Reproductive Donor Workshop Scenarios

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Required Donor Documents

- Physical Examination
- Donor Medical History Interview
- Test Results for Relevant Communicable Disease Agents and Diseases (RCDADs)
- Donor-Eligibility Determination
- Accompanying Records
- Summary of Records
- HCT/P Labeling

Physical Examination

- Performed within 6 months prior to HCT/P recovery
- Assess for physical signs of relevant communicable diseases and for signs suggestive of any risk factor for such diseases
- Should always include a genital exam for reproductive donors
- The firm may rely on records of a recent report of a physical examination by other health care professionals
- Because this is a step to determining donor eligibility, the firm must establish and maintain procedures for the conduct of the physical examination

Donor Medical History Interview

- Performed within 6 months prior to HCT/P recovery
- Documented dialogue concerning a donor's medical history and relevant social behavior
- May take place in person or by telephone
- If a donor medical history questionnaire is self-administered, the interviewer should review and verify the answers with the individual who filled out the questionnaire form
- Document should be reviewed to ensure all questions are answered
- The firm must establish and maintain procedures for the Donor Medical History Interview
- Refer to Guidance for Industry: Eligibility Determination for Donors of HCT/Ps, August 2007

Relevant Communicable Disease Agents and Diseases (RCDADs)

- **HIV, type 1 and HIV, type 2** (FDA-licensed screening test either for anti-HIV-1 and anti-HIV-2 or combination test for anti-HIV-1 and anti-HIV-2; and FDA licensed screening NAT test for HIV-1, or combination NAT)
- **HBV** (FDA-licensed screening test for Hepatitis B surface antigen (HBsAg) and for total antibody to Hepatitis B core antigen (anti-HBc)(IgG and IgM); and FDA-licensed screening NAT test for HBV, or combination NAT)
- **HCV** (FDA-licensed screening test for anti-HCV; and FDA-licensed screening NAT test for HCV, or combination NAT)
- **Treponema pallidum** (FDA-cleared screening test for syphilis)
- **WNV** (FDA-licensed screening NAT test): June 1st – October 31st (for donors residing in the US)
- **Chlamydia trachomatis**
- **Neisseria gonorrhea**

In addition, semen donors must also be tested for:

- **Human T-lymphotropic virus, types I and II** (FDA-licensed screening test for anti-HTLV I/II)
- **Cytomegalovirus** (FDA-cleared screening test for anti-CMV) (total antibody: IgG and IgM)

Scenario #1

Bill and Mike, a same-sex male couple and intended parents, created embryos using an anonymous oocyte donor and Bill's semen. Bill tested reactive for Hepatitis C. Resulting embryos will be transferred to a gestational carrier.

- What screening and testing are required?
- What should the accompanying Donor Eligibility and Summary of Records state for the oocyte and semen donations?
- How should the resulting embryos be labeled?
- Is donor-eligibility determination required for gestational or surrogate carriers?
- What if the intended parents decide to use an oocyte donor that they know, but is not known by the gestational carrier? How is this situation handled?

Anonymous Oocyte Donor

- **Physical Exam** – Donor CANNOT have any physical signs of a relevant communicable disease and any signs suggestive of any risk factor for such disease.
- **Donor Medical History Interview** – Donor CANNOT have a medical history, or any social behaviors considered to increase their relevant communicable disease risk.
- **RCDAD Testing** – Donor MUST be tested and CANNOT be reactive for HIV, HBV, HCV, Syphilis, Gonorrhea, Chlamydia, and/or WNV (June 1st – October 31st). Blood specimen for testing must be collected up to 30 days before or up to 7 days after recovery of oocytes.
- Anonymous Donors MUST be **Eligible** in order to be utilized.
- No Special Labeling or Warning Statements are required.

