Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps):

Reproductive HCT/P Virtual Workshop

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21 CFR Part 1271

Effective May 25, 2005

21 CFR Part 1271	Issues Addressed
Subpart A: General Provisions	Definitions, criteria for regulatory pathways determination (e.g. 361 tissue vs. 351 biologic)
Subpart B: Establishment Registration and Listing	Applicability: types and uses of products that will be regulated by these rules, requirements for registering and listing establishments/products
Subpart C: Donor Eligibility Determination	**Requirements for donor screening and testing for "relevant communicable disease agents and diseases"**
Subpart D: Current Good Tissue Practice (CGTP)	Handling and Process controls to prevent contamination and introduction, transmission, or spread of communicable diseases
Subpart E: Additional requirements	Adverse reactions and deviation reporting and labeling
Subpart F: Inspection and enforcement	Inspection, importation, orders of retention, recall, destruction and cessation of manufacturing

- Subparts E & F only apply to non-reproductive HCT/Ps regulated solely under section 361 of the PHS Act
- Subparts D & E do not apply to reproductive HCT/Ps (except 1271.150(c): Compliance with requirements & 1271.155: Exemptions and alternatives)

Subpart C: Donor Eligibility

- § 1271.45 General
- § 1271.47 Procedures
- § 1271.50 Donor Eligibility Determination
- § 1271.55 Records—accompanying and retained
- § 1271.60 Quarantine
- § 1271.65 Ineligible donors: Storage and Uses not prohibited
- § 1271.75 Donor Screening
- § 1271.80 Donor Testing—General
- § 1271.85 Donor Testing—All HCT/Ps and specific HCT/Ps
- § 1271.90 Exceptions for making DE Determination and Labeling

What requirements does this subpart contain?

21 CFR 1271.45(b) & (c)

General

§ 1271.45(b) – Donor eligibility determination required.

- Based on donor **screening and testing** for relevant communicable disease agents and diseases (RCDADs)
- Required for all donors of cells and tissues used in HCT/Ps, except as provided in § 1271.90
- In the case of an embryo or cells derived from an embryo, a donor-eligibility determination is required for both oocyte donor and semen donor.

§ 1271.45(c) – Prohibition on use

- An HCT/P must not be implanted, transplanted, infused, or transferred until the donor has been determined to be eligible, except as provided in § 1271.60(d), 1271.65(b), and 1271.90

How do I determine whether a donor is eligible?

21 CFR 1271.50

Donor Eligibility (DE) Determination

§ 1271.50 (a) – DE determination

- Based on the results of donor screening & testing
- Made & documented by a responsible person who is authorized to perform designated functions for which he or she is trained and qualified (§ 1271.3(t))

§ 1271.50 (b) – Eligible donor

- Donor is eligible only if:
  - Screening indicates donor is free of risk factors for & clinical evidence of RCDADs and risks associated with xenotransplantation (§ 1271.75)
  - Testing is negative or nonreactive (§ 1271.80 & 1271.85)
- Required for anonymous & directed donors
  - Anonymous donors: eligible only [§1271.45(c)]
  - Directed reproductive donors: eligible or ineligible. Use of HCT/P from ineligible directed donor not prohibited

DE Determination: Incomplete vs. Ineligible

- **Ineligible** – donor has complete testing and complete screening but there are risk factors or positive testing
  - § 1271.65(b)(1)(ii)- use of HCT/Ps from an ineligible directed reproductive donor is not prohibited
  - § 1271.65(b)(2)- must properly label HCT/P with biohazard & warnings
  - § 1271.65(b)(3)- must document physician was notified

- **Incomplete** – donor is missing testing for one or more required RCDADs and/or missing screening for all RCDADS
  - You cannot make a DE determination with incomplete screening or testing

Applying the Donor Eligibility (DE) Regulations
Q & A

Applying the Donor Eligibility (DE) Regulations

Question 1: If an anonymous donor of reproductive cells or tissue is determined to be ineligible, can their HCT/Ps be used?

Applying the Donor Eligibility (DE) Regulations

Answer 1: NO

- § 1271.45(c) - you must not implant, transplant, infuse, or transfer an HCT/P until the donor has been determined to be eligible. There are no exceptions that allow for the use of HCT/Ps from an ineligible anonymous donor

Applying the Donor Eligibility (DE) Regulations

Question 2: If a donor showed clinical evidence of a specific RCDAD but tested negative or non-reactive for that RCDAD, can the donor be determined eligible?

