to support the introduction of new software, hardware, or databases, or modifications of existing software, hardware, or databases relating to the requirements of these *HPC and Cellular Product Standards*. This process shall include the following:

- 1) Risk analysis, training, validation, implementation, and evaluation of postimplementation performance.
- 2) Description of system maintenance and operation.
- 3) Documentation that is written in language that is understandable to the user.
- 4) A system for display and verification of data before final acceptance when data are added or altered.
- 5) Description of how modifications to the system are authorized and documented.
- 6) Provisions to maintain appropriate levels of confidentiality and privacy.

9.3.1 Records of the following shall be maintained:

- 1) Validation of system software, hardware, databases, and user-defined tables.
- 2) Fulfillment of life-cycle requirements for internally developed software.
- 3) Numerical designation of system versions, if applicable, with inclusive dates of use.
- 4) Monitoring of data integrity for critical data elements.

9.3.2 Alternative Computer Systems

An alternative system that ensures continuous operation shall be available in the event that computerized data and computer-assisted functions are unavailable. The alternative system shall be tested periodically.

9.4 Donor Qualification Process

9.4.1 Qualification of Donors

The collecting HPC and cellular product service shall qualify all donors in conformance with Reference Standards 9R-A and 9R-B. Records of donor physician's approval of donor suitability prior to collection shall be maintained. Exceptions to the donor qualification process shall require written approval by the medical director and the recipient's physician. Records of HPC collection from donors who do not meet all criteria shall be maintained in the donor and recipient files. These HPCs and cellular products shall only be used with the informed consent of the recipient.

9.4.1.1 The HPC and cellular product service shall qualify autologous donors in conformance with Reference Standard 9R-A.

9.4.1.2 The HPC and cellular product service shall qualify allogeneic donors in conformance with Reference Standard 9R-B.

9.4.1.3 HLA

The HPC and cellular product service shall ensure that major histocompatibility antigens have been determined by a laboratory that is accredited by the American Society of Histocompatibility and Immunogenetics (ASHI) or by an equivalent organization.

9.4.2 Allogeneic Donor Testing

The HPC and cellular product service shall ensure that prior to myeloablative therapy, if intended, or otherwise prior to donation, the determinations listed in Standard 9.6.3 have been performed on the intended recipient and the prospective allogeneic donor. This information shall be

available to the intended recipient's physician and the cell processing laboratory. Each facility shall have a process to address the management of HLA type compatibility. The transplant facility shall be alerted to ABO/Rh typing of donor and intended recipient so that appropriate HPCs and cellular products can be provided to the intended recipient, if applicable. (See Section 10, Inspection and Testing.)

9.5 Collection of HPCs and Cellular Products

9.5.1 Preparation for the Collection Procedure

9.5.1.1 Collection Request

The HPC and cellular product service shall have a written request for collection of HPCs and cellular products from the recipient's physician before products are collected. Records shall be maintained in conformance with Section 16, Control of Records.

9.5.1.2 Medical Provisions

The HPC and cellular product service shall have provisions for medical care of donors in the case of adverse events.

9.5.1.3 Administration of Drugs or Growth Factors to the Donor

The HPC and cellular product service shall ensure that administration of drugs, growth factors, or other pharmacologic or biologic agents to the donor is under the supervision of a licensed physician experienced in the administration of these agents.

9.5.1.4 Placement of Central Venous Catheter for Cell Collection

The HPC and cellular product service shall ensure adequate line placement of the central venous catheter, if required for collection. Records of line placement

shall be maintained in conformance with Section 16, Control of Records.

9.5.1.5 Collection Endpoints

The HPC and cellular product service shall determine expected endpoints and objectives for the collection of HPCs and cellular products. Records shall be maintained in conformance with Section 16, Control of Records.

9.5.1.6 Collection Screening and Tests

The HPC and cellular product service shall perform pre-collection screening and tests to qualify the donor in conformance with Reference Standard 9R-A or 9R-B.

9.5.2 Collection Procedure

9.5.2.1 Lot Numbers and Expiration Dates

The HPC and cellular product service shall identify lot numbers and expiration dates of all disposables and solutions used in collection. Records shall be maintained in conformance with Section 16, Control of Records.

9.5.2.2 Collection Record

The HPC and cellular product service shall maintain a record of each procedure, including the details of the collection, the person responsible for each step, and all materials used during collection. Records shall be maintained in conformance with Section 16, Control of Records.

9.5.2.3 Unrealized Endpoints

The intended patient's physician shall be notified if expected collection endpoints are not met. Standard 13.2.3 applies.

9. Process Control

9.5.2.4 Review of Collection Records

After completion of collection, the collection record of each HPC or cellular product shall be reviewed.

9.6 Cell Processing

9.6.1 General

9.6.1.1 Test Suppliers

Tests required by these *HPC and Cellular Product Standards* shall be performed in a laboratory accredited by the American Association of Blood Banks or other equivalent accrediting body, certified by the CMS, or licensed or registered by the FDA. When an approved testing program is not available, there shall be a system for determining the accuracy and reliability of test results. There shall be a process for qualifying a test methodology for implementation.

9.6.1.2 Methods

The HPC and cellular product service shall use methods designed to result in acceptable HPC and cell product viability, recovery, function, and sterility, and designed to prevent cross contamination.

9.6.1.3 Processing Request

Before processing is initiated, the HPC and cellular product service shall obtain a written order (electronic signatures are acceptable) from the physician responsible for the recipient. Records of orders shall be maintained in conformance with Section 16, Control of Records.

9.6.1.4 Defined Processing Endpoints

The HPC and cellular product service shall define expected endpoints and objectives for processing HPCs and cellular products.

9.6.1.5 Irradiation or Damaging Conditions

The HPC and cellular product service shall ensure that products are not exposed to irradiation, inappropriate temperatures, or other damaging conditions that could harm viability, recovery, function, or sterility.

9.6.2 Processing

9.6.2.1 Lot Numbers and Expiration Dates

The HPC and cellular product service shall identify lot numbers and expiration dates of all materials used in processing. Records shall be maintained in conformance with Section 16, Control of Records.

9.6.2.2 Processing Record

The HPC and cellular product service shall maintain a record of each procedure, including each step, and of the person responsible for each step, and all materials used during processing. Records shall be maintained in conformance with Section 16, Control of Records.

9.6.2.3 Processing Tests

The HPC and cellular product service shall administer processing tests on each product in conformance with Reference Standard 9R-C. Additional tests will be performed when the procedure in use requires them.

9.6.2.4 Review of Processing Record

After completion of processing, the HPC and cellular product service laboratory director shall review the processing record.

9.6.2.5 Unrealized Endpoints

The HPC and cellular product service medical director shall notify the intended patient's physician if expected endpoints are not met. See Section 13, Deviations and Nonconforming Products and Services.

