

**Report from
ACD Working Group for
Human Embryonic Stem Cell
(hESC) Review**

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hESC Review**

**Advisory Committee to the Director
June 10, 2010**



Advisory Committee to the Director, NIH, 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
- 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
- John O'Shea, M.D., Scientific Director, NIAMS
- Carlos Pavão, M.P.A., Education Development Center Inc, Atlanta

Findings For Consideration

Working Group findings for 53 lines from 4 institutions are presented for ACD consideration today:

■ University of Connecticut

- Farmington, CT – 4 lines (2009-ACD-005)

■ Advanced Cell Technology

- Santa Monica, CA – 1 line (2010-ACD-007)

■ University of New South Wales

- New South Wales, Australia – 1 line (2010-ACD-008)

■ . Reproductive Genetics Institute

- Chicago, IL - 47 lines (2009-ACD-006, 2009-ACD-007)

Section IIB of NIH Guidelines for Human Stem Cell Research

For embryos donated anywhere before July 7, 2009 (if Section IIA is not met), ACD Working Group will take into account:

- Principles in Section IIA
- 45 CFR 46 Subpart A (Common Rule)
- Points to Consider: During informed consent process, whether donor(s) were:
 - Informed of other available options pertaining to use of embryos
 - Offered any inducements for the donation
 - Informed about what would happen to the embryos

University of Connecticut (U-CT) Submission

- Embryos donated by couples after IVF treatment at the Center for Advanced Reproductive Services at U-CT Health Center
- Covers 4 hESC lines (CT1 – 4) from embryos donated in the U.S. in 2008

WG Discussion of U-CT Submission

- Overall documentation was complete and clear, including a concise, focused embryo donation consent form.
- Upon initial review, WG noted that the date of the submitted consent form for donation of embryos appeared to be valid at a date later than the actual date of embryo donation. Upon NIH request, the submitters forwarded the versions of the consent and other forms used at time of donation.
- The WG agreed that Section IIB considerations were met and voted unanimously to put forward a positive finding to the ACD suggesting recommendation of the 4 cell lines (CT1 – 4) for use in NIH-funded research.

Note on U-CT Submission

- Restrictive language in consent?
 - “No human embryonic stem cell lines will be transplanted into a human being.”
 - “No animals transplanted with the human stem cells will be raised for reproduction.”

Submission from Advanced Cell Technology (ACT)

- Embryos transferred from separate IVF clinic to ACT after consent from couples.
- Covers 1 hESC line, MA135, from embryos donated in 2007.

WG Discussion of ACT Submission

- WG found the embryo donation consent form clear and thorough.
- WG asked for additional information from ACT to confirm that there was sufficient time between date of donation and actual embryo transfer to ACT (the point at which ACT stated the embryo donation could no longer be withdrawn). WG found information provided satisfactory.
- The WG agreed that Section IIB considerations were met and voted unanimously to put forward a positive finding to the ACD suggesting recommendation of the cell line MA135 for use in NIH-funded research.

Note on ACT submission

- Restrictive language in consent?
 - “...Advanced Cell Technology will use the stem cells to study the process of cell development and try to make cells and tissues that can be transplanted into humans to treat various diseases.”

University of New South Wales (UNSW) Submission

- Embryos transferred to UNSW from separate IVF clinic after consent from couples
- Covers 1 hESC line, Endeavour-2 (E-2), from embryos donated in Australia in 2006

WG Discussion of UNSW Submission

- While the consent form to donate embryos for research is not typical by U.S. standards, the WG agreed that it covers most relevant items and found it satisfactory.
- Point 8 on the research consent form states:
*“That embryonic stem cells produced may be used in the treatment of human diabetes and may result in financial gain to the researchers and/or their organizations. We understand that **we have no claim or interest** in such outcomes from this research and are donating our excess embryos for altruistic purposes.”*

WG Discussion of UNSW Submission (cont.)

- “Common Rule” 45 CFR 46 Section 46.116 states:
 - “No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.”

