FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY

Summary of Changes

Draft Ninth Edition FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration

and

Draft Third Edition FACT-JACIE International Immune Effector Cell Standards

This document summarizes the major changes proposed in the Ninth Edition *FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration* (HCT) and the Third Edition *FACT-JACIE International Immune Effector Cell Standards* (IEC). This summary does not list all proposed changes made to the Standards. Reorganization or clarified verbiage is not included unless considered to be a significant change to the intent of a standard. Refer to the Standards for all revisions.

The review for the ninth edition HCT Standards and third edition IEC Standards includes multiple structural and content changes. These include:

- A single collection section was created which includes apheresis, marrow, and other tissue sources. This change was introduced to reflect advances in the field and to incorporate evolving cell collection types and practices.
- Standards and edits were introduced to standardize practices related to Risk Evaluation and Mitigation Strategies (REMS).
- New audit requirements were added in Clinical, Collection, and Processing Standards 4.8.4 through 4.8.6.
- New Standards recommending a Chain of Identity Identifier (C7.1.3, C7.3.2, D7.1.3, and D7.3.2) to be assigned before or at the time of collection to each collection intended for further manufacturing were introduced.
- The Standard for Processing Facility Director qualifications (D3.1.1) has not changed. The committee did propose guidance to consider a pathway for individuals who do not possess a doctoral level degree to serve as the director.

The HCT and IEC sections of this document are organized into two primary sections and multiple subsections. "Major Changes" and its corresponding table identify concepts present throughout the document that impact all areas of cellular therapy, including new definitions. "Changes by Section" and the immediately following table examine Clinical Standards (Part B), including Quality Management, and details changes which impact the clinical program. The subsequent tables in this section summarize Standards specific to Collection (Part C) and Processing (Part D). Finally, major changes to the appendices are noted in the last table.

Each table includes the subject matter of the change, an explanation of its rationale or intention, and its location in the Standards. In the location column, the word "Standards" represents multiple Standards in the specified location which are related to the change.

Major Changes

Topic	Explanation	Related Standard(s)
New definition: *Assent*	New requirement to document minor's participation in their care.	A4, B6.2.6.1
New definition: *Clinical site*	To clarify the location where patient or donor services are received.	A4
New definition: *Collection Site*	Physical location where cells are collected.	A4
Revised definition: *Good Manufacturing Practice (GMP)*	Edited to match the current definition published by the US Food and Drug Administration	A4
New definition: *Investigator's Brochure*	Defined data for investigational products.	A4
New definition: *Package insert*	Defined information prepared by manufacturers for approved drugs.	A4
New definition: *Risk Evaluation and Mitigation Strategy (REMS)*	Drug safety program required by the US FDA	A4
New definition: *Risk management plan*	Process used to minimize risk associated with the use of a cellular therapy product	A4
Additional periodic audits	New audits to be performed periodically	B4.8.4 Standards C4.8.4 Standards D4.8.4 Standards
Audits as follow-up to occurrences	New Standard	B4.8.5 C4.8.5 D4.8.5
Management of external audits	New Standard	B4.8.6 C4.8.6 D4.8.6
Critical electronic records	Standard edited to include those systems under the control of the Facility.	B10.4.2 Standards C12.7.2 Standards D13.4.2 Standards