9.6.3 Testing of Allogeneic Donors

9.6.3.1 ABO Group and Rh Type

The HPC and cellular product service shall determine ABO group and Rh type.

9.6.3.2 Previous Records

If there are any previous records, the HPC and cellular product service shall compare HLA type, ABO group, and Rh type with the last available record. Any discrepancy shall be resolved prior to collection of the HPCs and cellular products.

9.6.3.3 Compatibility Determination

The HPC and cellular product service shall verify the degree of HLA match in allogeneic transplants between donor and intended recipient. The ABO group and Rh type of donor and intended recipient shall be compared and differences documented, including appropriate processing interventions, if any, needed to manage the difference.

9.6.3.4 Unexpected Antibodies for Allogeneic Donors

Serum or plasma from donors and intended recipients shall be tested for unexpected antibodies to red cell antigens using methods that demonstrate clinically significant antibodies.

9.6.4 Cryopreservation

The HPC and cellular product service shall use cryopreservation methods designed to preserve cellular product viability, recovery, and function.

9.6.4.1 Rate-Controlling Device

If a rate-controlling device is used for cryopreservation, the HPC and cellular product service shall monitor the cooling rate.

9.6.4.2 Alternative Cryopreservation

If alternative cryopreservation is used, records of the method and outcome of validation shall be maintained in conformance with Section 16, Control of Records.

9.6.4.3 Sample Aliquots

Sample aliquots from HPCs and cellular products shall be retained under the same storage conditions as the cellular product for possible future testing.

9.6.4.4 Records

The HPC and cellular product service shall maintain cryopreservation records in conformance with Reference Standard 9R-D and Section 16, Control of Records.

9.7 Product Release

The HPC and cellular product service shall inspect the conditions of HPCs and cellular products prior to release. Records shall be maintained in conformance with Reference Standard 9R-E and Section 16, Control of Records.

9.8 Thawing

The HPC and cellular product service shall either establish or approve thawing processes and procedures used by the transplant facility.

9. Process Control

6. The prospective donor shall acknowledge in writing that he/she has read and understood the educational material, has been given ample opportunity to ask questions, and has had those questions answered satisfactorily.
- B. Donor health history screening
1. Review of donor health to determine suitability shall be performed before the recipient receives marrow ablative therapy. The prospective donor's history shall be evaluated and the donor examined by a suitably qualified person. The donor qualification process shall include at a minimum:
 - a. The donor's general health and health history.
 - b. History of or risk factors for:
 - HIV
 - HBV
 - HCV
 - TSE
 - c. Assessment of risk behaviors for and exposure to infectious diseases transmissible by blood, body fluids, and/or tissue.
 - d. Evaluation of anesthesia risk for the prospective marrow donor.
 - e. Evaluation of peripheral venous access for potential apheresis donor.
 - f. A history of receipt of blood, blood components, blood derivatives, or tissue.
 - g. An immunization/vaccination history.
 2. Final approval of donor health for collection shall be given by the donor's physician prior to initiation of myeloablative therapy of the recipient. Interim health assessments shall be performed by a qualified person or persons through all phases of mobilization (if applicable) and collection.
- C. Testing
1. A determination of the donor's ABO group, Rh type, and HLA type shall be performed.
 2. A complete blood count, including platelet count, shall be performed within 24 hours preceding each collection.

3. The HPC and cellular product service shall have documented confirmation of a pregnancy assessment on all female donors. This documentation shall be obtained prior to mobilization, collection, or recipient myeloablation.

9. Process Control

Reference Standard 9R-C. Processing Tests

The following processing tests shall be performed on each cellular product:

1. Relevant cell count.
2. Antigen expression analysis appropriate for the cellular product.
3. Test(s) for cell viability.
4. Test(s) for product sterility.

Reference Standard 9R-D. Cryopreservation Records

The following information regarding cryopreservation shall be recorded for each HPC or cellular product:

1. Starting cell product and volume.
2. Relevant cell count.
3. Cell viability.
4. Cryoprotectant solution.
5. Cooling record from controlled-rate freezing, if applicable.
6. Endpoint temperature of cooling of the cellular product.
7. Storage temperature and conditions.

Reference Standard 9R-E. Verification of Products Upon Release

The following information shall be recorded at the time of product release:

1. Name of product.
2. Unique alpha and/or numeric identifier.
3. Date and time of release from storage, if applicable.
4. If patient-specific product, name and/or identifier of intended recipient.
5. Name of person and/or HPC and cellular product therapy service to whom the HPCs and cellular products were released and/or name of person delivering product to administration site.
6. Condition of container and label.
7. Name or identifier of person(s) releasing product from storage.

Reference Standard 9R-F. Verification of Product and Recipient Match

- A. The following information shall be recorded before administration of HPCs and cellular products:
 1. Recipient's name and identification number.
 2. Unique alpha and/or numeric identifier of a product.
 3. Date and time of administration.
 4. Identifier of person(s) administering the product.
- B. Adverse reactions suspected to be linked to the product shall be recorded during or after administration of HPCs and cellular products.
- C. If there are any erythrocytes or erythrocyte antibodies in the product, the following information shall be recorded:
 1. ABO group and Rh type of recipient.
 2. ABO group and Rh type of donor.

10. INSPECTION AND TESTING

10.1 General

The HPC and cellular product service shall establish and maintain policies, processes, and procedures for inspection and testing activities to verify that the specified requirements for products and services are met. Records of inspection and testing activities shall be maintained in conformance with Section 16, Control of Records.

10.2 Inspection and Testing on Receipt of Incoming Materials

10.2.1 Inspection of Incoming Materials Prior to Use

The HPC and cellular product service shall ensure that incoming materials that are incorporated into the final product or that directly affect the quality of the product are not used until they have been inspected or otherwise verified as conforming to requirements. Verification shall be in accordance with policies, processes, and procedures.

[Note 5: It is permissible to begin processing HPCs and cellular products before receipt of infectious disease testing results.]

10.2.2 Determination of Extent of Inspection

In determining the amount and nature of inspection required upon receipt of any material, consideration shall be given to the amount of control exercised at the supplier's premises and the recorded evidence of conformance provided.

10.2.3 Incoming Materials Released for Emergency Use

Where a material is used on an emergency basis, prior to verification, the material shall be positively identified and recorded in conformance with Section 16, Control of Records, to permit immediate recall and replacement in the

event that it is later determined not to conform to established requirements.

10.3 In-Process and Final Inspection and Testing of Products
[Note 6: For inspection of in-storage products, Standard 15.2 applies.]

