

# Attachment #1

## REPRODUCTIVE COUNCIL RESPONSES TO FDA'S GUIDANCE DOCUMENT FOR DONOR SUITABILITY RULES

### I. Section 1271.85(b)(2) Guidance Document V (B)(1)(b) pg. 32-33

“Special note on CMV: CMV is not a relevant communicable disease or disease agent. However, establishments are required to test donors of viable, leukocyte-rich cells or tissues for CMV. A donor who tests reactive for CMV is not necessarily ineligible to donate HCT/Ps. You must establish and maintain an SOP governing the release of HCT/Ps from donors whose specimens test reactive for CMV (§ 1271.85(b)(2)). We recommend that the SOPs be based on current information on the potential for disease transmission from the type of HCT/P to be made available for use and that the SOP limit use of an HCT/P based on the CMV-reactive status of the recipient.”

**Response:** Consistent with the response to Comment 40 with D Part 1271, Subpart C - Donor Eligibility, page 29802, it is unreasonable to hold a tissue banking establishment accountable for the responsibilities of the recipient's attending physician. The AATB requests the FDA replace the underscored language with the following: “it is the responsibility of the recipient's attending physician to determine the recipient's CMV- reactive status and to determine the potential risks of CMV transmission with use of a specific semen donor.”

### II. Guidance Document VII. Exceptions A, pg. 37-38

**Response:** Throughout this Guidance Document there are multiple references made to labeling and/or re- labeling containers. In the case of reproductive tissues stored in vials or straws, physical size limitations prohibit labeling containers with phrases such as those listed in 1271.90(b), “For Autologous Use Only”, or “Not Evaluated for Infectious Substances”, and/ or biohazard legend symbols. After cryopreservation, re-labeling and/or adding such information is also impossible without irreversibly compromising the specimens and/or risking loss of the new label. While we agree that this information is important and should be included, we recommend the Guidance Document contain language indicating it should be disseminated via package inserts or by attachment to an external shipping container. We suggest that a third option be added to the last sentence of the introductory paragraph, section VII. Exceptions; “or (3) a package insert included with the shipping container”.

III. 1271.85(d) Re-testing anonymous semen donors. Except as provided under 1271.90 and except for directed reproductive donors as defined in 1271.3(l), at least 6 months after the date of donation of semen from anonymous donors, you must collect a new specimen from the donor and test it for evidence of infection due to the communicable disease agents for which testing is required under paragraphs (a), (b), and (c) of this section.

Guidance Document (VI)(E) Is follow-up testing required for directed donors of semen? No, we do not require follow- up testing when semen is donated for directed use.

**Response:** We disagree with this language and recommend the following, "the quarantine requirement for directed semen donors should not be waived except for valid, documented medical and/ or scientific reasons and then only with informed consent of the recipient" (1271.90(a) Donor- eligibility determination not required).

IV. Guidance Document V. Donor Testing: Specific Requirements (1271.85), Nucleic Acid Testing (NAT). The last sentence reads: "FDA does recommend that living donors of HCT/Ps (e.g. hematopoietic stem/progenitor cell donors, semen donors) be tested with FDA-licensed NAT blood donor screening tests for HIV and HCV".

**Response:** It is our understanding, following discussions with FDA staff, that it is the intention of FDA to recommend that all living reproductive donors complete NAT for HIV and HCV. We recommend that for clarity, "embryo and oocyte" should be added to your list of examples.

V. Guidance Document VI. Additional Screening and Testing Requirements for Donors of Reproductive Cells and Tissues (1271.75, 1271.80, 1271.85 and 1271.90)

Sections B and C both address the screening/testing of donors of reproductive cells and tissues who are not sexually intimate partners. Chlamydia and Neisseria gonorrhea are listed under sections B and C as tests required for donation. Oocytes, if retrieved by laparoscopic procedures are exempted from this testing. Section E states that anonymous semen donors would be required to complete this testing while directed semen donors would not required to complete follow up testing for Chlamydia and Neisseria gonorrhea.

Section F discusses requirements for donation of reproductive tissue that was originally collected for use in sexually intimate partners. The first example listed discusses the requirements for testing of donors (anonymous or directed) of oocytes, semen and embryos cryopreserved by sexually intimate partners. The Guidance Document states that initial screening is required in all cases with follow up screening required by the semen provider in the case of embryos and anonymously donated semen.

**Response:**

It is our experience that sexually intimate partners who undergo infertility rarely, if ever, know if they would consider donating their cryopreserved cells or tissue at some time in the future. There concern is achieving a pregnancy and prior to their treatment, they have little idea if any of their semen or embryos will be cryopreserved. FDA's regulations do not require these individuals to be initially tested for any sexually transmitted disease. We strongly believe that the requirement for initial testing will greatly reduce embryo donation. However, we strongly support repeat serology testing (following a six month quarantine) of all embryo donors, not only the male gamete provider.

In the case of embryo donation, we do not support the requirement of Chlamydia and Neisseria gonorrhea testing after six months. Re-testing embryo donors six months after their IVF

procedure, or in most cases years later, would add little, if any, information regarding the safety of the tissue at the time of cryopreservation. Our experience indicates that while prior to an IVF procedure the oocyte provider may be tested for these two diseases, the sperm provider is rarely, if ever, tested because they are sexually intimate partners. AATB Standard D4.360 (R) states that Chlamydia and Neisseria gonorrhoea testing of semen donors shall be repeated at least every six months. The Standard further states that collected during intervals in which Chlamydia and Neisseria gonorrhoea cannot be ruled out shall be discarded. This assumes repeated donations by the semen donor over several months. Embryos considered for donation were created by one IVF procedure.

We recommend that FDA allow embryo donation with the following provisions:

1. Repeat serology testing six or more months after cryopreservation is required, if the donors are available for testing. If a donor is not available for repeat serology testing, initial serology testing results would be required.
2. Chlamydia and Neisseria gonorrhoea testing is not required initially or later at the time donor qualification.
3. An informed consent is required stating the testing completed and the testing not completed (including Chlamydia and Neisseria gonorrhoea). The recipient (s) and their transplanting physician would be required to sign the informed consent.
4. An initial and repeat physical examination of sexually intimate partners, who later become reproductive donors, would not be required as stated in 1271.47. However, a comprehensive three generation family medical/genetic history of each donor is required and must be reviewed and approved by the Medical Director of the cryobank and the transplanting physician.

The Guidance Document recommends that requirements for initial and repeat testing be provided to patients prior to infertility treatment so that they may participate in a donation program later. We do not believe IVF centers will have patient compliance with this procedure when at the same time the FDA is not requiring sexually intimate partners to complete testing prior to infertility treatment. We do not believe that IVF patients know or will have thought about possible donation prior to the IVF procedure. Formal physical examinations of IVF patients are not currently performed. We strongly believe that embryo donation will be severely decreased unless FDA's regulations are modified. We believe that the above recommendations will allow for continued embryo donation and will not increase the risk of transmitting infectious disease.