

Donor Eligibility Final Rule

Requirements for Cell Therapy Products

Karen Edward, Quality Assurance

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Today's Topics

- **Review Donor Eligibility Regulations**
- **FHCRC/SCCA experience with implementation of the rules**
- **Specifics regarding DE and immunotherapy products**

21 CFR 1271 Summary

- **Current Good Tissue Practice (cGTP)** regulations cover **Donor Eligibility (Subpart C), Establishment and Maintenance of a Quality Program, Personnel, Procedures, Facilities, Environmental Control and Monitoring, Equipment, Supplies and Reagents, Processing and Process Controls, Process Changes and Validation, Labeling Controls, Storage, Receipt and Distribution, Records, Tracking, Complaint File, and Reporting**
- Applicable to “manufacturers” of **most types of human cellular and tissue-based products (HCT/Ps)**
- **Other cell-based products are also regulated under current Good Manufacturing Practice (cGMP)**
- **cGTPs finalized May 25, 2005**

Donor Eligibility – General

1271.45

➤ Donor eligibility determination is required for all donors of HCT/Ps

▪ HCT/Ps mean human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient [1271.3(d)]

HCT/Ps: hematopoietic stem/progenitor cells derived from peripheral and cord blood

Not HCT/Ps: Minimally manipulated bone marrow for autologous use; Ancillary products used in the manufacture of HCT/Ps

Donor Eligibility – General (cont.)

1271.45

- Donor eligibility determination is required for HCT/Ps regulated under both sections 351 and 361 of the PHS Act.
- Donor Eligibility determination is not required for autologous donors (some labeling requirements)
- An HCT/P must not be administered until the donor has been determined to be eligible (with some exceptions)

Donor Eligibility – General (cont.)

1271.50

- **A donor is eligible only if:**
 - **Free from risk factors for and clinical evidence of relevant communicable disease agents and diseases,**
 - **Free from communicable disease risks associated with xenotransplantation, and**
 - **Tests negative or nonreactive for relevant communicable disease agents**

Donor Eligibility – General (cont.)

1271.50

➤ A responsible person must determine and document the eligibility of a donor

▪ Responsible person means a person who is authorized to perform designated functions for which he or she is trained and qualified
[1271.3(t)]



Accompanying Records

1271.55

- **Unique product identifier**
- **Must not contain the donor's name or other personal information that might identify the donor**
- **Statement whether the donor was determined eligible or ineligible**
- **Summary of Records**

Accompanying Records (cont.)

1271.55

➤ Summary of Records

- Statement that testing performed in CLIA certified lab
- Listing and interpretation of test results
- Name and address of establishment that made the donor eligibility determination
- If donor ineligible, a statement noting the reason

Donor Eligibility Incomplete

1271.60

➤ **Keep HCT/P in quarantine until donor eligibility is complete**

▪ **Quarantine means the storage or identification of an HCT/P to prevent the improper release, in a physically separate area clearly identified for such use [1271.3(q)]**

Donor Eligibility Incomplete (cont.)

1271.60

- Not prohibited from infusing an HCT/P if donor eligibility determination incomplete, if documented urgent medical need
 - *Urgent medical need* means that no comparable HCT/P is available and the recipient is likely to suffer death or serious morbidity without the HCT/P [1271.3(u)]

Donor Eligibility Incomplete (cont.)

1271.60

- **Label HCT/P “Not Evaluated for Infectious Substances) and “WARNING: Advise patient of communicable disease risks”**
- **Include in accompanying records list of screening and testing that has been completed**
- **Include list of donor screening and testing that has not been completed**

Ineligible Donors

1271.65

- **Products “quarantined” and stored in a physically separate area for such use to prevent improper release**
- **Limited uses of HCT/Ps from ineligible donors are not prohibited**
 - **Allogeneic use in a first-degree or second-degree relative**
 - **Documented urgent medical need**

Ineligible Donors (cont.)

1271.65

➤ **Label HCT/P with:**

▪ **Biohazard Legend**



▪ **“WARNING: Advise patient of communicable disease risks”**

▪ **“WARNING: Reactive test results for (name of disease agent or disease)” – if applicable**

Donor Screening

1271.75

- **Review relevant medical records for:**
 - **Risk factors for, and clinical evidence of relevant communicable disease agents and diseases**
 - **Includes for leukocyte-rich HCT/Ps**
 - **HIV, types 1 and 2**
 - **HBV**
 - **HCV**
 - **Human TSE, including CJD**
 - **Treponema pallidum (syphilis)**
 - **HTLV, types 1 and 2**

Relevant Medical Records

1271.75

- **Donor medical history interview**
 - **Documented dialogue concerning the donor's medical history and relevant social behavior**
- **Physical examination**
 - **Assessment of physical signs of relevant communicable disease and signs of any risk factors for such disease**

Donor Testing

1271.80

- **Timing of specimen collection**
 - **30 days before recovery for PBSC and bone marrow**
 - **7 days before or after recovery for cord blood and DLI**

- **For a donor 1 month of age or younger, test a specimen from the birth mother**

Donor Testing (cont.)