10.3.1 In-Process Inspection and Testing of Products

The HPC and cellular product service shall:

- 1) Inspect and test the product during processing as required by policies, processes, and procedures.
- 2) Quarantine the product until any required inspection and tests have been completed or necessary reports received and verified, except when the product is released pursuant to Section 10.2.3.

10.3.2 Final Inspection and Testing of Products

The HPC and cellular product service shall carry out all final inspection and testing for products in accordance with policies, processes, and procedures. These policies, processes, and procedures shall require that all specified inspection and tests, including those required for materials and in-process products, have been carried out and that the results meet specified requirements.

- 10.3.2.1** No product shall be released until the activities specified in processes or procedures, and the associated records have been completed.

10.4 Inspection and Testing of Services

The HPC and cellular product service shall carry out all inspection and testing for services, including laboratory testing services, in accordance with policies, processes, and procedures. These policies, processes, and procedures shall require that all specified inspection and tests, including any that might be re-

10. Inspection and Testing

quired during the provision of the service, have been carried out and that the service meets specified requirements.

10.5 Inspection and Test Records

The HPC and cellular product service shall maintain records in conformance with Section 16, Control of Records, that provide evidence that the product or service has been inspected or tested and the service has been provided in accordance with specified requirements. These records shall show clearly whether the product or service has passed or failed any inspection or tests or whether a service has been provided in accordance with specified requirements.

Where a product fails to pass any inspection or test, the policies, processes, and procedures for control of nonconforming product, Standards 13.1.2 and 13.2.

Where a service fails to pass any inspection or test, the policies, processes, and procedures for a nonconforming service, Standard 13.3, Review and Disposition of Nonconforming Services, shall apply.

Records shall identify the individual(s) responsible for the release of the product or provision of the service, as appropriate.

10.6 Testing

10.6.1 Accreditation of Testing Facilities

Tests required by these *HPC and Cellular Product Standards* shall be performed in a laboratory accredited by the AABB or other equivalent accrediting body, certified by the CMS, or licensed or registered by the FDA.

10.6.2 Tests Intended to Prevent Disease Transmission

10.6.2.1 Testing of Cellular Products

The HPC and cellular product service shall perform tests intended to prevent disease transmission within

10. Inspection and Testing

30 days prior to or concurrently with the collection for each donor as specified in Reference Standard 10R-A. Records of test results shall be maintained in conformance with Section 16, Control of Records.

10.6.2.1.1 Infectious disease testing of allogeneic donors shall be completed prior to myeloablative therapy of the recipient, if applicable.

10.6.2.2 Positive or Reactive Infectious Disease Tests Results

Allogeneic cellular products with a confirmed positive test for HIV-1/2, HBV, HCV, shall be released only for emergency administration. Standards 13.2.1 and 13.2.2 apply.

10.6.2.2.1 Products that have positive or reactive viral markers shall be labeled with biohazard labels in conformance with Reference Standard 10R-B. Records of the disposition of these products shall be maintained in conformance with Section 16, Control of Records.

10.6.2.2.2 The HPC and cellular product service shall ensure communication of abnormal or repeat reactive test results in conformance with Reference Standard 10R-C.

10.6.2.3 Untested products shall be labeled, "Donor Untested."

10.7 Inspection for Microbial Contamination

The HPC and cellular product service shall test each processed cellular component for microbial contamination. Records shall be maintained in conformance with Section 16, Control of Records.

10. Inspection and Testing

10.8 **Inspection Before Administration**

Prior to release of HPCs and cellular products for administration, the HPC and cellular product service shall review qualification, collection, and processing records to ensure that the HPCs and cellular products are issued for administration with sufficient information to permit positive identification of the intended recipient and HPCs and cellular products. The HPC and cellular product service shall compare the labeling information with the recorded test results for infectious diseases and sterility (when available.)

Reference Standard 10R-A. Tests Intended to Prevent Disease Transmission

Test for	Allogeneic Donor	Autologous Donor
HBV	X	X
HTLV-I/II	X	X
HIV-1/2	X	X
HCV	X	X
CMV	X	Not required
Syphilis	X	Not required

Reference Standard 10R-B. Biohazard Labels

The HPC and cellular product service shall affix biohazard labels to HPCs and cellular products when any of the following screening tests is repeatedly reactive and the confirmatory test is either positive or has not been performed.

- A. Test for:
- HBsAg
 - Anti-HBc
 - HIV-1/2
 - HCV
 - HTLV-I/II
 - Serologic test for syphilis*
- B. Health history of risk factors for:
- HIV
 - HBV
 - HCV
 - TSE

*If positive

10. Inspection and Testing

Reference Standard 10R-C. Notification of Test Results

Donation	Test Result	To Be Notified
Allogeneic	Positive infectious disease test results	Donor and recipient physician
Autologous	Abnormal results	Transplantation physician

11. CONTROL OF EQUIPMENT

11.1 Control of Equipment

The HPC and cellular product service shall establish and maintain policies, processes, and procedures to control, calibrate clean, and maintain critical equipment. Equipment that is used to inspect, measure, or test whether materials or products (incoming, in-process, or final) conform to the requirements established by the HPC and cellular product service shall be used in a manner that ensures that the measurement limitation is known and is consistent with the measurement capability that is required.

[Note 7: "Equipment that measures" includes measuring devices, such as thermometers, pipettes, cell cytometers, and balances.]

11.2 Calibration of Equipment

The HPC and cellular product service shall identify all equipment that requires calibration. For critical equipment, the HPC and cellular product service shall:

- 1) Prior to use and at prescribed intervals, calibrate and adjust equipment.
- 2) Define the process used for the calibration of equipment, including details of equipment type, unique identification, location, frequency of checks, check method, acceptance criteria, and the action to be taken when results are unsatisfactory.
- 3) Identify equipment so that the calibration status can be determined.
- 4) Maintain calibration records for equipment in conformance with Section 16, Control of Records.
- 5) Safeguard equipment from adjustments that would invalidate the calibration setting.
- 6) Assess the conformance of products and services provided when equipment is found to be out of calibration.

11. Control of Equipment

Records shall be maintained in conformance with Section 16, Control of Records.

11.2.1 Equipment Malfunction

Records of equipment malfunctions and any associated corrective actions shall be maintained in conformance with Section 16, Control of Records.

11.3 Control Processes and Procedures for Inspection, Measuring, and Test Equipment

For equipment used to inspect, measure, or test, the HPC and cellular product service shall also:

- 1) Determine the measurements to be made and the accuracy and precision required and then select appropriate equipment that is capable of meeting those requirements.
- 2) Assess the validity of previous inspection and test results when equipment is found to be out of calibration. Records shall be maintained in conformance with Section 16, Control of Records.
- 3) Calibrate the equipment using certified equipment that has a known valid relationship to nationally recognized standards. Where no such standards exist, the basis for calibration shall be recorded.
- 4) Ensure that environmental conditions are suitable for the calibrations, inspections, measurements, and tests carried out.