Directed Semen Donor (Known)

- Bill must be screened with a **Physical Exam** and **Donor Medical History Interview** within 6 months of semen recovery.
- **RCDAD Testing**: Must be tested for HIV, HBV, HCV, Syphilis, HTLV I/II, CMV, Gonorrhea, Chlamydia, and WNV (June 1st – October 31st). Blood specimen for testing must be collected up to 7 days before or after recovery of semen.
- Since Bill tested reactive for HCV and answered "yes" to the male-to-male sex question on the donor medical history interview, he would be determined **Ineligible** for donor eligibility.

Directed Semen Donor (Known) (Continued)

- Bill can still be utilized as a donor since he is directed and is known by the recipient (gestational carrier). A directed reproductive donor who is ineligible can be used under 21 CFR 1271.65.
- **Summary of Records** must state the reason for ineligibility; male-to-male sex and reactive for HCV.
- D-E determination must be made prior to HCT/P transfer.

HCT/P Labeling

Since Bill is ineligible due to male-to-male sex and testing reactive for HCV, the HCT/Ps (semen and resulting embryos) must be prominently labeled with:

- **Biohazard legend** (use when any screening/testing indicates the presence of and/or risk factor for any RCDADs)

- Statement: **“WARNING: Advise patient of communicable disease risk”** (use when D-E determination not is completed, or D-E determination reveals risk or positive test result)
- Statement: **“WARNING: Reactive test results for Hepatitis C”** (use when D-E determination revels positive or reactive test results)

Is DE required for gestational or surrogate carriers?

- No. Gestational or surrogate carriers are not considered to be donors according to the FDA definition of a donor (21 CFR 1271.3(m)).
- Gestational/surrogate carriers are not required to be screened and/or tested by FDA regulations.
- Gestational/surrogate carriers are considered to be HCT/P recipients.

What if the intended parents decide to use an oocyte donor that they know, but is not known by the gestational carrier?

- If the oocyte donor is NOT known by the recipient (gestational carrier) prior to donation, the oocyte donor must be considered as **Anonymous**.
- Donors are only classified as **Directed** if they are known by the **Recipient** (NOT the intended parents, if different) before donation.
- You should consider the relationship between the recipient (gestational carrier) and the oocyte and semen donors separately in order to determine which donor eligibility requirements apply.

Scenario #2

A couple, Pam and Bob, plan to conceive using Bob's semen (SIP) and oocytes from Pam's sister, Jane (directed oocyte donor). Jane recently traveled to an area with active Zika virus transmission. Pam plans to be the recipient of the resulting embryo.

- What screening and testing is required?
- What should the accompanying Donor Eligibility and Summary of Records state for the directed oocyte donation?
- How should the resulting embryos be labeled?

Required Documents for Directed Oocyte Donor

- Physical Examination
- Donor Medical History Interview
- Test Results for Relevant Communicable Disease Agents and Diseases (RCDADs)
- Donor-Eligibility Determination
- Accompanying Records
- Summary of Records
- HCT/P Labeling

Directed Oocyte Donor (Known)

- Jane must be screened with a **Physical Exam** and **Donor Medical History Interview** within 6 months of oocyte recovery.
- **RCDAD Testing**: Must be tested for HIV, HBV, HCV, Syphilis, Gonorrhea, Chlamydia, and WNV (June 1st – October 31st). Blood specimen for testing must be collected up to 30 days before or 7 after recovery of oocytes.
- Since Jane answered "yes" to the Zika travel question on the donor medical history interview, she would be determined **Ineligible** for donor eligibility.

Directed Oocyte Donor (Known) (Continued)

- Jane can still be utilized as a donor since she is directed and is known by the recipient (her sister Pam). A directed reproductive donor who is ineligible can be used under 21 CFR 1271.65.
- **Summary of Records** must state the reason for ineligibility; traveled to an area with active Zika virus transmission.
- D-E determination must be made prior to HCT/P transfer.

