FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY
AT THE UNIVERSITY OF NEBRASKA MEDICAL CENTER

FACT Common Standards for Cellular Therapies, Second Edition

Summary of Changes

This document summarizes major changes made to the Second Edition *FACT Common Standards for Cellular Therapies.* This summary does not list all changes made to the Standards; reorganization or clarified verbiage is not included unless considered to be a significant change. Refer to the final FACT Common Standards for all requirements.

Global Changes

1) Terminology

a) The term "Occurrence" was added to the FACT Common Standards, Second Edition. Occurrence has been defined as an incident or event that is out of compliance and may result in errors, accidents, deviations, adverse events, adverse reactions, or complaints. Where appropriate throughout the Standards, the term "Occurrences" replaces "errors, accidents, deviations, adverse events, adverse reactions, or complaints."
b) To provide clarity, the term "planned deviation" was introduced to replace "variance". Planned deviation is defined as an action allowed to occur with documented approval as the best course of action when adherence to the established course or accepted practice was not feasible or possible.

2) Quality Management (QM)

In addition to revising standards in the QM sections to explicitly and consistently state requirements, the following changes and additions were made:

a) Written agreements must be dated and reviewed on a regular basis, at a minimum every two years. (B/C/D4.6.3)
b) There must be an annual audit of:
    i. Infectious disease resulting from cellular therapy product collection or administration. (B4.8.3.4)
    ii. Documentation that external facilities performing critical services met the requirements of the written agreements. (B4.8.3.5)
    iii. Chain of custody of cellular therapy products. (B4.8.3.6)
c) Additional requirements for qualification include:
    i. The QM Plan must include policies and Standard Operating Procedures (SOPs) for qualification of critical manufacturers, vendors, equipment, supplies, reagents, facilities, and services. (B/C/D4.13)
    ii. Qualification plans, results, reports, and conclusions must be reviewed and approved by the Quality Manager and Clinical Program Director/Medical Director of collection activities/Processing Facility Director or designee. (B4.13.2, C4.13.1, D4.13.1)

d) Feedback must be obtained from associated programs and/or facilities in addition to donors and recipients or legally authorized representatives. This feedback may be obtained directly by the Clinical Program, Collection Facility, or Processing Facility; however, it is also acceptable to use hospital-wide systems, provided that issues relevant to the cellular therapy program can be readily identified. (B/C/D4.16)
e) QM activities must be reported, quarterly at a minimum, to representatives in key positions in all elements of the cellular therapy program to review the performance of the QM Program and its objectives. Meetings should have designated attendees, documented minutes, and assigned actions. Key performance data and review findings must be reported to staff. (B/C/D4.17)

3) *Additional Changes to Promote Consistency*

a) The following requirements from the Processing Facility Standards are now explicitly stated in the Clinical Program and Collection Standards:
    i. All waste generated by Clinical Program activities must be disposed of in a manner that minimizes hazard to facility personnel and to the environment in accordance with Applicable Law. (B2.12, C2.11)
    ii. Gloves, personal protective equipment, including protective clothing must be used while handling biological specimens. Such protective clothing shall not be worn outside the work area. (B2.13, C2.12)
    iii. The facility must document cleaning and sanitation and maintain order sufficient to achieve adequate conditions for operation. (B2.4, C2.6)
    iv. Cleaning and sanitation records must be retained for a minimum of three (3) years or longer in accordance with Applicable Law. (B10.1.2, C11.2.2)
b) Cellular therapy product transportation and shipping requirements in section C were updated to be consistent and include all requirements outlined in section D. (C10)

Changes to Clinical Program Standards

1) Products from Third-Parties (B1.2.1)

a) The Clinical Program's responsibilities when they directly receive a cellular therapy product for administration from a third-party or when it is routed through an intermediary facility such as a blood bank, tissue bank, or hospital pharmacy have been clarified. Additional responsibilities as required by the Second Edition include:
    i. Traceability and chain of custody of the cellular therapy product.
    ii. Cellular therapy product storage and distribution.
    iii. Verification of cellular therapy product identity.
    iv. Review and verification of product specifications provided by the manufacturer, if applicable;
    v. Readily available access to a summary of documents used to determine allogeneic donor eligibility; and
    vi. Documented evidence of donor eligibility screening and testing in accordance with applicable laws and regulations.