12. INSPECTION AND TEST STATUS

The inspection and test status of all materials and HPCs and cellular products shall be identifiable throughout collection, processing, storage, distribution, and administration to ensure that only materials and products that have passed the required inspections and tests are released and administered.

The inspection or test status of all HPCs and cellular products shall be identified by suitable means to indicate the conformance or nonconformance. In the case of a nonconformance, the reason for the nonconformance shall be identified and documented.

13. DEVIATIONS AND NONCONFORMING PRODUCTS AND SERVICES

13.1 **Deviations**

The HPC and cellular product service shall have a process to capture, assess, investigate, and monitor events that deviate from accepted policies, processes, or procedures, or that fail to meet the requirements of the HPC and cellular product service, these *HPC and Cellular Product Standards*, or applicable laws and regulations. Deviations shall be reported in accordance with specified requirements.

13.1.1 **Control of Nonconforming Products or Services**

The HPC and cellular product service shall establish and maintain policies, processes, and procedures to ensure that materials and products or services that do not conform to specified requirements are prevented from unintended use or unintended product administration. This control shall provide for identification, documentation, evaluation, segregation (when practical), and disposition of nonconforming material and products. The HPC and cellular product service shall establish and maintain policies, processes, and procedures to address nonconforming services.

13.1.2 **Review and Disposition of Nonconforming Materials and Products**

The responsibility for review of and authority for the disposition of nonconforming materials or products shall be defined. A nonconforming material or product shall be evaluated for appropriate disposition in accordance with policies, processes, and procedures. A nonconforming material or product may be:

- 1) Reprocessed, retested, or reworked to meet the specified requirements.
- 2) Accepted by the customer, after disclosure of the nonconformance.

13. Deviations and Nonconforming Products and Services

- 3) Relabeled, in conformance with applicable requirements.
- 4) Destroyed.

Products that are determined after release not to conform to specified requirements shall be evaluated to determine the effect of the nonconformance on the quality of the product. In cases where quality may have been affected, the nonconformance shall be reported to the customer. Records of the nature of nonconformances and subsequent actions taken, including acceptance for use shall be maintained in conformance with Section 16, Control of Records. The HPC and cellular product service shall notify all facilities to whom the product was distributed.

Reprocessed, retested, or reworked products shall be re-inspected in accordance with policies, processes, and procedures.

13.2 Nonconforming HPC Products

The HPC and cellular product service shall ensure that the medical director discusses deviations from established processes and procedures that may affect the safety and efficacy of HPCs and cellular products when identified with the recipient's physician and prior to initiation of myeloablative therapy, if intended. Records shall be maintained in conformance with Section 16, Control of Records.

13.2.1 Nonconforming Infectious Products

The HPC and cellular product service shall ensure that HPCs and cellular products that are nonconforming due to positive cultures and/or positive or repeatedly reactive markers for tests required under Section 10, Inspection and Testing, are administered only with the informed consent of the recipient and the approval of the recipient's physician. Records shall be maintained in conformance with Section 16, Control of Records.

13. Deviations and Nonconforming Products and Services

13.2.2 Shipping Nonconforming Infectious Products

When HPCs and cellular products will be shipped, the HPC and cellular product service shall notify the administering facility and the patient's physician of any HPC products that are nonconforming due to positive markers for infectious agents, including those listed in Reference Standard 10R-B.

13.2.3 Unrealized Endpoints

The HPC and cellular product service, in consultation with the patient's physician, shall determine the acceptability of products for which expected endpoints are not realized during collection and/or processing.

13.3 Review and Disposition of Nonconforming Services

The responsibility for review of and authority for the handling of nonconforming services shall be defined. A nonconforming service shall be evaluated for appropriate action in accordance with policies, processes, and procedures. A nonconforming service may be: 1) repeated or 2) accepted by the customer.

Where required by agreement, the proposed repeat of a service that does not conform to specified requirements shall be reported to the customer. The description of any nonconforming service that has been accepted shall be recorded in conformance with Section 16, Control of Records, to denote the actual condition.

Repeated services shall be reinspected in accordance with policies, processes, and procedures.

- 13.3.1** The HPC and cellular product service shall have a process to notify the original collecting HPC and cellular product service of confirmed cases of an infectious disease in a recipient that could be attributed to the HPCs and cellular products.

13.4 Adverse Events

The HPC and cellular product service shall establish a process for the detection, reporting, and evaluation of adverse reactions suspected to be linked to donations, and administrations/transplantations. Records of such events, and the related investigations, evaluations, and notifications, shall be maintained in conformance with Section 16, Control of Records. Deviations shall be reported as required in accordance with specified requirements.

13.4.1 Recipient adverse reactions associated with the progenitor cell products shall be reported to the HPC service for evaluation. These events shall be tracked and analyzed for trends and repeated frequent deviations.

13.4.2 The administering medical facility shall have a process to notify the collecting and processing HPC and cellular product service of all significant adverse events, including, but not limited to, infusion reactions, confirmed cases of infectious disease, failure to engraft, or other product failure. Standard 3.5.1 applies.

14. CORRECTIVE AND PREVENTIVE ACTION PLANS

14.1 General

The HPC and cellular product service shall establish and maintain policies, processes, and procedures for implementing corrective and preventive action plans. Management personnel 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.

The HPC and cellular product service shall implement any changes to the policies, processes, and procedures resulting from corrective and preventive action. Records shall be maintained in conformance with Section 16, Control of Records.

14.2 Corrective Action

The process for corrective action shall include:

- 1) The effective handling of deviation reports and product nonconformances.
- 2) Investigation of the cause of nonconformances relating to product, process, and the quality system. Records shall be maintained in conformance with Section 16, Control of Records.
- 3) Investigation of customer complaints.
- 4) Determination of the corrective action needed to eliminate the cause of nonconformances.
- 5) Ensuring that corrective action is taken and that it is effective.

14. Corrective and Preventive Action Plans

14.3 Preventive Action

The process for preventive action shall include:

- 1) The use of appropriate sources of information (such as policies, processes, and procedures that affect product or service quality, assessment results, proficiency testing results, quality control records, and customer complaints) to detect, analyze, and eliminate potential causes of nonconformances.
- 2) Determination of steps needed to deal with any problems requiring preventive action.
- 3) Initiation of preventive action and application of controls to ensure that it is effective.

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16.4 Record Retention

Records as defined in Reference Standard 16R-A and 16R-B shall be retained for appropriate periods of time in conformance with these reference standards.