WG Discussion of UNSW Submission (cont.)

- WG believes this consent language appears to border on exculpatory, but is appropriately intended to inform donors that they will not benefit financially.
- WG is not aware of any Australian research regulations that parallel the U.S. regulations (45 CFR 46) prohibiting exculpatory language.
- The WG agreed that Section IIB considerations were met and voted unanimously to put forward a positive finding to the ACD, suggesting recommendation of the cell line Endeavour-2 for use in NIH-funded research.

Note on UNSW Submission

- Restrictive language in consent?
 - Consent is titled “Creating Human Embryonic Stem Cell Lines for the Treatment of Diabetes.”

Submissions from Reproductive Genetics Institute (RGI)

- Embryos donated by couples at risk for conceiving children with genetic diseases
- IVF treatment and hESC derivation were at RGI, a private clinic and research facility
- Submissions cover 47 hESC lines from embryos donated in the U.S. in 2003-2009 (prior to July 7, 2009)
- 42 cell lines carry disease-specific mutations

WG Discussion of RGI submission

- WG was concerned that RGI IRB had not conducted annual reviews of research protocols, abrogating opportunity for IRB to review concerns/complaints that may have arisen.
- WG had general discussion about how to consider submissions from entities with IRBs not subject to 45 CFR 46 (when conducting human subjects research).
- WG examined dates of consent for clinical treatment and consent for donation of embryos; in 4 cases, occurred on the same day.
- WG was concerned about language in “Discoveries and Patents” section of consent to donate embryos for research.

RGI Consent Form

“DISCOVERIES AND PATENTS

By choosing to enroll in this research study, we acknowledge and agree that we will receive no payment of any kind for donation of our embryos and/or for participation in this study. We further acknowledge that RGI may realize monetary or other benefits and awards from its research utilizing our donated embryos and that RGI will be the sole and exclusive owner of any such monetary or other benefits and awards. We further agree that we, our heirs, successors, relatives, representatives and/or agents have no interest in, and will make no claim to, any monetary or other benefits and awards which RGI may derive, in whole or in part, from use of our donated embryos. We further agree that we, our heirs, successors, relatives, representatives, and/or agents will not bring any action in law or in equity, or in any administrative setting, related to our participation in this study.”

WG Discussion of RGI Consent Language

- Majority opinion: Consent language is exculpatory
 - 1) Donors appear to be asked to relinquish rights to sue for negligence or harm.
 - 2) Other language in section appears sufficient to address property rights, suggesting that language in question intended to address the broader issue of liability for negligence or harm.

- Minority opinion: Consent Language is not exculpatory as
 - 1) placement under “Discoveries & Patents” sub-heading makes it clear that it relates to property interests, not to the right to sue for negligence or harm;
 - 2) there is no agreed-upon legal or moral right to the financial rewards stemming from tissue donation

WG Discussion of RGI submission (cont)

- The WG found that Section IIB considerations were not met. Based primarily on concerns about exculpatory language in the consent form and failure to review the research protocol on an annual basis, the WG voted to put forward a negative finding to the ACD, suggesting recommendation that the RGI cell lines be disapproved for use in NIH-funded research.
- WG concerns could be sufficiently addressed through appropriate re-consent of donors (without exculpatory language); submission should be reconsidered by the WG and ACD following re-consent.

Note on RGI Submission

- Restrictive language in consent?
 - None. RGI states that lines cannot be used for experimental nuclear transfer and chimera production.

Summary Working Group Findings

- ACD should consider recommending to NIH Director that the following lines be **approved** for use in NIH-supported research:
 - **University of Connecticut:** CT1, CT2, CT3 and CT4
 - **Advanced Cell Technology:** MA135
 - **University of New South Wales:** Endeavour-2 (E2)

- ACD should consider recommending to NIH Director that the following lines be **disapproved** for use in NIH-supported research:
 - **Reproductive Genetics Institute (RGI):** 47 lines (in the two submissions considered today)