HCT/P Labeling

For this scenario, since the oocyte donor is ineligible and traveled to an area of active Zika virus transmission, the HCT/Ps must be prominently labeled with:

- **Biohazard legend** (use when any screening/testing indicates the presence of and/or risk factor for any RCDADs)

- Statement: **"WARNING: Advise patient of communicable disease risk"** (use when D-E determination not completed, or DE determination reveals risk or positive test result)

Zika Virus (ZIKV) Testing

- Although nucleic acid tests (NAT) for donor screening are available, they are not considered appropriate for preventing transmission of ZIKV through HCT/Ps

- If an establishment chooses to test donors for ZIKV:
  - Donors still must be screened for ZIKV risks
  - A negative/nonreactive test DOES NOT override recommendations in the 2016 ZIKV Guidance (updated May 2018)
  - A donor with a positive/reactive test is considered ineligible even if no screening risks were identified

Reproductive Donor Workshop Scenarios

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Scenario #3: Subsequent Donation

- A couple, Pam H. and Bob H., used the husband's semen and an anonymous oocyte donor (instead of Pam's sister) to create a family with Pam being the recipient.
- Their family is now complete and they have one remaining embryo in storage. They decide to donate the embryo to another couple they do not know. This is referred to as a "subsequent" anonymous donation.

Scenario #3: Subsequent Donation (Continued)

- **What accompanying records and/or labeling is required of the subsequently donated embryo before transfer to an anonymous recipient?**
  - Hint: Consider both gametes separately (after recovery and before transfer to Pam)
    - Anonymous oocyte donor
    - The husband (sexually intimate partner or SIP for the semen)
  - Hint: First determine whether a Donor-Eligibility (D-E) determination was required (after recovery and before transfer to Pam)

This example assumes all required steps were performed correctly

Scenario #3: Subsequent Donation (Continued)

- **Did the anonymous oocyte donor require a Donor-Eligibility (D-E) determination?**
  - Yes
  - No
  - N/A
- **If yes, what could the D-E determination have been? (select one)**
  - Eligible
  - Ineligible
  - Either is fine
  - N/A
- Regulatory cite(s): _____

Scenario #3: Subsequent Donation (Continued)

- **Did the anonymous oocyte donor require a Donor-Eligibility (D-E) determination?**
  - Answer: **Yes**
- **If so, what could the D-E determination have been?**
  - Answer: **Eligible**
- Regulatory cite(s):
  - **1271.45(b)** – a Donor-Eligibility determination is required of all donors; exceptions listed do not apply to anonymous oocyte donors
  - **1271.45(c)** – an HCT/P must not be transferred until the donor has been determined to be eligible; exceptions listed do not apply

Scenario #3: Subsequent Donation (Continued)

- **Did the oocytes from the anonymous donor require any labeling (warning statements)?**
  - Yes
  - No
  - N/A

- Regulatory cite(s): _____

Scenario #3: Subsequent Donation (Continued)

- **Did the oocytes from the anonymous donor require any labeling (warning statements)?**
  - Answer: **No**
- Regulatory cite(s):
  - **Since this was an anonymous donor, there are no labeling/warning statements in 1271.90(c) that applied.**

Scenario #3: Subsequent Donation (Continued)

- **What information must the accompanying records for the anonymous oocytes include?**
  1. _____
  2. _____
  3. _____

- Regulatory cite(s) _____

Scenario #3: Subsequent Donation (Continued)

- **What information must the accompanying records for the anonymous oocytes include?**
  1. **ID Code** (e.g., alphanumeric); does not include name, MRN, SSN
  2. **Eligibility Statement** (e.g., based on the results of screening and testing, the donor was determined eligible or ineligible)
  3. **Summary of Records**
     a. **Testing lab statement** (e.g., communicable disease testing was performed in a lab that is CLIA certified or equivalent)
     b. **Listing & interpretation of test results** (includes all RCDAD testing performed)
     c. **Name and address** (of firm making the Donor-Eligibility determination)
- Regulatory cite(s) **1271.55(a)(1)-(3) and 1271.55(b)**