16.4.1 Records not included in the Reference Standards 16R-A and 16R-B shall be retained by the HPC and cellular product service for a length of time determined by the facility's individual business needs.

16.4.2 Divided Responsibilities

If two or more facilities are involved in the collection and processing of a product, records shall show the responsibilities of each. Each facility shall provide a copy of any requested records to the final receiving facility except for those compromising donor confidentiality.

Reference Standard 16R-A. Record Retention for Processing and Collecting HPC and Cellular Product Services

- A. Records that shall be retained for at least 10 years after the transplantation or final disposition of the HPC or cellular product include:
1. Donor Records
 - a. For autologous donors
 - 1) Identifying information sufficient to attempt to contact the donors.
 - 2) Medical history, interview, physical examination, physician approval.
 - 3) Informed consent.
 - 4) Adequate line placement of central venous catheter, if applicable
 - 5) Interpretations of ABO group, Rh type, and HLA type (including comparisons to previous records), and tests for infectious disease markers, if applicable.
 - 6) Adverse reactions or donor complaints.
 - 7) Notification to donor-patient's physician of products that are lost, damaged, or otherwise unsuitable for administration.
 - b. Allogeneic donors
 - 1) Identifying information sufficient to attempt to identify and contact the donors.
 - 2) Recipient information sufficient to permit tracing of the product.
 - 3) Medical history, interview, physical examination, physician approval.
 - 4) Informed consent.
 - 5) Adverse reactions or donor complaints.
 - 6) Interpretation of ABO group, Rh type, and HLA type (including comparisons to previous records), tests for infectious disease markers, detection and identification of unexpected red cell antibodies

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- and, if performed, red cell compatibility testing with a sample from the intended recipient.
- 7) Notification from administering medical facility of confirmed cases of infectious disease in recipient.
- c. For allogeneic donor found unsuitable by the collection/processing service, records of:
 - 1) Reason for deferral.
 - 2) Donor notification of deferral.
 - 3) Products from unacceptable donors.
 - 4) Notification to receiving facility when a previous donor is subsequently found positive for HCV, HIV-1/2, HTLV-I/II, or HBV.
- 2. Supplier Records
 - a. Identifying information for all acceptable suppliers providing:
 - 1) Donor selection information, product collection, processing or testing.
 - 2) Identifying information for all facilities providing recipient selection information, compatibility testing, record-keeping, treatment for disease, or transplantation of HPCs and cellular products.
 - 3) Agreements, reviews of, and changes to agreements.
- 3. Additional Collection and Processing Records
 - a. Physician authorization/order(s) for collection and processing.
 - b. Product name, unique numeric or alphanumeric identification, preparation volume and additives, date of collection, and date of processing.
 - c. Procedure record, including the person responsible for each step.
 - d. Details of product collection and processing, including the following results:
 - 1) Measurements of established collection and processing parameters.
 - 2) Manipulations other than minimal.

- 3) Name, lot number, and expiration date of all reagents, supplies, and materials used during collection and processing.
- 4) Identification of any materials used on an emergency basis.
- e. Labeling, including identity of individuals performing any container transfer.
- f. Verification of the accuracy of the final container label prior to issue.
- g. Name and address of collection and processing facility.
- 4. Quarantine Records
 - a. Quality assurance and technical review of the donor chart.
 - b. Medical director review and approval.
 - c. Authorization to release any product with a positive infectious disease marker test.
 - d. Inspection of container at issue.
- 5. Storage, Distribution, or Disposal Records
 - a. Reissuance, including temperature records.
 - b. Final disposition of each product.
 - c. Storage history of each product.
 - d. Product verification information when released.
 - e. Method and date of disposal for discarded products or disposition of products released for research.
 - f. Death or no need of HPCs or cellular product, and notification of appropriate parties.
- 6. General Records
 - a. Names, signatures, and initials or identification codes, qualifications, and inclusive dates of employment of those authorized to perform or review critical processing steps, including technical personnel, temporary personnel, and independent contractors.
 - b. Reports of unsatisfactory or mislabeled products or adverse reactions, including reports of investigation.
 - c. Verification of purchased materials (Reference Standard 6R-A applies).

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- d. Notification to the collection facility by the administering facility when a donor or patient seroconverts.
- e. Obsolete policies, processes, and procedures.
- B. Records that shall be retained for 10 years by the collecting service include:
 - 1. Storage temperature charts and records, including temporary transport storage.
 - 2. Quality control records
 - a. Calibration of equipment.
 - b. Performance checks of equipment and reagents.
 - c. Periodic check of sterile technique.
 - d. Periodic tests of transport equipment.
 - e. Quality control testing results, interpretation, and corrective action for out-of-range values.
 - f. Results of external proficiency testing, if performed.
 - g. Validation of equipment.
 - 3. General Records
 - a. Technical personnel
 - 1) Training and continuing education.
 - 2) Periodic competency testing.
 - b. Maintenance records for equipment, including preventive maintenance.
 - c. Sterilization of supplies and reagents.
 - d. Disposition of rejected supplies and reagents.
 - e. Management review of quality system.
 - f. Annual review of policies, processes, and procedures.
 - g. Design output, review, verification, validation, changes and approvals for new or changed HPCs and cellular products.
 - h. Validation of new policies, processes, and procedures.
 - j. Monitoring of environmental conditions.
 - j. Corrective actions taken.
 - k. Results and executive management review of internal assessments.

Reference Standard 16R-B. Record Retention for the Cellular Product Administration

Records that shall be retained indefinitely by the administering HPC and cellular product service include:

- A. Autologous Recipient Records
 - 1. Patient identification and diagnosis.
 - 2. Medical history and physical examination.
 - 3. Informed consent.
 - 4. Interpretation of ABO group and Rh type, and tests for infectious disease markers.
 - 5. Any adverse reaction suspected to be linked to the cellular product administration.
 - 6. Outcomes of transplantation, including engraftment data on the HPC transplant recipient.
 - 7. Any data required to be maintained by IRB-, IND-, IDE-approved or other protocol.
- B. Allogeneic or Syngeneic Recipient Records
 - 1. Patient identification and diagnosis.
 - 2. Medical history and physical examination.
 - 3. Informed consent.
 - 4. Interpretation of ABO group and Rh type, and tests for infectious disease markers; detection and identification of unexpected red cell antibodies; HLA determinations; and red cell compatibility testing with the intended donor.
 - 5. Any adverse reaction suspected to be linked to the administration.
 - 6. Outcomes of transplantation, including engraftment data on the HPC transplant recipient.
- C. Administration Records
 - 1. Identification of all cellular products administered, traceable to all donor information.
 - 2. Visual inspection prior to administration.
 - 3. All pertinent administration event information, including patient vital signs and time of all recorded events.

