

6 June 2012

**Advisory Committee to the Director (ACD)  
Working Group for Human Embryonic Stem Cell Eligibility Review**

**Findings and Minutes of Discussion Regarding  
GENEA Submissions 2012-ACD-002 and 2012-ACD-003**

Finding regarding all lines in GENE A submissions 2012-ACD-002 and 2012-ACD-003

The ACD should consider recommending that the NIH Director approve the use of these nine cell lines in NIH-funded research under the Section IIB criteria of the NIH Guidelines for Human Stem Cell Research.

Summary of Discussion

The Working Group reviewed all documents in support of these two new requests from GENE A (formerly Sydney IVF) for a total of nine cell lines to be approved for use in NIH-funded research. Submission 2012-ACD-002 includes three cell lines derived from embryos affected by Huntington's disease, cystic fibrosis, and Wilms' tumor. The consent form uses the phrase "genetically abnormal (affected)" to describe these embryos. Submission 2012-ACD-003 includes six cell lines derived from embryos affected by Huntington's disease, cystic fibrosis, facioscapulohumeral muscular dystrophy, Van Hippel-Lindau disease, and Charcot-Marie-Tooth disease; the consent form describes these embryos as "affected by a genetic condition." Aside from these two differing phrases, the two submissions contain materials that are substantively identical, including the embryo donation consent, information for participants, and license documents. Therefore, the comments below apply to both submissions.

All embryos were created for reproductive purposes, using in vitro fertilization. Derivation occurred in 2007, from the inner cell mass at the blastocyst stage. The donors gave written consent for research purposes, and it was clear that the embryos would be used for stem cell research, that the cell lines made from the embryos would be kept for years, and that donation was made without restriction. The consent form stated clearly that there would be no direct benefit to the donor but that there may be commercial benefits to GENE A. The consent form discussed confidentiality, and the subjects were informed of other options, with no inducements. The separation between clinical care and decision to donate the embryo for research was stated clearly.

The two submissions were initially submitted for administrative review under Section IIA of the NIH Guidelines for Human Stem Cell Research, but were moved to Working Group review based on language pertaining to withdrawal of consent. Specifically, the embryo donation consent document states: "If you do decide to donate your embryos affected by a genetic condition they will be cryostored ('frozen') for at least two weeks before use. You can withdraw your consent at any time during this two weeks period." The consent also states "It is for this reason that embryos will not be used for at least two weeks after you have given your consent,

which gives you this time to reconsider your decision.” Later in the consent, there is the statement: “Because the process of deriving embryonic stem cells will destroy our embryos, Sydney IVF will not use our embryos until 2 weeks after we give our consent, in case we decide to withdraw our consent.” In response to a question from the NIH staff, GENE explained that, in practice, the patients were informed verbally that withdrawal could occur until the embryo was actually used for stem cell derivation.

The Working Group discussed the discrepancy between the language in the consent form and the information provided to the patients verbally. Several Working Group members commented that verbal communication can never be as effective as a written document, which can be taken home, read, and reconsidered. However, the overall Working Group did not consider the 2-week interval to be a significant problem given that the stem cells were derived in 2007 and that the consent form could not be expected to meet the Guidelines criteria exactly. Therefore, the submission meets the Section IIB criteria. In a way, the 2-week reference could be seen as a helpful illustration, informing the subjects about the nature of the research process and their rights. This is consistent with the thoughtful and stepwise approach demonstrated throughout the submission, including the description of the two-stage consent process.

The submission is clear and concise, and the Working Group had no major concerns about the verbal assurance of the timeline for withdrawal of consent. The Working Group voted unanimously to present a positive finding to the ACD (under the Section IIB criteria) for the use of these nine cell lines in NIH-funded research.

#### Additional Discussion

After having arrived at a positive finding for the cell lines submitted under 2012-ACD-002 and 2012-ACD-003, the NIH staff then asked the Working Group to consider the separate matter of future referral of applications with similar issues. For example, do these two submissions meet Section IIA criterion regarding withdrawal of embryo donation, and if so, would the Working Group be comfortable with having future applications with similar language undergo administrative review, bypassing review by the Working Group entirely?

The Working Group members discussed their level of comfort with having applications with issues similar to those identified for 2012-ACD-002 and 2012-ACD-003 referred to administrative review as opposed to review by the Working Group. In favor of the latter option, the point was made that review under Section IIB criteria allows the submission to be looked at in a broader context. This is clearly important for submissions with cell lines derived before the Guidelines were published. Also, Working Group members expressed their belief that this would not place a significant workload burden on them; if NIH believes that it would be helpful for the Working Group to deliberate, then the members are pleased to do so. Arguments were also offered in support of the blanket referral to administrative review for applications with required information missing from the consent documents but present either in other materials or through verbal assurances. The point was made that, if the applicant has done an excellent job overall in communicating with subjects and has been thoughtful about the process, then the location of the information within the materials may not be critical.

The Working Group expressed its belief that submissions 2012-ACD-002 and 2012-ACD-003 probably met the Section IIA criteria, but the members did not feel comfortable making a formal motion to that effect. Instead, the Working Group proposed that the ACD weigh in on this matter and the implications for the referral of future submissions, with the understanding that the Working Group is flexible on this issue. The Working Group supports the ability of the NIH staff and administrative review to evaluate documents beyond the informed consent, in conjunction with assurances, in making a determination about whether Section IIA criteria are met.

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