Applying the Donor Eligibility (DE) Regulations

Answer 2: NO

- § 1271.50(a) – DE determination is based on the results of both screening and testing
- § 1271.50(b) – A donor is only eligible if screening shows no risk factors or clinical evidence of RCDADs AND test results for required RCDADs are negative or non-reactive

Applying the Donor Eligibility (DE) Regulations

Question 3: If a responsible person did not yet document that the donor was determined eligible, can their HCT/Ps be used?

Applying the Donor Eligibility (DE) Regulations

Answer 3: NO

- § 1271.50(a) - a responsible person must determine & document DE
- § 1271.45(c) – - you must not implant, transplant, infuse, or transfer an HCT/P until the donor has been determined to be eligible. There are no exceptions that allow for the use of HCT/Ps from an ineligible anonymous donor

Donor Eligibility Determination

Donor Type	Is a DE determination required?	Can HCT/Ps be used if donor is ineligible?	Regulations
Anonymous	Yes	No	§ 1271.45(b)&(c) § 1271.50 (a)&(b)
Directed	Yes	Yes	§ 1271.45(b)&(c) § 1271.50(a)&(b) § 1271.65 (b)(1)(ii)

What records must accompany an HCT/P after the donor eligibility (DE) determination is complete; and what records must I retain?

21 CFR 1271.55

Accompanying Records

§ **1271.55(a)**

Once the DE determination has been completed and documented, the following must accompany the HCT/P at all times:

- Distinct ID code affixed to HCT/P container
  - e.g., alphanumeric, that relates the HCT/P to the donor and to all the records pertaining to the HCT/P, and except in the case of autologous and directed reproductive donations, does not include an individual's name, social security number, or medical record number
- Statement whether donor has been determined eligible or ineligible based on screening & testing
- Summary of records used to make DE determination

Summary of Records (SOR)

§ **1271.55(b)**

- Statement that communicable disease testing done by CLIA-certified lab
- Listing & interpretation of results of all communicable disease tests performed
- Name & address of establishment that made DE determination
- Statement noting reason for determination of ineligibility for ineligible directed reproductive donors

Summary of Records (SOR)

- The SOR is not labeling – it is a record
- 21 CFR 1271.55(b) states what information must be contained in the SOR but FDA does not require a specific format or template for the SOR
- You may choose to include any required labeling/warning statements on the SOR but this isn't the only option for labeling
- The SOR is required after the DE determination is complete
  - Donors for whom a DE determination is not required are not required to have a SOR

Record Retention

§ **1271.55(d)**

You must retain:

- Results & interpretation of all required donor testing & screening
- Name & address of testing laboratory
- DE determination including name of responsible person who made determination & date

Record Retention

§ 1271.55(d)

- Records must be available during FDA inspections
  - Records that can be readily retrieved from another location by electronic means are considered "retained“
- Must be retained for at least 10 years after date of administration or date of distribution, disposition, or expiration
  - If the date of administration is not known, then at least 10 years after the date of the HCT/P's distribution, disposition, or expiration, whichever is latest
  - For labs that perform donor testing, 10 years after creation of record is acceptable (DE Guidance, III.H)

Are there exceptions from the requirements for determining donor eligibility?

21 CFR 1271.90

Donor Eligibility Determination Not Required

§ 1271.90(a)

- You are not required to make a DE determination:
  1. Cells and tissues for autologous use
  2. Reproductive cells or tissue donated by a sexually intimate partner (SIP) of the recipient for reproductive use
  3. Cryopreserved oocytes or semen originally excepted under #1 or #2 above and subsequently for directed donation
     - Additional donations unavailable & appropriate measures are taken to screen test donor(s) before transfer
  4. Cryopreserved embryos, originally excepted under #2 above and subsequently for directed or anonymous donation
     - When possible, screen and test donors before transfer

Exceptions for Reproductive Use

§ 1271.90(b)

Embryo originally intended for reproductive use for a specific individual or couple that is subsequently intended for directed or anonymous donation for reproductive use is excepted from prohibitions in 1271.45(c) even when donor eligibility requirements are not met

- This exception allows for the use of embryos even when the required donor testing and/or donor screening for one or both of the gamete donors was not performed as required or was incomplete

Resources

Tissue Homepage
http://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/default.htm

Code of Federal Regulations Title 21
http://www.ecfr.gov/cgi-bin/text-idx?SID=ae1deecc79a9f185d48af015ae277f5d&mc=true&tpl=/ecfrbrowse/Title21/21cfr1271_main_02.tpl

New Embryo Rule: Revisions to Exceptions Applicable to Certain Human Cells, Tissues, and Cellular and Tissue-Based Products
https://www.gpo.gov/fdsys/pkg/FR-2016-06-22/pdf/2016-14721.pdf

Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products
http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM091345.pdf

Summary

- Donor Eligibility Determination
- Records—accompanying and retained
- Exceptions for making DE Determination


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