Changes by Section

Part B: Clinical Program Standards	
Topic	**Related Standard(s)**
New Standards: General Clinical Program	B1.4, B1.8, B1.9
Lineage specific chimerism	B2.18.1
Director requirements	B3.1.1
Physician specialty requirements for non-transplant therapies	B3.2.1.1, B3.2.1.2
Attending physician knowledge requirements	B3.3.6 Standards
Nurse training requirements	B3.6.2.2, B3.6.2.4
Care interventions to manage complications. Examples previously in the Standard will now be in guidance. Additional examples added to address REMS.	B3.6.2.6
Pharmacist training requirements	B3.7.2.2, B3.7.2.3
Consultant specialty	B3.8.1.18
GxP training (new requirement)	B4.4.2.5
Program audits. Note that both the US and JACIE have new form names for reporting clinical data.	B4.8.3 Standards
Management of products with positive microbial culture results	B4.9.2, B4.9.5
Documentation	B4.10.3.1
Required qualifications in the Quality Management Plan	B4.13
Standard Operating Procedures: • Informed consent • Management of complications • Chain of Identity • Chain of Custody	 B5.1.3 B5.1.12 B5.1.21 B5.1.22
Donor evaluation	B6.1.2 Standards, B6.3.3 Standards
Donor consent	B6.2.1.2
Pregnancy testing prior to mobilization	B6.3.5.1
Donor follow-up, adverse events	B6.3.11.1
Donor retention records	B6.5 Standards
Recipient informed consent	B7.1.2
Safe administration policies	B7.6.3
Management of IEC complications	B7.8
Discharge/follow-up care	B7.9.2.1, B7.11.1, B7.11.2, B7.11.3.7
Informed consent for a research subject	B8.3.2 Standards
Clinical Program data accuracy. Note: the form names have changed.	B9.1 Standards, B9.2
Records management system	B10.1 Standards, B10.2

Part B: Clinical Program Standards	
Topic	**Related Standard(s)**
Records to be maintained	B10.3.1
Electronic records	B10.4.1 Standards

Part C: Collection Facility Standards	
Topic	**Related Standard(s)**
Site qualifications	C1.5, C1.7
Facility Standards	C2.1
Facility, Marrow Facility, and Other Tissue Facility Director requirements	C3.1.1 Standards, C3.2.4
Medical Director requirements	C3.2.1 Standards
Director and Medical Director training requirements	C3.1.3 Standards, C3.2.5
Facility and Medical Director responsibilities	C3.1.2, C3.2.2 Standards
Standard Operating Procedures: • Qualifying critical supplies/equipment	C4.13.1
Standard Operating Procedures: Critical aspects of operations: • Storage • Product disposal • Cleaning and sanitation • Environmental control • Extracorporeal photopheresis • Chain of Identity • Chain of Custody	 C5.1.11 C5.1.14 C5.1.17 C5.1.18 C5.1.22 C5.1.23 C5.1.24
Donor evaluation and management	C6.1.1
Donor consent	C6.2.1.6
Risks of collection	C6.3.2.3, 6.3.2.4
Hemoglobinopathy risk	C6.3.3.1
Donor suitability	C6.3.6, C6.3.7
Allogeneic donor requirements	C6.4.2.1
ISBT 128 Chain of Identity Identifier	C7.1.3, C7.3.2 Standards, C7.3.5
Label content	C7.4.1.1, C7.4.2.1, C7.4.7
Equipment and supply qualification	C8.1
Inventory control	C8.3 Standards
Equipment management	C8.4.1 Standards, C8.4.2 Standards
Use of critical reagents and supplies	C8.5
Inventory of critical reagents and supplies	C8.6 Standards

Part C: Collection Facility Standards	
Topic	**Related Standard(s)**
Blood count criteria	C9.4 Standards
Donor identity	C9.9
Collection containers	C9.11 Standards
Records in case of divided responsibility	C9.15.1
Additional requirements for apheresis collection	C9.16 Standards
Additional requirements for bone marrow collection	C9.17 Standards
Additional requirements for other tissue collection	C9.18 Standards
Storage temperature	C10.3 Standards
Storage monitoring	C10.4 Standards
Transportation and shipping: • Product integrity and safety • Internal transport • Transport/ship on public roads • Temperature range • Transit time • Contingency plans • X-Ray irradiation	 C11.3 C11.4 Standards C11.5 Standards C11.6 C11.9 C11.10 C11.13
General records	C12.1
Records to be maintained	C12.3 Standards
Electronic records	C12.7 Standards