Summary of Records

Anonymous Oocyte Donor ID: 33XX9921

Based on results of Screening and Testing, this donor is: **eligible**

Infectious disease testing:

Anti-HIV 1/2	Non-reactive
Anti-HCV	Non-reactive
HBc antibody (total)	Non-reactive
HBsAg	Non-reactive
NAT for HIV-1, HCV, and HBV	Non-reactive
Syphilis	Non-reactive
NAT for Chlamydia	Negative
NAT for Gonorrhea	Negative

All communicable disease testing was performed by a laboratory certified by CLIA

Donor-Eligibility determination made by:

IVF Clinic

123 Reproductive Blvd.

Anywhere, FL 12345

Scenario #3: Subsequent Donation (Continued)

- **Did Bob H. (the husband) require a Donor-Eligibility determination?**
  - Yes
  - No
  - N/A
- **If yes, what could the D-E determination have been? (select one)**
  - Eligible
  - Ineligible
  - Either is fine
  - N/A
- Regulatory cite(s): _____

Scenario #3: Subsequent Donation (Continued)

- **Did Bob H. (the husband) require a D-E determination?**
  - Answer: **No**
- **If so, what could the D-E determination have been?**
  - Answer: **N/A**
- Regulatory cite(s):
  - **1271.45(b)** – a D-E determination is required of all donors but exception 1271.90(a)(2) applied to Bob.
  - **1271.90(a)(2)** – Bob was "originally excepted" from screening, testing, and a D-E determination because he was a SIP to recipient (Pam) when he donated his semen for reproductive use to her.

Scenario #3: Subsequent Donation (Continued)

- **Did the semen from Bob H. (the husband) require any labeling (warning statements)?**
  - Yes
  - No
  - N/A

- Regulatory cite(s): _____

Scenario #3: Subsequent Donation (Continued)

- **Did the semen from Bob H. (the husband) require any labeling (warning statements)?**
  - Answer: **Yes**
- Regulatory cite(s):
  - **Labeling (warning statements) are found in 1271.90(c)(1)-(6) and list required labeling based on various circumstances, including Bob's situation.**

Scenario #3: Subsequent Donation (Continued)

- **So what accompanying records and/or labeling is required of the subsequently donated embryo before transfer to an anonymous recipient?**
  - Anonymous oocyte portion:
    - Accompanying records or labeling (warnings) or both
  - The semen portion (Bob's semen, previously SIP):
    - Accompanying records or labeling (warnings) or both

This example assumes all required steps were performed correctly

Scenario #3: Subsequent Donation (Continued)

- **So what accompanying records and/or labeling is required of the subsequently donated embryo before transfer to an anonymous recipient?**
  - Anonymous oocyte portion:
    - **Accompanying records**
  - The semen portion (Bob's semen, previously SIP):
    - **Labeling (warnings)**

This example assumes all required steps were performed correctly

Scenario #3: Subsequent Donation (Continued)

- **What labeling (warning statements) does the subsequent anonymous embryo donation require for the semen portion?**
  - Bob was "originally excepted" in 1271.90(a)(2) because he was a SIP.
  - 1271.90(a)(4) indicates when possible appropriate measures *should* be taken before transfer to screen and test the donor(s) of a cryopreserved embryo originally excepted under 1271.90(a)(2) when subsequently donating as an anonymous or directed donation.
  - 1271.90(a)(4) does not require screening and testing at this point; it is recommended.

Scenario #3: Subsequent Donation (Continued)

- **How is the embryo labeled when Bob H. is *not* subsequently screened and tested?**

Labeling includes	Regulatory cites
a. _____	a. _____
b. _____	b. _____

Scenario #3: Subsequent Donation (Continued)

- **How is the embryo labeled when Bob H. is *not* subsequently screened and tested?**

Labeling includes	Regulatory cite
"NOT EVALUATED FOR INFECTIOUS SUBSTANCES"	1271.90(c)(2) since all screening and testing was not done.
"WARNING: Advise recipient of communicable disease risks"	1271.90(c)(3)(i) since the D-E determination was not performed.

