

# Industry Workshop for Reproductive HCT/Ps Establishments: HCT/P Labeling

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# Abbreviations



- **FDA** – Food and Drug Administration
- **CFR** – Code of Federal Regulations
- **HCT/P** – Human cells, tissues, or cellular or tissue-based products
- **DE** – Donor Eligibility
- **SOR** – Summary of Records
- **RCDAD** – Relevant Communicable Disease Agents and Diseases
- **SIP** – Sexually Intimate Partners

# Labeling of Reproductive HCT/Ps Under Subpart C: Donor Eligibility



- What is labeling?
- Labeling of HCT/Ps from an Ineligible Donor
- Exceptions & Labeling Requirements
- Labeling examples

# Labeling of Reproductive HCT/Ps

- Labeling of the following HCT/Ps
  - Semen
  - Oocytes
  - Embryos
- Labeling for the following donors
  - Autologous donors
  - Anonymous donors
  - Directed reproductive donors
  - SIP (sexually-intimate partners) donors – when donating embryos for anonymous or directed donation

\*We will not be covering labeling of HCT/Ps strictly for SIP use

# What is Labeling?



- “Label” is defined as:
  1. Printed label affixed to the HCT/P container; or
  2. Printed label affixed as a tie-tag to the HCT/P container; or
  3. If #1 or #2 not possible because container is too small or is frozen, the “Warning” statements may accompany the HCT/P
- The Summary of Records is not labeling – it is a record
  - Labeling statements and/or biohazard legend can be included on the Summary of Records
  - Establishments may decide how/where to apply the required labeling statements

# Labeling Includes



- A distinct identification code affixed to the HCT/P container, e.g. alphanumeric, that relates the HCT/P to the donor & to all records pertaining to the HCT/P
  - Except for autologous & directed reproductive donations, the code must not include the donor's name, SSN, or medical record number
- As applicable, specific statements described in:
  - 1271.65(b) – (c)
  - 1271.90(c)
- Biohazard legend – 1271.3(h) (as applicable)

# Donor Eligibility & Labeling



- Eligible Donor
  - Donor has a **complete** screening and **complete** testing and there are no risk factors for RCDADs
- Ineligible Donor
  - Donor has a **complete** screening and **complete** testing but there are risk factors for RCDADs present
  - 1271.65(b)(1)(ii): allows for use of HCT/Ps from an ineligible directed reproductive donor
- Incomplete Donor Eligibility Determination
  - Donor is missing testing results for one or more required tests for RCDADs and/or is missing screening for one or more risk factors for RCDADs
  - DE determination cannot be made when info is missing

## **21 CFR 1271.65(b)(2)-(3)**

# **Labeling of HCT/Ps from an Ineligible Donor**

# Labeling of HCT/Ps from an Ineligible Donor



## Under 1271.65(b)(2) - (3):

- Directed Reproductive Donors who have been determined ineligible:
  - Biohazard legend shown in 1271.3(h)
  - “WARNING: Advise patient of communicable disease risks”
  - “WARNING: Reactive test results for (name of disease or disease agent)” - when RCDAD testing is reactive
- Document that you notified physician using HCT/P of results of testing/screening

# Labeling of HCT/Ps from an Ineligible Donor



## Under 1271.65(c):

- HCT/Ps for non-clinical purposes
  - “For Nonclinical Use Only”
  - Biohazard legend - 1271.3(h)

## **21 CFR 1271.90**

**Are there exceptions and what labeling requirements apply?**

# Donor Eligibility Determination Not Required



## Under 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 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



## Under 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

# Exceptions for Reproductive Use (Continued)



## Under 1271.90(b) (continued):

- Nothing in this paragraph creates an exception for deficiencies that occurred in making the DE determination for the oocyte or semen donor or for deficiencies in required donor screening and/or testing in 1271.75, 1271.80 & 1271.85
  - Does not excuse establishments from performing all donor testing, screening, and DE in compliance with 21 CFR 1271
  - Establishments can be cited during an inspection for deviations related to donor screening, testing, & DE



## Required Labeling – 1271.90(c)(1) – (6)

- Labeling is based on the results of donor screening and donor testing, or lack thereof
- For embryos, the labeling should specify which gamete donor the statement(s) applies to
- No requirement to re-screen or re-test donors whose embryos are used under 1271.90(a)(4)
- No exemption request is required to use embryos under 1271.90(b)

# Required Labeling – 1271.90(c)(1) – (6) (Continued)



## Cells or tissue for autologous use - 1271.90(a)(1)

- “FOR AUTOLOGOUS USE ONLY”
- “NOT EVALUATED FOR INFECTIOUS SUBSTANCES”  
Unless you have performed ALL testing and screening in accordance with 21 CFR 1271

# Required Labeling – 1271.90(c)(1) – (6) (Continued)



## **Cryopreserved semen or oocytes, originally excepted for autologous or SIP use, and subsequently intended for directed donation - 1271.90(a)(3)**

