

*FACT-JACIE International Standards for Cellular Therapy Product  
Collection, Processing, and Administration*  
**SIGNIFICANT CHANGES FROM 3<sup>RD</sup> EDITION TO 4<sup>TH</sup> EDITION**

This document is intended to outline the significant changes made to the FACT-JACIE Standards during the 4<sup>th</sup> edition standards development process. The outline includes global changes and specific changes to the Clinical, Collection, and Processing sections. These do not include every change made to the Standards. Refer to the draft *FACT-JACIE International Standards for Cellular Therapy Product Collection, Processing, and Administration, 4<sup>th</sup> Edition* to review all changes.

### **Global changes:**

Quality Management and Policies and Procedures: In the fourth edition, the QM standards were realigned to reduce redundant references to QM topics, yet still maintain the rigorous assurances of a QM Program that results in high-quality cellular therapy. The QM standards were organized in each section on a topical basis, and standards pertaining to operational quality control were relocated to the operational sections to which they pertain. Specific examples include:

- Streamlined standards to reduce redundancies within the Quality Management section and between the Quality Management section and Policies and Procedures section.
- Moved operational quality control activities out of the Quality Management sections and into the applicable operational sections.
- Dispersed repeated requirements across the Clinical, Collection, and Processing sections as they apply to those sections (specifically, Quality Management requirements for management of products with positive microbial culture results).
- Changed SOP review requirement from annually to biannually (or upon procedural changes, whichever is sooner).

Donor Selection, Evaluation, and Management: The Donor Selection, Evaluation, and Management sections in the Clinical Program and Collection Facility sections were modified to reflect the usual delineation of such responsibilities between clinical programs and collection facilities. The Collection Facility standards focus more on donor evaluation and management, with less emphasis on donor selection activities. To account for situations in which the Collection Facility is primarily responsible for donor selection activities, standards were included to establish that the Collection Facility in those situations are required to comply with the applicable Clinical Program standards. Specific examples include:

- Reorganized and reworded standards throughout section to clarify when requirements are applicable to allogeneic donors, autologous donors, or both.
- Limited scope of Collection Facility Requirements to “Donor Evaluation and Management,” and required compliance with Clinical Program standards pertaining to donor selection activities if the Collection Facility is primarily responsible for donor selection.

Appendices: Appendices were revised to clarify requirements and simplify the Standards. Appendices that are external tables and forms were removed and replaced with a reference table indicating the websites where the current versions can be found. This is in response to

situations in which external tables and forms are updated within months of publication of FACT-JACIE Standards, which causes the appendices to become extremely out of date over time. Specific examples include:

- Revised existing FACT-JACIE tables to clarify the difference between label content and accompanying documentation.
- Added “Accompanying Documents at Distribution” table.
- Removed external tables and forms (i.e. Modified Circular of Information Biohazard and Warning Label Table, TED forms, and MED-A forms) and inserted an appendix titled “External Tables and Forms,” which includes a reference table that directs readers to the website where the current versions of each of these tables and forms are found. (**Note:** Per Zbigniew Szczepiorkowski, the COI committee will retain ultimate responsibility for keeping this current.)
- Added the Circular of Information Testing Table to the External Tables and Forms appendix.
- Removed detail in Standards that contained duplicate information in the appendices and simply referenced the appendices.

Expanded Requirements: While a significant effort was placed upon simplifying the Standards under the idea that FACT-JACIE Standards are intended to be minimum standards rather than best practices, some requirements were expanded. Specific examples include:

- Written agreements (places responsibility of ensuring external entities comply with Standards and governmental laws and regulations on the Clinical Program/Collection Facility/Processing Facility).
- Disaster plans (explicitly states in standard the requirement to include the response of the Clinical Program/Collection Facility/Processing Facility as applicable).
- Concurrent plasma and samples required to have the same identifier as the cellular therapy product.

Terminology: Several uses of specific terminology were clarified in order to 1) reduce misinterpretations commonly found during the inspection and accreditation process and 2) account for international variations. Specific examples include:

- Changed “HPC” to “CTP” where applicable. In instances where only HPC applies, “HPC” is specifically referenced.
- Redefined “Distribution,” “Transportation,” and “Shipping” to clarify when a product is out of a responsible person’s control.
- Redefined “Available for Distribution” and “Release” to clarify instances where a product is distributed before meeting release criteria (e.g., cases requiring urgent medical need).
- Board eligibility/certification references changed to “specialist certification” to accommodate international education.
- References to specific governmental agencies and accrediting bodies (e.g., FDA, JCAHO, etc.) changed to verbiage similar to “appropriate governmental authorities” or “certified as required by governmental authorities.”
- Redefined validation to include only processes (including intended uses of equipment) and qualification to include only equipment, supplies, and reagents (in alignment with FDA interpretation).

- “Metropolitan Statistical Areas” in Clinical standard B1 replaced with “defined networks” to accommodate the international community. Examples of defined networks are explained in the guidance information.

## **Specific sectional changes:**

### Clinical Program Standards

- General reorganization to make requirements more parallel to Collection and Processing sections.
- New standards requiring minimum volumes for programs requesting accreditation for only autologous transplants.
- New requirements for cases involving planned pre-engraftment discharges.

### Collection Facility Standards

- Collection Facility Director not required to have doctoral degree if he/she possesses relevant degree qualified by experience and training.
- Clarification of minimum volume requirements for facility and minimum experience of Directors for apheresis collection procedures and bone marrow collection procedures.

### Processing Facility Standards

- Required to audit external facilities under written agreements with the Processing Facility.
- Expanded requirements for aliquots.
- Clarification that ready-access to and/or summarized documentation of required accompanying documentation (such as electronic access) is sufficient.