Part D: Processing Facility Standards	
Topic	**Related Standard(s)**
Oxygen sensors alarms	D2.11.1
Facility and Medical Director requirements	D3.1.1, D3.2.1, D3.2.3, D3.2.4
New Guidance establishing a process through accreditation to approve a Processing Facility Director who does not possess a doctoral level degree. **Explanation:** The Processing Facility Director must be an individual with a medical degree, doctoral degree, or an equivalent degree in a relevant science with appropriate experience. A director without a doctoral degree will require documentation of additional experience and competency. The relevant Accreditation Committee will consider the documentation to determine suitability to perform the role of the Director.	D3.1.1 guidance

Part D: Processing Facility Standards	
Topic	**Related Standard(s)**
The Processing Facility Director must be qualified by training or experience (or combined training and experience) for the scope of activities carried out by the Processing Facility. The director must demonstrate competency according to the scope of his/her responsibilities. The director should understand the procedures, identify critical points and expected outcomes, be capable of making improvements and corrections in procedures and accompanying documents, and understand basic laboratory techniques used by the laboratory. In addition, he/she must have practical training, experience, and be knowledgeable for each new procedure that is introduced into the facility, even if he/she is not responsible for performing the procedure (e.g., DC vaccines, MSC culture, flow cytometry). Experience requirements may exceed those required by the Standards based on Applicable Law.	D3.1.1 guidance (continued)
Quality Management Plan, qualification of critical equipment/services	D4.13 Standards
Qualification plan reports	D4.14 Standards
Reviewing feedback	D4.16
Standard Operating Procedures for critical aspects of operation	D5.1.10.1, D5.1.21, D5.1.22
Supply and equipment inventory control	D6.3 Standards
Equipment maintenance, cleaning, and calibration	D6.4 Standards
Inventory critical equipment	D6.6 Standards
ISBT 128 Chain of Identity Identifier	D7.1.3, D7.3.2 Standards
Product labels from third-party manufacturers	D7.4.8
Evaluation of cellular therapy products	D8.1.3 Standards, D8.1.4
Storage duration	D9.2.1
Expiration date for non-cryopreserved products	D9.2.3
Alarm system signals. New Standards addressing safety in areas where liquid nitrogen is present.	D9.6.2 Standards, D9.6.3
Temperature during product shipment	D10.6 Standards, D10.7
Shipping cellular therapy products	D10.11, D10.12
Electronic records	D13.4 Standards
Critical electronic records	D13.4.2 Standards

APPENDICES		
Number/Name	**Topic**	**Change**
Appendix I: Minimum Number of New Patients, Adult or Pediatric	Single site, IEC	• 3 during 12 months prior to accreditation • 3 average per year
	Multiple sites, Allogeneic and Autologous	• 10 allogeneic recipients, each site, prior to accreditation • 10 per year
	Multiple sites, IEC	• 3 each site, prior to accreditation • 3 each site, per year
Minimum Number of New Patients, Combined Adult and Pediatric	Single site, IEC	• 6 prior to accreditation, at least one in each population • 3 pediatric and 3 adults, each site, per year
	Multiple sites, Allogeneic and Autologous	• 5 adult and 5 pediatric allogeneic, 5 adult autologous, prior to accreditation
	Multiple sites, IEC	• 3 pediatric and 3 adults, each site, prior to accreditation • 3 pediatric and 3 adults, each site, each year
Minimum Number of New Patients, IEC Stand Alone		• 5 each population prior to accreditation • 5 each population, each year
Appendix II: Cellular therapy product labeling		• Label requirements for expiration date and time