- “NOT EVALUATED FOR INFECTIOUS SUBSTANCES”
  - Unless you have performed ALL testing and screening in accordance with 21 CFR 1271
- “WARNING: Advise recipient of communicable disease risks”
  - When DE determination is not completed or not performed OR screening/testing indicate presence of or risk factor for RCDAD
- Biohazard legend shown in 1271.3(h)
  - Only if testing or screening indicate presence of relevant communicable disease agents or risk factors for RCDADs

# Required Labeling – 1271.90(c)(1) – (6) (Continued)



## Cryopreserved semen or oocytes, originally excepted for autologous or SIP use, and subsequently intended for directed donation - 1271.90(a)(3) (continued)

- “WARNING: Reactive test results for (name of disease or disease agent)”
  - **Only when** RCDAD testing is positive
- “Advise recipient that screening and testing of the donor(s) were not performed at the time of recovery or cryopreservation of the reproductive cells or tissue but have been performed subsequently.”
  - **Only when performed**
  - If using this labeling, the “NOT EVALUATED FOR INFECTIOUS SUBSTANCES” labeling does not apply

# Required Labeling – 1271.90(c)(1) – (6) (Continued)



## Cryopreserved embryos, originally excepted for SIP use, and subsequently intended for directed or anonymous donation - 1271.90(a)(4)

- “NOT EVALUATED FOR INFECTIOUS SUBSTANCES”
  - Unless you have performed ALL testing and screening in accordance with 21 CFR 1271
- “WARNING: Advise recipient of communicable disease risks”
  - When DE determination is not complete or not performed
- Biohazard legend shown in 1271.3(h)
  - Only if testing or screening indicate presence of relevant communicable disease agents or risk factors for RCDADs

# Required Labeling – 1271.90(c)(1) – (6) (Continued)



## Cryopreserved embryos, originally excepted for SIP use, and subsequently intended for directed or anonymous donation - 1271.90(a)(4) (continued)

- “WARNING: Reactive test results for (name of disease or disease agent)”
  - **Only when** RCDAD testing is positive
- “Advise recipient that screening and testing of the donor(s) were not performed at the time of recovery or cryopreservation of the reproductive cells or tissue but have been performed subsequently.”
  - **Only when performed**
  - If using this labeling, the “NOT EVALUATED FOR INFECTIOUS SUBSTANCES” labeling does not apply

# Embryo Labeling Example #1



- Scenario:
  - Stored embryos
  - Gamete donors are SIPs - embryos originally for SIP use, subsequently for directed or anonymous donation
  - Gamete donors NOT subsequently screened and/or tested
- Applicable labeling:
  - “NOT EVALUATED FOR INFECTIOUS SUBSTANCES”
  - “WARNING: Advise recipient of communicable disease risks”

# Embryo Labeling Example #2



- Scenario:
  - Stored embryos
  - Gamete donors are SIPs - embryos originally for SIP use, subsequently for directed or anonymous donation
  - Both donors subsequently screened and tested - NO risk factors for RCDADs + testing is negative
- Applicable labeling:
  - “Advise recipient that screening and testing of the donor(s) were not performed at the time of recovery or cryopreservation of the reproductive cells or tissue but have been performed subsequently.”

# Embryo Labeling Example #3

- Scenario:
  - Stored embryos
  - Gamete donors are SIPs - embryos originally for SIP use, subsequently for directed or anonymous donation
  - Both donors subsequently screened and tested – RCDAD risk factor identified or testing is POSITIVE
- Applicable labeling:
  - “WARNING: Advise recipient of communicable disease risks”
  - Biohazard legend shown in 1271.3(h)
  - “WARNING: Reactive test results for (name of disease or disease agent)” (if testing was positive)
  - “Advise recipient that screening and testing of the donor(s) were not performed at the time of recovery or cryopreservation of the reproductive cells or tissue but have been performed subsequently.”

# Embryo Labeling Example #4



- Scenario:
  - Stored embryos
  - Both gamete donors were anonymous or directed donors
  - Donor testing performed with kits that were NOT FDA-licensed, approved, or cleared
- Applicable labeling:
  - “NOT EVALUATED FOR INFECTIOUS SUBSTANCES”
  - “WARNING: Advise recipient of communicable disease risks”

# Embryo Labeling Example #5



- Scenario:
  - Stored embryos
  - Both gamete donors were anonymous or directed donors
  - Donor screening was incomplete – did not include evaluation for all risk factors for RCDADs (INCOMPLETE DE)
- Applicable labeling:
  - “NOT EVALUATED FOR INFECTIOUS SUBSTANCES”
  - “WARNING: Advise recipient of communicable disease risks”

# Public Access to FDA



## **CDER website:**

<http://www.fda.gov/BiologicsBloodVaccines/default.htm>

## **Consumer Affairs Branch (CAB):**

Email: [ocod@fda.hhs.gov](mailto:ocod@fda.hhs.gov)

Phone: 800-835-4709 or 240-402-8010

## **Manufacturers Assistance and Technical Training Branch (MATTB)**

Email: [industry.biologics@fda.gov](mailto:industry.biologics@fda.gov)

Phone: 240-402-7800

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