1271.80

- **Use FDA-licensed, approved or cleared donor screening tests, according to manufacturer's instructions**
- **FDA recommends the use of NAT testing for living donors, if available**
- **Use a laboratory that is CLIA certified or equivalent**

Donor Testing (cont.)

1271.85

- **For viable, leukocyte-rich HCT/P donors**
 - **HIV, types 1 and 2**
 - **HBV**
 - **HCV**
 - **Treponema pallidum (syphilis)**
 - **HTLV, types 1 and 2**
 - **CMV – can use HCT/P where donor tests reactive, need to establish and maintain SOP governing the release of a CMV reactive HCT/P**

FHCRC/SCCA Facilities Overview

➤ Apheresis Unit

- 800 PBSC/DLI collections
- 10 nursing staff

➤ Cellular Therapy Laboratory

- 1200 products, approx. 500 infusions/transplants (50% allogeneic and URD transplants)
- Minimal Manipulation, Cell Enrichment/Reduction
- 12 technical staff

➤ Cellular Processing Facility

- Currently ramping up for production, (“More than minimally manipulated products”, e.g. Dendritic cell vaccines, T cell cloning, cord blood expansion)
- Class 10,000 production suites
- 4 technical staff

FHCRC/SCCA Donor Eligibility Implementation

- **Read and understand the relevant regulations**
- **Defined Scope – Autologous, Allogeneic and URD donors**
- **Created process flow of donor screening, testing and product handling**
- **Defined SOPs, forms and labels for creation and revision**
- **Assigned resources**
- **Set timelines**
- **Wrote, reviewed and approved SOPs**
- **Trained staff**
- **Implemented**

FHCRC/SCCA Donor Eligibility Implementation (cont.)

➤ Personnel Involved

- Apheresis Unit**
- Cellular Therapy Laboratory**
- Cellular Processing Facility**
- Transplant MDs**
- Mid-level Providers**
- Nurses – Inpatient and outpatient**
- VA, other area hospitals**
- URD Collection Centers**
- URD Coordinators**

FHCRC/SCCA Donor Eligibility Implementation (cont.)

- **Declaration of donor eligibility made by attending physician – created new form**
- **Added donor H&P supplemental checklist**
- **Revised “Justification for Collection” form (urgent medical need)**

DE Declaration Form

- **Check that donor is eligible with expiration date (30days for PBSC, 7 days for DLI)**
- **Check if donor is ineligible then state the reasons**
 - **Due to donor screening**
 - **History and physical**
 - **Reactive ID testing**
 - **Donor testing incomplete, pending or outdated**
 - **Check that Justification for Collection and Infusion form completed (urgent medical need)**

Summary of Records Form

- **Completed for all products – autologous, allogeneic, URD and bone marrow**
- **Includes only recipient name and MRN and product identifier, no donor information**
- **Maintained in recipient medical record (copies in collection and laboratory records)**

Summary of Records (cont.)

- **Donor Eligibility Statement – includes attending MD who determined eligibility (N/A for autologous products)**
 - **For incomplete or ineligible donors include attending MD who released the HCT/P under urgent medical need**
- **Donor screening results and reason if donor ineligible (N/A for autologous products)**
- **Donor testing results including reactive results, if applicable**
- **Statement to attach appropriate labeling**

Documentation tracking

- **Many new forms to maintain! More and more paperwork!**
- **What happens if the form doesn't accompany the Product?**
 - **Contact the collection site**
 - **Contact the URD coordinator**
 - **Last resort contact attending physician for orders to release the product**

Labeling Issues

➤ Labeling

- 6 different labels
- All URD products from Europe from ineligible donors (due to TSE) so warning labels apply and must be on all of these products
- Labeling of products with reactive tests a concern at the bedside; created a fold-over label for in-house products (where donor is family member)

DE and Immunotherapy Products

- For autologous immunotherapy products DE not required
- Feeder cells used for culturing considered ancillary products not subject to DE determination, but donors still need to be screened and tested
- Immunotherapy product similar to DLI
 - Donor testing requirements 7 days “before or after recovery”

DE and Immunotherapy Products (cont.)

- **For allogeneic immunotherapy products**
 - **DE rules apply, include accompanying records with the product**
 - **Information regarding DE should be included in IND or BLA**