2) *Pharmacists (B3.7)*

a) Pharmacist standards were added and outline specific requirements including:
    i. Pharmacists must be licensed to practice in the jurisdiction of the Clinical Program and must be limited to a scope of practice within the parameters of their training and licensure.(B3.7.1)
    ii. Training and knowledge of designated must include: (B3.7.2)
        a) An overview of the process of cellular therapy. (B3.7.2.1)
        b) Pharmacological management of expected complications, if applicable. (B3.7.2.2)

3) *Recipient Care (B7.6, B7.7, B7.8)*

a) New requirements for recipient care were introduced in the Second Edition. The Clinical Program must have policies and Standard Operating Procedures for addressing appropriate follow-up after the administration of cellular therapy products; in place for the planned discharge and provision of follow-up care; and in place for the provision of appropriate long-term follow-up care to recipients.

4) *Data Management (B9)*

a) The First Edition of FACT Common Standards required Clinical Programs to collect all the data necessary to complete the Cellular Therapy Essential Data Forms of the CIBMTR for Regenerative Medicine or the Minimum Essential Data-A forms of the EBMT. The Second Edition expands these requirements to include:
    i. Clinical Programs must submit the data specified in B9.1 to a national or international database if required by Applicable Law.
    ii. Clinical Programs should collect the data specified in B9.1 for all patients for at least one (1) year following administration of the cellular therapy product.
    iii. The Clinical Program must define staff responsible for collecting and reporting data.
    iv. Defined data management staff should annually participate in continuing education.

5) *Clinical Program Electronic Records (B10.4)*

a) Electronic record requirements (similar to those applicable to cellular therapy collection and processing facilities) were added to the clinical section to address systems used to support cellular therapy-specific activities. It is not the intent of these Standards to include hospital-based electronic medical records, but only those electronic systems that are under the control of the Clinical Program. Critical electronic record systems may include commercial software, custom-made software, or databases and spreadsheets.

Changes to the Collection Activities Standards

1) *Collection Activities (C2)*

   a) New requirements were added for the use of collection kits. These requirements include:
      i. When a collection kit is prepared and sent to collection staff, there must be adequate instructions and materials to collect, label, store, pack, and transport or ship the cellular therapy product and associated samples to the Processing Facility. (C2.2)
      ii. The collection kit must be transported or shipped under conditions validated to maintain the designated temperature range from the time it leaves the Processing facility until it is received by the collection staff. (C2.2.1)

2) *Process Controls (C8)*

   a) The First Edition Common Standards required a process for inventory control that encompass equipment, supplies, and reagents. In the Second Edition, this was expanded to include a process to control storage areas to prevent mix-ups, contamination, and cross-contamination. (C8.2.4)
   b) Two new standards were added to the Second Edition FACT Common Standards requiring that:
      i. Equipment must be inspected for cleanliness and verified to be in compliance with the maintenance schedule prior to each use. (C8.3)
      ii. Equipment must be standardized and calibrated on a regularly scheduled basis and after critical repair or move as described in SOPs and in accordance with the manufacturer's recommendations. (C8.4)

Changes to the Processing Facility Standards

1) *Processing Facility (D2)*

   a) New requirements were added for the use of collection kits. These requirements include:
      i. When a collection kit is prepared and sent to collection staff, there must be adequate instructions and materials to collect, label, store, pack, and transport or ship the cellular therapy product and associated samples to the Processing Facility. (D2.2)
      ii. The collection kit must be transported or shipped under conditions validated to maintain the designated temperature range from the time it leaves the Processing facility until it is received by the collection staff. (D2.2.1)
      iii. Identity of the supplies and reagents including manufacturer, lot number, and expiration date must be documented for each collection. (D2.2.2)
      iv. Supplies and reagents shipped to the collection staff from the Processing Facility shall be in an outer container validated to maintain the designated temperature range. (D2.2.3)

2) *Reagents (D6.2.4)*

a) Requirements for use of supplies and reagents coming into contact with cellular therapy products during processing, storage, or administration that are sterile and of the appropriate grade for the intended use have been clarified.
   i. Reagents must undergo initial qualification for the intended use. (D6.2.4.1)
   ii. Where there are no suitable clinical or pharmaceutical grade reagents available, reagents must undergo lot-to-lot functional verification to confirm that new lots perform as expected. (D6.2.4.2)