

NIH Guidelines for Human Stem Cell Research

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Chair, ACD Working Group for
hESC Review**

**Advisory Committee to the Director
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Working Group for hESC Eligibility Review

- Jeffrey Botkin, M.D., M.P.H., University of Utah School of Medicine
- Dena Davis, J.D., Ph.D., Cleveland-Marshall College of Law
- Pamela Davis, M.D., Ph.D., Case Western Reserve University
- David Grainger, M.D., M.P.H., University of Kansas School of Medicine-Wichita; Center for Reproductive Medicine
- Richard Lifton, M.D., Ph.D., Yale School of Medicine
- Bernard Lo, M.D., University of California, San Francisco
- Terry Magnuson, Ph.D., University of North Carolina (Chapel Hill)
- Jeffrey Murray, M.D., University of Iowa Children's Hospital
- Carlos Pavão, M.P.A., Education Development Center

Working Group Process

- All conflicts of interest are disclosed
- Each working group member reads all applications
- Each application is assigned to a member of the working group as a “primary reviewer.”
- 3 potential outcomes: Positive, negative, or table.
 - Additional information from the applicant may be requested through NIH staff.
- The findings will include majority and minority opinions, as appropriate.
- Materials submitted by the applicants are treated as confidential.

Status of Review

- Working Group is reviewing materials from a number of submissions and is scheduled to conduct reviews on a rolling basis
- Clarifying information has been requested from several submitters
- General challenges in reviewing submissions:
 - Consent for clinical services distinct from consent for research
 - Documentation of options presented to patients
 - Information on the timing of consent relative to treatment
 - Anonymization limits ability to obtain documentation

Findings For Consideration

Working Group findings for 28 lines submitted by Harvard University presented for ACD consideration today.

Submission from Harvard University

(2009-ACD-003)

- Covers 28 hESC lines from embryos donated in the U.S. prior to July 7, 2009 under single IRB-approved protocol and informed consent form
- Protocol designed in 2000-2001
- 2000 NIH Guidelines followed, e.g., only frozen embryos donated

Submission from Harvard University

- Embryos originated at multiple U.S. IVF clinics and at a Collaborating IVF Clinic
 - Consent obtained by Collaborating Clinic staff (except 1 line)
 - Anonymized
 - No ability to identify individual or clinic source of each line
- Clarifying information requested and provided regarding:
 - Timing of consent
 - Options available to patients
 - Financial and academic relationship of Collaborating IVF Clinic staff with Harvard

Submission from Harvard University

- Line #25: consent obtained during lapse in IRB approval of consent and protocol
 - Harvard IRB approved continued use of Line #25 based on:
 - Donors signed a consent form
 - No changes in protocol or consent during the lapse
 - No ability to re-consent embryo donor
 - Human subject regulations permit the IRB to determine what should happen in this circumstance

II(B) Requirements

■ hESCs must have been derived from human embryos:

(1) that were created using in vitro fertilization for reproductive purposes

(2) that were donated by donor(s) who gave voluntary written consent for the human embryos to be used for research purposes.

II(B) Considerations

- Principles articulated in Section II (A)
- 45 C.F.R. Part 46, Subpart A
- Points to Consider

II(B) Points to Consider

- During the informed consent process, including written or oral communications, whether the donor(s) were:
 - (1) informed of other available options pertaining to the use of the embryos;
 - (2) offered any inducements for the donation of the embryos; and
 - (3) informed about what would happen to the embryos after the donation for research.

Additional Considerations

- Although relevant to use rather than approval, the ACD should note that:
 - the consent form states: *“These cells will be used to study the embryonic development of endoderm with a focus on pancreatic formation. The long-term goal is to create human pancreatic islets that contain β cells, the cells that produce insulin, for transplantation into diabetics.”*
 - the Harvard IRB determined it was acceptable to use the cells more broadly based on interpretation of the Common Rule regarding use of “anonymized” tissue
- The use of “anonymized” biospecimens for research that was not addressed in the consent process is under active discussion at other federal agencies at present.

WG Findings

- The ACD should consider recommending that 27 of the 28 lines submitted by Harvard be eligible for use in NIH-supported research.
- Line 25 should not be approved for this purpose.