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
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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 and Center for Reproductive Medicine, Wichita
- 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

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; one set raises an additional question for ACD about flexibility of Section IIA review.

NIH Human Embryonic Stem Cell Registry

- Approved: 163 lines
  - 48 lines approved after ACD review
  - 115 lines approved after NIH administrative review
- Disapproved: 65 lines
  - All lines disapproved after ACD review
  - Includes lines referred to ACD after NIH staff determined did not meet administrative review criteria

Findings For ACD Consideration Today

Working Group findings on 10 lines from 2 institutions:

- GENEA, Sydney, Australia, 9 lines
  - Submissions 2012-ACD-002, -003
- California Stem Cell Inc., Irvine, California, 1 line
  - Submission 2012-ACD-001

GENEA Submissions
2012-ACD-002, -003

- GENEA (formerly Sydney IVF) is IVF clinic in Sydney, Australia
- Embryos with disease-specific mutations donated in 2007 by patients at GENEA
- hESC derivation at GENEA under license from National Health and Medical Research Council of Australia, per national law
  - Ethics committee approval required
  - Inspection and reporting process

GENEA Submissions

- 2-part consent process:
  - Donors sign “Declaration of Excess PGD Embryos” and choose option to consider donating embryos to specific research project
  - Donors sign consent for hESC derivation & research
- Initially submitted for administrative review under Section IIA of Guidelines
- Two submissions have nearly identical documentation

GENEA Submissions

- Section IIA requires donors be informed can withdraw embryo donation until hESCs derived (or embryo deidentified)
  - GENEA consent said had 2 weeks to withdraw
  - GENEA policy, explained verbally to donors, is can withdraw up until the time the hESCs derived.

- Moved to Working Group review/IIB because language in the consent regarding withdrawal of consent not completely consistent with Section IIA, although the verbal assurance is consistent.

WG Discussion of GENEA Submissions

- Working Group judged overall submission to be clear and concise.
- Discrepancy in the withdrawal information not viewed as a significant problem.
- The Working Group voted unanimously under Section IIB to suggest that the ACD recommend approval of these lines for use in NIH-funded research.

WG Discussion of GENEA Submissions

- Question from NIH

Could NIH use Section IIA to approve future submissions that present a similar issue: verbal consent is in accordance with Section IIA withdrawal requirement, but written consent is not completely consistent?

- Working Group did not make a motion on this question, but is comfortable with NIH evaluating documents beyond the embryo donation consent to determine whether Section IIA criteria are met.

California Stem Cell Inc.
Submission 2012-ACD-001

- Single line from embryo donated in 2006 at California IVF clinic
- Initially submitted for administrative review/IIA
  - IIA requires donors be informed can withdraw embryo donation until hESCs derived or embryo deidentified.
  - No information in consent regarding withdrawal; company states there is no evidence that donors were informed.
- Moved to Working Group review under IIB because of withdrawal issue.

WG Discussion of California Stem Cell Submission

- Working Group also concerned about lack of withdrawal information.
- Undated protocol and process documents discuss withdrawal procedures, but company has no evidence that either document was in effect at time.
- In addition, consent contained exculpatory language: donors give up rights under Federal law to control use of cell lines.
  - While no such law exists, such language could nonetheless cause further confusion about withdrawal ability.

WG Discussion of California Stem Cell Submission

- IRB approval occurred 3 years after embryo donation
  - Company not required to obtain IRB review since no HHS funds or federal assurance with OHRP
  - Lack of impartial review presents ethical problem
- Other options for embryos listed in embryo disposition form but not in consent; Working Group agreed that key information can be presented in forms other than consent.
- Due to multiple concerns, Working Group voted unanimously under Section IIB to suggest that the ACD recommend disapproval of these lines for use in NIH-funded research.

Proposed Actions for ACD

- Recommend to NIH Director that 9 lines from GENEA (submissions 2012-ACD-002, -003) be approved for use in NIH-supported research.

- Recommend to NIH Director that 1 line from California Stem Cell Inc. (submission 2012-ACD-001) be disapproved for use in NIH-supported research.

- Provide advice regarding whether NIH may use Section IIA to approve future submissions where verbal consent is in accordance with Section IIA withdrawal requirement, but written consent not consistent.