17. QUALITY ASSESSMENTS

17.1 General

The HPC and cellular product service shall perform quality assessments that verify whether the quality system and the collection, processing, storage, distribution, and administration of HPCs and cellular products and the provision of related services comply with requirements, and that determine the effectiveness of the quality system.

The HPC and cellular product service shall establish and maintain policies, processes, and procedures for scheduling and conducting external and internal quality assessments. These internal quality assessments shall verify whether the quality system and the collection, processing, storage, distribution, and administration of HPCs and cellular products and services comply with requirements and shall determine the effectiveness of the quality system.

Internal quality assessments shall be planned on the basis of the importance of the activity to the quality of the product or service. The results of the internal quality assessment shall be reviewed by personnel independent of those having direct responsibility for the activity being assessed.

The results of internal quality assessments shall be reviewed by executive management. The results of the assessments shall be recorded in conformance with Section 16, Control of Records, and reviewed by the personnel having responsibility for the area being assessed. The management personnel responsible for the area shall take timely corrective action on nonconformances found during the assessment.

Follow-up action shall verify and record the implementation and effectiveness of the corrective action and preventive action taken.

17.2 External Quality Assessments

The HPC and cellular product service shall successfully participate in an external quality assessment program. The results of external quality assessments shall be reviewed by executive management. Records shall be maintained in conformance with Section 16, Control of Records.

17.3 Engraftment Data and Outcomes of Administration and/or Transplantation

The HPC and cellular product service shall review information relating donor and collection outcomes to methods of HPC mobilization and other manipulations and review information relating recipient outcomes to the variables in collection, processing, storage, distribution, and administration of HPCs and cellular products.

- 17.3.1** The outcome parameters for HPCs and cellular products shall be stated in agreements with the administering or transplanting facility, in conformance with Standard 3.5.1.

18. TRAINING

18.1 **General**

The HPC and cellular product service shall establish and maintain policies, processes, and procedures for identifying training needs and provide for the training of all persons performing activities affecting quality. Persons performing specific assigned tasks shall be qualified on the basis of appropriate education, training, or experience. Records shall be maintained in conformance with Section 16, Control of Records.

18.2 **Competence**

Evaluation of continued competence shall be performed. Records shall be maintained in conformance with Section 16, Control of Records.

19. STATISTICAL TECHNIQUES

19.1 Identification of Need

The HPC and cellular product service shall identify the need for statistical techniques required to establish, control, and verify process performance and product characteristics.

19.2 Application of Statistical Techniques

When statistical techniques are used, the HPC and cellular product service shall establish and maintain policies, processes, and procedures to implement and control the application of the statistical techniques.

20. SAFETY

20.1 General

The HPC and cellular product service shall establish and maintain policies, processes, and procedures designed to minimize risks to the health and safety of employees, donors, volunteers, and, where applicable, patients and other persons affected within the work environment. Suitable quarters, environment, and equipment shall be available to maintain safe operations.

The policies, processes, and procedures shall address biological, chemical and, where applicable, radiation safety and appropriate intervention to mitigate exposure, and shall include a system for monitoring training and compliance.

HPCs and cellular products and other biohazardous materials shall be handled and discarded in a manner that minimizes the potential for human exposure to infectious products.

20.2 Compliance with External Safety Requirements

The HPC and cellular product service shall comply with all applicable requirements relating to safety issued by the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), and the Occupational Safety and Health Administration (OSHA).

20.3 Handling Products

The HPC and cellular product service shall ensure proper handling of cellular products in recognition of the potential for exposure to infectious agents.

20.3.1 Discarding Products

Products shall be discarded according to applicable laws.

20.3.2 Discarding Infectious Products

The HPC and cellular product service shall obtain the approval of the medical director and/or recipient's physician for the discard or release of HPCs and cellular products to be used for research purposes. Records shall be maintained in conformance with Section 16, Control of Records.



GLOSSARY

Activity: A defined and organized process with intended results or outcomes.

Adverse Reactions: A noxious or unintended response to any HPC and cell product for which there is a reasonable possibility that the response may have been caused by the product.

Agreement: A contract or order that is a binding understanding between two or more parties, including a facility and one of its customers.

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

Allogeneic Donor: A person who donates blood or tissue to a recipient, who may be genetically related or unrelated.

Analyte: Substance or chemical constituent that is assayed.

Aseptic Methods: Methods designed to eliminate the risk of microbial contamination to a product, reagent, specimen, or person in a laboratory or clinical care setting.

Assessment: A systematic and independent examination to determine whether quality activities comply with planned activities and whether these activities are implemented effectively and are suitable to achieve objectives. Assessments also include comparison of results to expected results. Types of assessments include external assessments, internal assessments, peer review, and self-assessments.

Autologous Donor: A person who acts as his/her own blood or tissue donor.

Calibrate: To set measurement equipment against a known standard.

CD34: A cell surface antigen present on HPCs, expressed in decreasing quantity as progenitor cells differentiate and mature. This antigen is used

in flow cytometric identification and quantitation of HPCs and as the basis for selection methods that isolate HPCs.

Certified by CMS: Having met the requirements of Clinical Laboratory Improvement Amendments of 1988 through inspection by CMS (formerly HCFA), a deemed organization, or an exempt state agency.

Compliance: See Conformance.

Conformance: Fulfillment of requirements.

Competence: Ability of an individual to perform a specific task according to procedures.

Corrective Action: An activity performed to eliminate the cause of an existing nonconformance or other undesirable situations in order to prevent reoccurrence.

Critical Equipment: A piece of equipment that can affect the quality of the facility's products or services.

Cross Contamination: Transmission of infectious or contaminating agents among reagents, product, or supplies.

Cryopreservation: The process of low-temperature freezing and storage of cellular products that preserves cells which, after thawing, retain a significant measure of their pre-freeze viability and function.

Cryoprotectant: A solution or additive which, when combined with living cells, provides protection from damage otherwise induced by the freezing and/or thawing process.

Customer: The receiver of a product or service. A customer may be internal, ie, another department within the same organization, or external, ie, another organization.

Design Control: Procedures to control, verify, and validate product, service, design, and supporting software.

Design Goals: A list of physical and performance requirements, including regulatory and customer requirements, that shall be included in de-

signing a new product or service. The design input may also list the expected goals of a new product or service.

Design Output: The results of a design effort. The finished design output consists of documents used to meet physical and performance requirements defined in design input for the product or service, and includes packaging and labeling specifications, if applicable.

Design Validation: Design validation typically follows successful design verification and is normally performed under defined operating conditions. It is normally performed on the final product, but may be necessary in earlier stages prior to product completion. Multiple validations may be performed if there are different intended uses.