Major Changes

Topic	Explanation	Related Standard(s)
New definition: *Assent*	New requirement to document minor's participation in their care.	A4, B6.2.6.1
New definition: *Clinical Site*	To clarify the location where patient or donor services are received	A4
Revised definition: Collection ~~Service~~ Facility	The field of cellular therapy has advanced and the concept of where care is provided requires updating.	A4
New definition: Collection Site	Physical location where cells are collected.	A4
Additional periodic audits	New audits to be performed periodically	B4.8.4 Standards C4.8.4 Standards D4.8.4 Standards
Audits as follow-up to occurrences	New Standards	B4.8.5 C4.8.5 D4.8.5
Critical electronic records	Standard edited to include those systems under the control of the Facility	B10.4.2 Standards C12.7.2 Standards D13.4.2 Standards

Changes by Section

Part B: Clinical Program Standards	
Topic	**Related Standard(s)**
General Clinical Program	B1.7, 1.9
Laboratory requirements	B2.16
Attending physician requirements	B3.2.1.2, 3.3.6 Standards
Director and attending physician training requirements	B3.3.4.12, B3.3.4.22
Nurse training requirements	B3.6.2 Standards
Pharmacist training requirements	B3.7.2 Standards
Data management staff training requirements	B3.10.2
Review of product outcome analysis	B4.7.3.1
Program audits. Note that both the US and JACIE have new form names for reporting clinical data.	B4.8.3 Standards
Management of external audits	B4.8.6
Documentation	B4.10.3.1
Required qualifications in the Quality Management plan	B4.13

Part B: Clinical Program Standards	
Topic	**Related Standard(s)**
Standard Operating Procedures: • Lymphodepletion regimen • Management of complications • Chain of Identity • Chain of Custody	 B5.1.6 B5.1.12 B5.1.21 B5.1.22
Donor evaluation	B6.1.2 Standards, B6.3.3 Standards
Donor consent	B6.2.1.2
Donor follow-up, adverse events	B6.3.10.1
Donor retention records	B6.5.1
Recipient informed consent	B7.1.2
Safe administration policies	B7.6.1
Recipient discharge and follow-up	B7.7.5, B7.9.1.1, B7.11.1, B7.11.2, B7.11.3.7
Management of IEC complications	B7.8
Informed consent for research subject	B8.3.2 Standards
Clinical Program data accuracy. Note: the form names have changed.	B9.1 Standards
Records to be maintained	B10.3.1
Electronic records	B10.4.1.8, B10.4.2 Standards

Part C: Collection Facility Standards	
Topic	**Related Standard(s)**
Site qualifications	C2.1.1, C2.4 Standards
Collection Facility Director-New requirement. This person can be the same person as the Medical Director.	C3.1 Standards
Medical/Marrow Director requirements	C3.2.1 Standard, C3.2.3, C3.2.4
Medical Director responsibility	C3.2.2 Standard
Medical Director training requirements	C3.2.5
Documentation	C4.10.3 Standards
Reporting requirement	C4.10.4.1
Standard Operating Procedures: • Qualifying critical supplies/equipment • Feedback	 C4.13 C4.16

Part C: Collection Facility Standards	
Topic	**Related Standard(s)**
Standard Operating Procedures: Critical aspects of operations: • Donor specific issues • Administration of blood products • Product disposal • Cleaning and sanitation • Chain of Identity • Chain of Custody	 C5.1.4 C5.1.7 C5.1.14 C5.1.18 C5.1.23 C5.1.24
Donor evaluation and management	C6.1.1
Donor consent	C6.2.1.6
Donor suitability	C6.3.4, C6.3.6
Donor eligibility determination	C6.4.6
Retention of donor records	C6.5.1, 6.5.3
ISBT 128 Chain of Identity Identifier	C7.1.3, C7.3.2 Standards, C7.3.5
Label content	C7.4.1.1, C7.4.2 Standards, C7.4.7
Equipment and supply qualification	C8.1
Inventory control	C8.3 Standards
Equipment management	C8.4.1 Standards, 8.4.2 Standards
Use of critical reagents and supplies	C8.5
Inventory of critical reagents and supplies	C8.6 Standards
Blood count criteria	C9.4 Standards
Donor identity	C9.9
Collection containers	C9.11 Standards
Additional requirements for apheresis collection	C9.16 Standards
Additional requirements for bone marrow collection	C9.17 Standards
Additional requirements for other tissue collection	C9.18 Standards
Storage temperature	C10.3 Standards
Storage monitoring	C10.4 Standards