Labels for Bob's semen when the embryo is subsequently donated as anonymous or directed and subsequent screening or testing is NOT performed

"NOT EVALUATED FOR INFECTIOUS SUBSTANCES"

"WARNING: Advise recipient of communicable disease risks"

Scenario #3: Subsequent Donation (Continued)

- **How is the embryo labeled if Bob H. *is* subsequently screened and tested and *no* risk factors or evidence of infection are identified?**

Labeling includes	Regulatory cite
a. _____	a. _____

Scenario #3: Subsequent Donation (Continued)

- **How is the embryo labeled, if Bob H. *is* subsequently screened and tested and *no* risk factors or evidence of infection are identified?**

Labeling includes	Regulatory cite
"Advise recipient that the screening and testing of the donor was not performed at the time of recovery or cryopreservation of the reproductive tissue, but have been performed subsequently"	1271.90(c)(6) since screening and testing was performed at some point after recovery or cryopreservation.

Scenario #3: Subsequent Donation (Continued)

- **How is the embryo labeled if Bob H. *is* subsequently screened and tested and *screening risk factors are identified*?**

Labeling	Regulatory cites
a. _____	a. _____
b. _____	b. _____
c. _____	c. _____

Scenario #3: Subsequent Donation (Continued)

- **How is the embryo labeled, if Bob H. *is* subsequently screened and tested and *screening risk factors are identified*?**

The label should include:	Regulatory cites
"Advise recipient that the screening and testing of the donor was not performed at the time of recovery or cryopreservation of the reproductive tissue, but have been performed subsequently"	1271.90(c)(6) since screening and testing was performed at some point after recovery or cryopreservation.
"WARNING: Advise recipient of communicable disease risks"	1271.90(c)(3)(ii)(B) since risk factors were identified in screening.
Biohazard Legend	1271.90(c)(4)(ii) since risk factors were identified.

Scenario #3: Subsequent Donation (Continued)

- **How is the embryo labeled if Bob H. *is* subsequently screened and tested and testing reveals *positive test result(s)?***

Labeling	Regulatory cites
a. _____	a. _____
b. _____	b. _____
c. _____	c. _____
d. _____	d. _____

Scenario #3: Subsequent Donation (Continued)

- **How is the embryo labeled, if Bob H. *is* subsequently screened and tested and testing reveals *positive test result(s)?***

The label should include:	**Regulatory cites**
"Advise recipient that the screening and testing of the donor was not performed at the time of recovery or cryopreservation of the reproductive tissue, but have been performed subsequently"	1271.90(c)(6) since screening and testing was performed at some point after recovery or cryopreservation.
"WARNING: Advise recipient of communicable disease risks"	1271.90(c)(3)(ii)(B) for the positive test.
"WARNING: Reactive test results for (insert RCDAD)"	1271.90(c)(5) for the positive test.
Biohazard Legend	1271.90(c)(4)(ii) for the positive test.

Reproductive Donor Workshop Scenarios

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Scenario #4

Mary and John are trying to conceive. Due to John's low sperm count, his brother Steve agrees to be a directed donor for the couple. Mary's oocytes and Steve's sperm are used to form embryos. Some embryos are transferred to Mary and the other embryos are cryopreserved.

