



AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

Formerly *The American Fertility Society*

Administrative Office
1209 MONTGOMERY HIGHWAY
BIRMINGHAM, ALABAMA 35216-2809
TEL 205/978-5000 • FAX 205/978-5005

EMAIL: asrm@asrm.org • WEB SITE: <http://www.asrm.org>

J. Benjamin Younger Office of Public Affairs
409 12th STREET SW, SUITE 203
WASHINGTON, D.C. 20024-2155
TEL 202/863-4985 • FAX 202/484-4039
EMAIL: asrm-dc@asrm-dc.org

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KAMRAN S. MOGHISSI, M.D.

August 23, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Draft "Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products"

To Whom It May Concern:

The American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART) are pleased to submit comments to the Food and Drug Administration (FDA) on the agency's draft "Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products" (69 Fed. Reg. 29835 (May 25, 2004)).

ASRM is a non-profit organization dedicated to advancing knowledge and expertise in reproductive medicine and biology, and is the foremost organization promoting the study of reproduction and reproductive disorders. ASRM has approximately 8000 members throughout the United States and in 99 foreign countries, the great majority of whom are physicians practicing in the fields of obstetrics and/or gynecology. ASRM's membership also includes others involved in reproductive medicine, such as doctoral level scientists, nurses and technicians.

SART is an affiliated society of ASRM whose members are medical practices actively engaged in performing assisted reproductive technology ("ART"), as well as individuals who are participants in or

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employees of SART member practices. SART currently has 390 medical practice members representing ART practices in 46 states, the District of Columbia and Puerto Rico. SART programs are responsible for approximately 90% of the ART treatment cycles performed in the US each year.

ASRM and SART submitted comments on FDA's proposed rule regarding "Suitability Determination for Donors of Human Cellular and Tissue-Based Products", and we appreciate that in the final rule and draft Guidance FDA has responded to, and addressed, many of the concerns we raised. As we have noted in our past comments, and in several meetings with FDA, reproductive cells and tissues are special, and in many respects cannot be treated like other types of tissues. We hope that FDA will continue to acknowledge and accommodate this reality going forward, and will continue to work with ASRM and SART in developing further guidance.

With respect to the draft "Guidance for Industry", we have the following comments:

Donor Eligibility Determinations and Emerging Infectious Diseases – In addition to the infectious diseases specifically identified in the regulations, the draft Guidance also lists several other diseases that FDA believes meet the standards for "relevant communicable disease agents or diseases". FDA also notes that it intends to recommend screening and testing for additional infectious diseases if the agency believes a disease meets the definition of "relevant communicable disease" (see, *e.g.*, section II.D.). Prior to recommending screening and testing for additional diseases, we request that FDA confer with representatives of the establishments that would be affected by such changes.

Identifying HCT/Ps - There are several references in the draft Guidance to use of "automated designation" systems to accurately identify and prevent improper release of HCT/Ps (see, *e.g.*, sections II.H. and J.). We are requesting that FDA clarify that an automated system is not required and that a manual system of check-offs to determine valid identification of HCT/Ps also would meet FDA's requirements.

Storage of HCT/Ps - The draft Guidance indicates that with respect to HCT/Ps for which a donor-eligibility determination has not yet been completed, and for HCT/Ps that have been determined to be ineligible, the establishment must store or identify those HCT/Ps in a physically separate area or use other procedures to prevent improper release. (see, *e.g.*, sections II.H. and J.) We are requesting that FDA clarify that at least with respect to reproductive cells and tissues, compliance would not require establishments to maintain separate liquid nitrogen tanks for quarantined and ineligible HCT/Ps. Such a requirement would be very burdensome and costly for many smaller reproductive medicine practices and is unnecessary.

The identification system and current storage procedures should address this concern since each cane in the tank is clearly identified and would contain a single patient's specimen(s). A cane is a metal rod designed to secure one or more cryovials or straws submerged in liquid nitrogen, and eligible specimens would not be placed on the same cane with specimens that are ineligible or for which an eligibility determination has not yet been completed.

Donor Screening Review of "Relevant Medical Records" – In the list of "other records" that should be reviewed as part of the donor screening process, if they are available, FDA includes police records (see, *e.g.*, section III.C.3.). We assume that this is included because, with respect to cadaveric donors, the existence of such records may be known and could provide relevant information. However, we request that the Guidance document make clear that establishments generally are not required to seek police records as part of the donor screening process, unless they have reason to know that such records exist and are likely relevant to donor screening.

Donor Screening Review of "Physical Evidence" – The regulations and the draft Guidance state that donor screening requires review of the donor's relevant medical records, which is defined to include a report of the physical assessment of a cadaveric donor or the physical examination of a living donor (see, *e.g.*, section III.G.). We request that FDA clarify that the establishment conducting the donor screening is not required to conduct the physical exam of the potential donor, but can rely on the records prepared by some other individual or entity that performed the examination. For example, a physician who has obtained donor sperm or donor oocytes may not have an opportunity to physically examine the donor and may, instead, rely on the examination records provided by a sperm bank or other facility from which the sperm or oocytes were obtained.

Donor Testing and the Timing of Specimen Collection – As we have expressed previously in comments to FDA, we continue to be concerned about the requirement that donor specimens for testing must be collected at the time of recovery of cells or tissues, or up to 7 days before or after recovery (see, *e.g.*, section IV. F.). With respect to donor oocytes, this requirement is not practicable, will result in costly, duplicative testing, and is not necessary to protect oocyte recipients. Oocyte donors typically are screened and tested prior to being matched with a recipient couple since it would make no sense to have the donor and recipient couple go through the sometimes lengthy and emotional process of making a match if the donor then might be determined ineligible. And once a donor and recipient are matched, the donor then is placed on medications for several weeks before the oocytes can be recovered. Requiring that the specimen for donor testing be collected no more than 7 days before recovery will mean that donors will have to undergo two complete sets of costly donor eligibility tests; one prior to being matched with a

recipient and then an identical set of tests several weeks later, just prior to oocyte recovery.

Donor Testing for Hepatitis B – The final regulation requires that all donors be tested for Hepatitis B virus, and the draft Guidance recommends that testing be done for both Hepatitis B surface antigen and for total antibody to Hepatitis B core antigen (see, e.g., section V.A.). We believe this requirement is duplicative, and that the antigen test alone should be sufficient, as patients who have been vaccinated for hepatitis B will have a positive antibody test. The antigen test would evaluate for the presence of the virus.

HCT/Ps Collected for Use in a Sexually Intimate Partner, but Subsequently Intended for Anonymous or Directed Donation - We very much appreciate that FDA is exempting from regulation HCT/Ps collected for use in a sexually intimate partner, and has included regulatory exceptions to allow directed donation of HCT/Ps. However, the requirement that embryos originally created for use in sexually intimate partners may later be donated for anonymous or directed use only if both donors were initially screened and tested at the time of the *in vitro* treatment cycle will dramatically reduce the number of embryos available for such donations. Since donor testing is not required for sexually intimate partners, very few couples will be willing to incur the extra costs of screening and testing merely on speculation that they may ultimately have embryos that they wish to donate at some point in the future.

Again, we appreciate the opportunity to provide these comments. We welcome the opportunity to work with FDA in further refining this Guidance document, and we would be pleased to meet with FDA to discuss any questions.

Sincerely,

 RA

Marian Damewood, M.D.
President, ASRM

 BO

Owen Davis, M.D.
President, SART