Design Verification: Design verification may include performing alternative calculations, comparing the new design with a similar proven design, if available, undertaking tests and demonstrations, and reviewing the design-stage documents before release.

Deviation: An unexpected or unplanned undesirable event.

Disposition: The final status or control of an HPC or cellular product in a given facility.

Distribute: To transfer a finished product or deliver a service to an external customer.

Document (noun): Written or electronically generated information. Examples of documents include quality manuals, policies, processes, procedures, labels, or forms.

Donor-Patient: A person whose blood, tissue, or HPCs are collected for possible autologous transfusion or administration.

Engraftment: In-vivo proliferation and differentiation of infused HPCs, in an autologous or allogeneic recipient, typically assessed by recovery of circulating blood cell counts.

Establish: To define, document, and implement.

Ex Vivo: Outside of a living body, denoting removing of cell or tissue for manipulation, after which it is returned to the living body.

Executive Management: The highest level personnel within an organization, including employees 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: That part of the organization that is assessed and accredited by the AABB. A location or operational area within an organization. AABB accreditation is granted to specified facilities for specific activities.

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 conformity is achieved for each characteristic.

Function: The special, normal, or proper physiologic activity of an HPC or cellular product that can be qualitatively or quantitatively evaluated (for example by in-vitro, in-vivo, and/or ex-vivo assays).

Growth Factors: Recombinant cytokines that promote proliferation and/or differentiation of specific cell types or lineages. Certain growth factors are used in vivo for mobilization of HPCs.

Hematopoietic Progenitor Cells (HPCs): Cells that are capable of proliferation and differentiation into one or more of the hematopoietic lineages, which include granulocytes, monocytes, erythrocytes, and platelets. Marrow, mobilized peripheral blood, or umbilical cord blood may be collected as an HPC source for clinical transplantation.

HPC and Cellular Product Service: A facility involved in 1) qualifying donors, 2) performing one or more of the manufacturing steps for HPC products (including collection, processing, and storage), or 3) distributing these products.

In Vitro: Observable in an artificial environment.

In Vivo: Within the living body.

Inspect: To measure, examine, or test one or more characteristics of a product or service and compare results with specific requirements.

Label: An inscription affixed 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 dates, cautionary statements, or indications for use.

Laboratory Director: A qualified individual holding a relevant doctoral degree who is responsible for all technical aspects of the HPC and Cellular Product Service.

Maintain: To keep in the current state; to preserve or retain; to keep in a state of validity.

Material: A good or supply item used in a process or procedure to prepare the final product or service. Reagents are a type of material.

Medical Director: A qualified licensed physician who has overall responsibility and authority for all medical aspects of the HPC and Cellular Product Service.

Medical Therapy: The direct provision of a medical intervention ordered by a physician, eg, therapeutic phlebotomy, issuing a unit for infusion.

Myeloablative Therapy: Treatment of a patient with an agent (eg, chemotherapy or gamma irradiation) that causes marrow aplasia reversible only with administration and engraftment of HPCs.

Nonconforming: A product or service that does not satisfy one or more specified requirements, such as an unacceptable blood product, blood sample, test run, or apheresis procedure.

Organization: An institution, or part thereof, that has its own functions and executive management.

Output: Information or product that results from a process.

Patient-Specific Product: A product collected and/or prepared exclusively for a particular autologous or allogeneic recipient.

Policy: A documented general principle that guides present and future decisions.

Preventive Action: An activity performed to eliminate the potential for nonconformance or other undesirable situations.

Procedure: A description of how an activity is to be performed, ie, a standard operating procedure.

Process: The transformation of input into output. This transformation can be achieved by an activity or a series of interrelated activities.

Process Control: Efforts made to standardize and control processes in order to produce predictable output.

Product: The tangible result of a process.

Proficiency Testing: The structured evaluation of laboratory methods that assesses the suitability of processes, procedures, equipment, supplies, and reagents.

Quality: Characteristics of a product or service that bear on its ability to meet requirements, including those defined during agreement review.

Quality Assurance: Confidence that the policies, processes, and procedures that influence the quality of the product and service are working as expected, both individually and collectively.

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

Quality Manual: A document that describes the facility's quality system.

Quality Planning: Activities that identify the requirements and the intended method of achieving those requirements prior to the production of a new or changed product or service.

Quality Policy: A documented general principle expressed by executive management that guides present and future decisions regarding quality.

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

Quarantine (verb): To isolate nonconforming materials or products in a clearly marked area so that they cannot accidentally be used in a downstream process.

Rate-Controlling Device: The process of freezing products at a specified rate of temperature change.

Reagent: A substance used to perform an analytical procedure. A substance used (as in detecting or measuring a component or preparing a product) because of its biological or chemical activity

Record: Information captured in writing or electronically that provides objective evidence of activities that have been performed or results that have been achieved, such as test records or audit results. Records do not exist until the activity has been performed.

Recovery: The proportion of a starting cell population remaining after one or more ex vivo manipulations.

Reference Standard: Specified requirements defined by AABB (see Specified Requirements). Reference requirements define how or within what parameters an activity shall be performed and are more detailed than system requirements contained in these AABB standards.

Regulation: Law promulgated by federal, state, or local authorities.

Related Donor: An allogeneic donor who is a blood relative of the recipient.

Release: Removal of product from quarantine or in-process status for distribution.

Service: The intangible result of a process. Services may include contracted laboratory testing services, gamma irradiation services for blood components, or reference laboratory services.

Shall: A term used to indicate a requirement.

Specified Requirements: Any requirement in these AABB standards and including but not limited to FDA requirements, specific customer requirements, and requirements of other accrediting organizations.

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

Statistical Techniques: Established mathematical methods used to collect, analyze, and present data.

Sterility: Free from living micro-organisms.

Supplier: An organization that provides a product or service.

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.”

Traceability: The ability to trace the history, application, or location of a product by means of recorded identification.

Tracking: To follow all steps of a process or procedure from the beginning to end.

Trend: A movement of measurement data in a specific direction over a period of time.

Unrelated Donor: An allogeneic donor who is not a blood relative of the recipient.

Validation: Ensuring that identified product or service parameters are capable of being met prior to the implementation of new or changed processes and procedures.

Verification: Affirmation of the accuracy of something. New or changed processes are verified against the design goals before being implemented.

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

**CROSSWALK BETWEEN 2ND AND 3RD EDITIONS OF
STANDARDS FOR HEMATOPOIETIC PROGENITOR
CELL AND CELLULAR PRODUCT SERVICES**

The following “crosswalk” traces each standard in the 2nd and 3rd editions of *HPC and Cellular Product Services Standards*. Each standard in the 3rd edition corresponds with its predecessor in the 2nd edition. The “crosswalk” is offered as assistance to those who will be updating their facility’s procedures to be compliant with the most current edition of *HPC and Cellular Product Services Standards*. Its use should not take the place of a thorough, line-by-line analysis of each standard.