Part C: Collection Facility Standards	
Topic	**Related Standard(s)**
Transportation and shipping: • Product integrity and safety • Internal transport • Transport/ship on public roads • Temperature range • High-dose therapy • X-Ray irradiation	 C11.3 C11.4 Standards C11.5 Standards C11.6 C11.8 C11.13
General records	C12.1
Records to be maintained	C12.3.1
Electronic records	C12.7 Standards

Part D: Processing Facility Standards	
Topic	**Related Standard(s)**
Oxygen sensor alarms	D2.11.1
New Guidance establishing a process through accreditation to approve a Processing Facility Director who does not possess a doctoral level degree. **Explanation:** The Processing Facility Director must be an individual with a medical degree, doctoral degree, or an equivalent degree in a relevant science with appropriate experience. A director without a doctoral degree will require documentation of additional experience and competency. The relevant Accreditation Committee will consider the documentation to determine suitability to perform the role of the Director. The Processing Facility Director must be qualified by training or experience (or combined training and experience) for the scope of activities carried out by the Processing Facility. The director must demonstrate competency according to the scope of his/her responsibilities. The director should understand the procedures, identify critical points and expected outcomes, be capable of making improvements and corrections in procedures and accompanying documents, and understand basic laboratory techniques used by the laboratory. In addition, he/she must have practical training, experience, and be knowledgeable for each new procedure that is introduced into the facility, even if he/she is not responsible for performing the procedure (e.g., DC vaccines, MSC culture, flow cytometry). Experience requirements may exceed those required by the Standards based on Applicable Law.	D3.1.1 guidance
Facility and Medical Director requirements	D3.1 Standards, D3.2.1, D3.2.3
Facility Director training requirements	D3.1.4

Part D: Processing Facility Standards	
Topic	**Related Standard(s)**
Standard Operating Procedures for products with positive microbial culture results	D4.9 Standards
Quality Management Plan, qualification of critical equipment/services	D4.13
Reviewing feedback	D4.16
Standard Operating Procedures for critical aspects of operation	D5.1.10.1, D5.1.21, D5.1.22
Supply and equipment inventory control	D6.3 Standards
Equipment maintenance, cleaning, and calibration	D6.4 Standards
Inventory critical equipment	D6.6 Standards
ISBT 128 Chain of Identity Identifier	D7.1.3, D7.3.2 Standards
Evaluation of cellular therapy products	D8.1.4 Standards
Storage duration	D9.2.1
Expiration date for non-cryopreserved products	D9.2.3
Stability program	D9.2.4.1
Alarm system signals. New Standards addressing safety in areas where liquid nitrogen is present.	D9.6.2 Standards, D9.6.3
Temperature during product shipment	D10.6 Standards, D10.7
High-dose therapy	D10.8
Shipping cellular therapy products	D10.11, D10.12
Electronic records	D13.4 Standards
Critical electronic records	D13.4.2 Standards

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Minimum Number of New Patients, Combined Adult and Pediatric	Single site, IEC	• 6 prior to accreditation, at least one in each population • 3 pediatric and 3 adults, each site, per year
	Multiple sites, IEC	• 3 pediatric and 3 adults, each site, prior to accreditation • 3 pediatric and 3 adults, each site, each year
Minimum Number of New Patients, IEC Stand Alone		• 5 each population prior to accreditation • 5 each population, each year
Appendix II: Cellular therapy product labeling		• Label requirements for expiration date and time • Donor identifier • Biohazard warning labels