

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

**Jeffrey R. Botkin, M.D., M.P.H.
Chair, ACD Working Group for
hESC Eligibility Review**

**Advisory Committee to the Director
December 9, 2011**



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., Lehigh University
- 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
- Anne Drapkin Lyerly, M.D., MA., University of North Carolina Chapel Hill
- 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., National Institute of Arthritis and Musculoskeletal and Skin Diseases

NIH Guidelines for Human Stem Cell Research

- Effective July 7, 2009
- All hESCs must be:
 - Derived from embryos created by IVF for reproductive purposes and no longer needed for that purpose
 - Donated by individual(s) who sought reproductive treatment and who gave voluntary written consent for human embryos to be used for research purposes

Types of Review

- **NIH administrative review** under “Section IIA”: specific requirements for donation process
 - required for current/future US donations
 - optional review path for older lines or foreign lines
- **ACD Working Group review** for older lines under “Section IIB”: more flexible
- **ACD Working Group review** for current/future lines from outside of US under “Section IIC”: equivalency
- **NIH Director makes final decisions** on eligibility of hESC lines for use by NIH-funded researchers

Section IIB of NIH Guidelines for Human Stem Cell Research

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

All submissions presented today reviewed under IIB

NIH Human Embryonic Stem Cell Registry

- **Approved:** 136 lines
 - 44 lines approved after ACD review
 - 92 lines approved after NIH administrative review
- **Disapproved:** 59 lines
 - All lines disapproved after ACD review
 - Includes lines referred to ACD after NIH staff determined did not meet administrative review criteria
- **Submitted:** 39 lines

Findings For ACD Consideration Today

Working Group findings on 10 lines from 2 institutions:

- University of Queensland, Brisbane, Australia, 4 lines
- Guangzhou Medical College, Guangdong, China, 6 lines

University of Queensland Submission

- Submission originally from Australian Stem Cell Centre: ownership recently transferred to University of Queensland
- 4 normal lines from frozen embryos donated in 2004-2005 from patients at Melbourne IVF fertility clinic
- Derivation of hESCs done by Stem Cell Science Ltd. under license from Embryo Research Licensing Committee of National Health and Medical Research Council of Australia

WG Discussion of University of Queensland Submission

- Initially submitted under administrative review; moved to Working Group review because of borderline exculpatory language
- 3-part embryo donation consent process:
 - Consent to dispose or use excess embryos (with options)
 - Plain language statement about stem cell research
 - Consent to use embryos for derivation of stem cell lines

WG Discussion of University of Queensland Submission

- Working Group discussed borderline exculpatory language in the plain language document and stem cell research consent
 - language similar to New South Wales submission, which was approved through ACD
 - concluded that language was intended to let donors know that they would not benefit financially from the research
- The Working Group voted unanimously to suggest that the ACD recommend approval of these lines for use in NIH-funded research.

Guangzhou Medical College Submission

- Initially presented to the ACD on December 9, 2010
- Six lines from embryos donated in 2007
 - non-clinical grade embryos not usable for fertility treatment
- Embryo donation consent signed at the same time as IVF consent
- Approval and ongoing monitoring by hospital IRB
- Working Group noted that couples may have limited options with respect to clinical grade embryos in China due to the one child policy
 - Not a relevant issue for these lines derived from non-clinical grade embryos

WG Discussion of Guangzhou Submission

- Reasonable to agree to donate nonclinical grade embryos in advance of treatment
- Donation rate is 7-8% for research
 - Supports voluntariness of decisions
- Problematic statements in IVF treatment consents, in particular:
 - Multifetal pregnancy reduction necessary in case of pregnancy with more than two fetuses (*WG believes such a provision would be unacceptable in the U.S.*)

WG Discussion of Guangzhou Submission

2 translations of key terms in *The Subject's Acknowledgement*

Guangzhou translation

"The discarded **embryos** can not be available to any individual or research units without our consent. The discarded **embryos** can not be used to other experiment without our consent."

NIH translation

"The **specimens** may not be provided to any individual or research institution without our consent. The **specimens** may not be used in any other test in the laboratory without our consent."

WG Discussion of Guangzhou Submission

- Working Group voted 7-2 to put forward a positive finding to the ACD. Members voting in the minority felt that restrictions on choice in the clinical IVF clinical consent process were potentially coercive. Members voting in majority also expressed concern.
- December 9, 2010 ACD meeting: ACD raised concerns about what donors understood about use of the embryos. ACD tabled the submission and sent back to Working Group for further consideration.
- Working Group subsequently consulted 4 outside experts who are fluent in Chinese language, familiar with culture, and knowledgeable about IVF practices

WG Discussion of Guangzhou Submission

- 4 reviewers: consent form was more accurately translated as “specimen” as opposed to “embryo”
- 2 reviewers: ambiguous language on sharing cell lines with investigators at outside institutions
- 2 reviewers: overall consent form ambiguous and inadequate to enable couples to make an informed choice about the use of their embryos for stem cell research.
- Working Group agreed that the consent was ambiguous about what would be the product of the research and what could be distributed outside Guangzhou. **The Working Group voted unanimously to present a negative finding to the ACD.**

Summary Working Group Findings

- ACD should consider recommending to NIH Director that 4 lines from **University of Queensland**, Brisbane, Australia be **approved** for use in NIH-supported research
- ACD should consider recommending to NIH Director that 6 lines from **Guangzhou Medical College**, Guangdong, China, be **disapproved** for use in NIH-supported research