3RD	2ND	3RD	2ND	3RD	2ND
1	1	3.5.1	3.5.1	5.1	5.1
1.1	1.1	3.5.2	3.5.2	5.2	5.2
1.2	1.2		3.5.2.1	5.3	5.3
1.2.1	1.2.1	3.5.2.1	3.5.2.1	5.4	5.4
1.2.2	1.2.2	3.5.2.2	New	5.5	5.4
1.2.3	1.2.3	3.5.3	New	5.6	5.5
1.2.4	1.2.4	3.5.4	9.3.2	6	6
1.2.5	1.2.5	3.5.4.1	9.3.2.1	6.1	6.1
1.2.5.1	1.2.5.1	3.6	New	6.2	6.2
1.2.5.2	1.2.5.2	3.7	New	6.3	6.3
1.2.5.3	1.2.5.3	3R-A	9R-A	6.4	6.4
1.2.5.4	1.2.5.4	4	4	6.4.1	6.4.1
2	2	4.1	4.1	6.4.2	New
2.1	2.1	4.2	4.2	6.5	New
2.2	2.2	4.3	4.3	6R-A	New
2.3	2.3	4.4	4.4	7	7
2.4	2.4	4.5	4.5	7.1	7.1
3	3	4.6	4.6	7.1.1	7.1
3.1	3.1	4.7	4.7	7.2	7.2
3.2	3.2	4.8	4.8	7.2.1	7.2.1
3.3	3.3	4.9	4.9	7.2.2	7.2.2
3.4	3.4	4.9.1	4.9.1	7.2.2.1	7.2.2.1
3.5	3.5	5	5	7.2.3	7.2.3

Crosswalk

3RD	2ND	3RD	2ND	3RD	2ND
8	8	9.3.2	9.2.1	9.6.3.3	9.5.3.4
8.1	8.1	9.4	9.3	9.6.3.4	9.5.3.5
8.2	New	9.4.1	9.3.3	9.6.4	9.5.4
8.2.1	8.2.1.2	9.4.1.1	9.3.3.1	9.6.4.1	9.5.4.1
8.2.2	8.2.1.1	9.4.1.2	9.3.3.2	9.6.4.2	9.5.4.2
8.2.2.1	8.2.1.1.1	9.4.1.3	9.5.3.1	9.6.4.3	9.5.4.3
8.2.2.2	New	9.4.2	9.5.3	9.6.4.4	9.5.4.4
8.2.2.3	8.2.1.2.1	9.5	9.4	9.7	9.6
8.2.3	8.2.1.3	9.5.1	9.4.1	9.8	9.7
8.3	8.2.2	9.5.1.1	New	9.9	9.8
8.3.1	8.2.2.1	9.5.1.2	9.4.1.1	9.9.1	New
8.3.1.1	New	9.5.1.3	9.4.1.2	9R-A	9R-B
8.3.2	8.2.3	9.5.1.4	9.4.1.3	9R-B	9R-C
8.4	New	9.5.1.5	New	9R-C	9R-E
8R-A	8R-A	9.5.1.6	New	9R-D	9R-G
8R-B	8R-A	9.5.2	New	9R-E	9R-H
9	9	9.5.2.1	New	9R-F	9R-I
9.1	9.1	9.5.2.2	New	10	10
9.1.1	9.1.1	9.5.2.3	9.5.2.6	10.1	10.1
9.1.1.1	9.1.1.1		13.2.2	10.2	10.2
9.1.1.2	New	9.5.2.4	New	10.2.1	10.2.1
9.1.1.3	9.1.1.2	9.6	9.5	10.2.2	10.2.2
9.1.2	17.4	9.6.1	9.5.1	10.2.3	10.2.3
	17.4	9.6.1.1	9.5.1.1	10.3	10.3
9.1.3	17.4	9.6.1.2	9.5.1.2	10.3.1	10.3.1
9.1.4	9.1.2	9.6.1.3	9.5.2.1	10.3.2	10.3.2
9.1.5	9.1.3	9.6.1.4	9.5.1.3	10.3.2.1	10.3.2
9.1.6	9.1.4	9.6.1.5	9.5.1.4	10.4	10.4
9.1.7	New	9.6.2	9.5.2	10.5	10.5
9.1.7.1	9.1.5	9.6.2.1	9.5.2.2	10.6	10.6
9.1.7.2	New	9.6.2.2	9.5.2.3	10.6.1	New
9.2	New	9.6.2.3	9.5.2.4	10.6.2	10.6.1
9.2.1	New	9.6.2.4	9.5.2.5	10.6.2.1	10.6.1.1
9.2.2	New	9.6.2.5	9.5.2.6	10.6.2.1.1	New
9.2.3	New	9.6.3	New	10.6.2.2	10.6.1.3
9.3	New	9.6.3.1	9.5.3.2	10.6.2.2.1	10.6.1.3.1
9.3.1	New	9.6.3.2	9.5.3.3	10.6.2.2.2	10.6.1.3.2

3RD	2ND	3RD	2ND	3RD	2ND
10.6.2.3	New	13.4.2	14.2.1.1	16.3.1	New
10.7	10.7	14	14	16.4	16.4
10.8	10.8	14.1	14.1	16.4.1	16.4.1
10R-A	10R-A	14.2	14.2	16.4.2	New
10R-B	10R-B	14.3	14.3	16R-A	16R-A
10R-C	10R-C	15	15	16R-B	16R-B
11	11	15.1	15.1	17	17
11.1	11.1	15.2	15.2	17.1	17.1
11.2	11.2	15.2.1	15.2.1		17.2
11.2.1	New	15.2.1.1	New	17.2	17.3
11.3	11.2	15.2.2	15.2.2	17.3	17.5
12	12	15.2.2.1	15.2.2.3	17.3.1	New
13	13	15.2.2.2	15.2.2.2	18	18
13.1	New	15.2.2.3	15.2.2.1	18.1	18.1
13.1.1	13.1	15.2.3	15.2.3	18.2	18.2
13.1.2	13.2	15.3	15.3	19	19
13.2	13.2.1	15.3.1	15.3.1	19.1	19.1
13.2.1	13.2.1.1	15.3.1.1	New	19.2	19.2
13.2.2	13.2.1.2	15.3.1.2	15.3.1.1	20	20
13.2.3	13.2.2	15.4	New	20.1	20.1
13.3	13.3	16	16	20.2	20.2
13.3.1	New	16.1	16.1	20.3	20.3
13.4	14.2.1	16.2	16.2	20.3.1	New
13.4.1	14.2.1	16.3	16.3	20.3.2	20.3.1



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