Scenario #4: Question #1

A donor-eligibility (D-E) determination based on screening (1271.75) and testing (1271.80 & 1271.85) under 1271.50(a) is required for:

a) Mary
b) Steve
c) John
d) None of the above because they are relatives

Scenario #4: Question #1

A donor-eligibility (D-E) determination based on screening (1271.75) and testing (1271.80 & 1271.85) under 1271.50(a) is required for:

a) Mary
b) Steve
c) John
d) None of the above because they are relatives

Scenario #4: Question #2

Mary was not screened or tested for communicable diseases. Select the most appropriate labeling for Mary's oocytes. Select all that apply.

a) "FOR AUTOLOGOUS USE ONLY" (1271.90(c)(1))

b) "NOT EVALUATED FOR INFECTIOUS SUBSTANCES" (1271.90(c)(2))

c) "WARNING: Advise recipient of communicable disease risks" (1271.90(c)(3))

d) Biohazard legend (1271.90(c)(4))

Scenario #4: Question #2

Mary was not screened or tested for communicable diseases. Select the most appropriate labeling for Mary's oocytes. Select all that apply.

a) "FOR AUTOLOGOUS USE ONLY" (1271.90(c)(1))

b) "NOT EVALUATED FOR INFECTIOUS SUBSTANCES" (1271.90(c)(2))

c) "WARNING: Advise recipient of communicable disease risks" (1271.90(c)(3))

d) Biohazard legend (1271.90(c)(4))

Scenario #4: Question #3

After a D-E determination is made for Steve, the accompanying records and summary of records must accompany the semen at all times (1271.55). Select the most appropriate labeling for Steve's semen if the communicable disease test results indicate the presence of a communicable disease.

a) "FOR AUTOLOGOUS USE ONLY" (1271.90(c)(1))

b) "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" (1271.90(c)(6))

c) Include the Biohazard legend with the statement, "WARNING: Advise patient of communicable disease risks," and, in the case of reactive test results, "WARNING: Reactive test results for (name of disease agent or disease)" (1271.65(b)(2))

d) "For Nonclinical Use Only" (1271.65(c)(1))

Scenario #4: Question #3

After a D-E determination is made for Steve, the accompanying records and summary of records must accompany the semen at all times (1271.55). Select the most appropriate labeling for Steve's semen if the communicable disease test results indicate the presence of a communicable disease.

a) "FOR AUTOLOGOUS USE ONLY" (1271.90(c)(1))

b) "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" (1271.90(c)(6))

c) Include the Biohazard legend with the statement, "WARNING: Advise patient of communicable disease risks," and, in the case of reactive test results, "WARNING: Reactive test results for (name of disease agent or disease)" (1271.65(b)(2))

d) "For Nonclinical Use Only" (1271.65(c)(1))

Scenario #4

After several embryo transfer attempts, Mary and John decide to transfer the cryopreserved embryos to a gestational carrier/surrogate who is known to them. Steve was determined eligible, but Mary was not screened and tested at the time of oocyte recovery because she was originally an autologous donor; however, Mary agreed to subsequently undergo screening and testing. Mary's screening indicates risk factors for or clinical evidence of communicable disease.

Scenario #4: Question #4

A D-E determination is NOT required for the gestational carrier/surrogate.

True

False

Scenario #4: Question #4

A D-E determination is NOT required for the gestational carrier/surrogate.

True

False

Scenario #4: Question #5

Select the most appropriate labeling for the embryos if Mary's screening indicates risk factors for or clinical evidence of communicable disease. Select all that apply.

a) "WARNING: Advise recipient of communicable disease risks" (1271.90(c)(3))

b) Biohazard legend (1271.90(c)(4))

c) "WARNING: Reactive test results for (name of disease agent or disease)" (1271.90(c)(5))

d) "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" (1271.90(c)(6))

Scenario #4: Question #5

Select the most appropriate labeling for the embryos if Mary's screening indicates risk factors for or clinical evidence of communicable disease. Select all that apply.

a) "WARNING: Advise recipient of communicable disease risks" (1271.90(c)(3))

b) Biohazard legend (1271.90(c)(4))

c) "WARNING: Reactive test results for (name of disease agent or disease)" (1271.90(c)(5))

d) "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" (1271.90(c)(6))


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