November 28, 2011

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

Findings and Minutes of Discussions Regarding
University of Queensland Submission 2011-ACD-006

Finding Regarding All Lines in University of Queensland[1] Submission 2011-ACD-006

The ACD should consider recommending that the NIH Director approve the lines in this submission for use in NIH-funded research

First Discussion

The Working Group reviewed all documents in support of this request for four cell lines to be approved for use in NIH-funded research. This request was initially submitted for Administrative Review under Section IIA consideration, then moved to review under Section IIB because the embryo donation consent form was deemed to contain borderline exculpatory language. Notably, the language is similar to that of an earlier submission from the University of New South Wales that was moved from Administrative Review to the Working Group for the same reason and ultimately approved for listing on the NIH Registry.

The four cell lines were derived in 2004 (lines MEL-1 and MEL-2) and 2005 (lines MEL-3 and MEL-4) from embryos donated from patients at the fertility clinic, Melbourne IVF. The National Health and Medical Research Council's Licensing Committee approved the use of embryos for the period 2004-2008, which covers the donation and derivation timeline for all lines described in this submission. All four lines have been demonstrated to have a normal human diploid karyotype.

Stem Cell Science Ltd (SCS) was responsible for the isolation and identification of the cell lines, and the Australian Stem Cell Centre provided financial support for these efforts. The documents state that neither the employees of SCS nor the employees of the Australian Stem Cell Centre were involved in the consent process.

The Australian Stem Cell Centre distributes all four MEL lines to Australian researchers through its StemCore facility, while international distribution is provided by Millipore (lines MEL-1 and

[1] After the discussions were finished, Australian Stem Cell Centre notified NIH that it is ceasing its operations and ownership and responsibility for distribution of the MEL lines has been transferred to Stem Cells Ltd, a not-for-profit company operating within the University of Queensland. Thus, the minutes below refer to the Australian Stem Cell Centre but the submission title has been changed to the University of Queensland.

MEL-2) and StemCore (lines MEL-3 and MEL-4). International researchers can also obtain the MEL-1 and MEL-2 lines through the UK Stem Cell Bank.

The submission provides three documents related to consent, the first of which, "Consent to the Disposal or the Use of Excess Frozen Embryos" is a short, straightforward form. The form states that the individuals "no longer require the embryo(s) to be transferred to the woman" and it asks the individuals if they want the frozen embryo(s) to be: a) thawed and discarded; b) made available for research; or, c) donated to another couple. There is no option for long-term storage on this form.

Individuals who selected the research option were then referred to the "Plain Language Statement." This 2-page document is clear overall, but contains the following language that could possibly be interpreted as exculpatory: "Excess embryos must be donated altruistically for the project. While no commercial gains will result from the derivation of ES lines, the embryo donors will have no claim now or in the future on any financial benefits that may be generated from the use of these cell lines." The Working Group agreed this language is similar to an earlier submission from the University of New South Wales which was approved after a thorough discussion of this point; this issue is discussed in more detail below.

Through a third consent document entitled "Consent for the Use of Embryos for the Derivation of Embryonic Stem Cell Lines," the couple selected a research project and documented that they understood that the embryos would be destroyed in the derivation process and that any cell lines that are created would be used for "basic" and "general" stem cell research. This form also includes text similar to that referred to above: "We acknowledge that while no commercial gains will result from the derivation of ES cell lines, we have no claim now or in the future on any financial benefits that may be generated from the use of these lines." Their signatures on this form completed the consent process. Also, in answering a question from NIH staff, the submitters indicated that the lines are not appropriate for clinical use as they were not derived under GMP conditions.

The primary discussion of the Working Group centered on whether the text referred to above within the second and third consent documents could be considered exculpatory. The Working Group considered this thoroughly and agreed that it is not exculpatory. However, the Working Group was puzzled by the phrase: "While no commercial gains will result from derivation of these cell lines…." This wording appears to imply that no one will derive commercial gain; this does not seem likely. For example, Millipore, a private enterprise, might profit financially from their distribution of lines MEL-1 and MEL-2. It is possible the phrase "no commercial gain" refers to nonclinical use, but again this is unclear.

The Working Group voted unanimously to present a positive finding to the ACD. It was agreed that the consent language that donors will have no claim on financial benefits is appropriately intended to let the individuals know they will not benefit financially, and the Working Group is comfortable with the language as written. The NIH will need to work with the submitter to develop an appropriate statement about allowable use, in the event that the lines are posted on the Registry.

Second Discussion

At the prior meeting, the Working Group voted unanimously to present a positive finding to the ACD. Following that meeting the submitter conveyed two points of clarification which were brought to the second discussion for informational purposes.

First, as part of the consent process, the donor couple documented that they understood that any cell lines that are created would be used for "basic" and "general" stem cell research. At the earlier meeting the Working Group stated that the NIH would need to work with the submitter to develop an appropriate statement about allowable use, in the event that the lines are posted on the Registry. NIH staff noted that the submitter indicated that the lines are not suitable for clinical purposes. In response to NIH, the submitter agreed that "not for clinical use" should be indicated in the "Provider Restrictions" field on the Registry. As part of a brief follow-on discussion of this point, NIH staff reminded the Working Group of the process for placing restrictions on eligible cell lines.

Second, at the earlier meeting the Working Group had questioned apparently contradictory statements pertaining to potential commercial gains. Specifically, the consent documents provided in the original submission included the statement: "We acknowledge that while no commercial gains will result from the derivation of ES cell lines, we have no claim now or in the future on any financial benefits that may be generated from the use of these lines." The submitter provided a clarification of this language, stating that the wording "no commercial gains will result from the derivation of ES cell lines" was included to address potential concerns from the donors that the derivation may have been a commercial arrangement, given the involvement at that time of Stem Cell Sciences Pty, Ltd. Therefore, the statement pertained to the parties involved in the derivation, and the submitter wanted to make it very clear that the project was an altruistic undertaking by all parties.

The submitter also verified that the phrase "…we have no claim now or in the future on any financial benefits that may be generated from the use of these lines" was indeed aimed at potential concerns related to the use of the cell lines. Since the intent from the outset was to share the cells widely, this statement was included to make it clear that the donors should not expect any financial benefit from discoveries made through the use of the cell lines.

The Working Group appreciated the clarification of these issues, and they found no reason to reconsider their previous positive finding.

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