

## **GESCR PROCEDURE: REVIEW PROCESS AND LEVELS OF REVIEW**

Office of Origin: Human Research Protection Program

Effective Date: June 2009

### **I. Introduction**

The Human Gamete, Embryo and Stem Cell Research (GESCR) Committee functions as the Stem Cell Research Oversight (SCRO) Committee for the University of California, San Francisco (UCSF).

### **II. Purpose**

This procedure document describes the GESCR Committee's process for review of stem cell protocols, as well as the varying levels of review that are applied to these research protocols.

### **III. Review Process**

To initiate review of a protocol by the GESCR Committee, the applicant must submit the following forms:

- Committee on Human Research (CHR) [Application Form](#): Submit to Human Research Protection Program (HRPP). Simultaneously, submit a copy of the cover page of the CHR Application Form to the Office of Research Compliance Coordinator;
- [Human Stem Cell Research Supplement](#): Submit to HRPP and Office of Research Compliance Coordinator;
- [Request for hESC Equipment Approval](#) (if applicable): Submit to the HRPP and to the Office of Research Compliance Coordinator.

On receipt of the materials described above, the GESCR Coordinator:

- Reviews the information provided;
- Forwards the CHR Application Form, Human Stem Cell Research Supplement and, if provided, the Request for hESC Equipment Approval, (collectively, the Application) to the GESCR Committee Chair (Chair), and;
- Suggests the appropriate level of review to the Chair. There are three levels of review applied to research protocols submitted to the GESCR Committee for review. In summary, these are:

**Administrative Review:** Research protocols that involve purely in vitro research and that use pre-existing stem cell lines are eligible for "administrative review". This is an accelerated review process.

**Expedited Review:** Research protocols that involve injection of human stem cells into post-natal animals, as well as some protocols involving injection of human stem cells into non-human blastocysts, embryos or fetuses, may be eligible for "expedited review". The "expedited review" process involves more scrutiny than administrative review, but less than "full review".

**Full Review:** Where a protocol is not eligible for administrative or expedited review, it is subject to full review by the GESCR Committee.

**A full description of the levels of review is detailed in Section IV of this document.**

*Please note: GESCR-specific application and renewal forms are under development and, when completed, will be published on the Office of Research website.*

#### **A. Administrative Review**

The Chair and the GESCR Coordinator review and approve protocols that are eligible for administrative review. All administrative review approvals are then formally reported in writing to the GESCR Committee at regularly scheduled review meetings. Reports include the name of PI, title of protocol, and short description of the protocol.

#### **B. Expedited Review**

The Chair reviews protocols that are eligible for expedited review and also designates one other Committee member, with scientific expertise relevant to the protocol, to review the protocol.

The GESCR Coordinator distributes the Application to the Chair and the designated reviewer. At the next Committee meeting, the Chair and the designated reviewer present the protocol and their opinions to the Committee. After appropriate deliberation, the Chair, designated reviewer, GESCR Coordinator and any other Committee members who choose to participate decide on the outcome of the review.

### **C. Full Review**

The Chair designates three Committee members as lead reviewers to review protocols that require full review; one with scientific expertise pertinent to the protocol, one with ethics expertise and one nonaffiliated GESCR Committee member.

The GESCR Coordinator distributes the Application to all GESCR Committee members. At a Committee meeting, the three lead reviewers present the protocol and their analysis to the Committee. After deliberation, those committee members present (who must include a quorum in order to take official action), vote on the outcome of the review.

### **D. Additional Information**

At any stage in the review process, the Chair or another Committee member who has been selected by the Chair to review the Application may require the applicant to submit additional information or documentation to the GESCR Committee in support of the Application.

### **E. Additional Review**

If the Chair determines, at the Chair's discretion, that a protocol requires additional review, he or she may forward the Application to an ad hoc reviewer or to one or more additional Committee members for additional review on an expedited basis or to the Committee for full review.

If the Chair or the designated reviewer determines that a protocol that is undergoing expedited review raises concerns about transferring human characteristics into non-human animals, he or she must forward the Application to the Committee for full review.

### **F. Additional Approval**

Final approval of the protocol by the GESCR Committee is contingent on receipt by the GESCR Committee of documentation of other required approvals, such as approval by the CHR, the Institutional Animal Care and use Committee or the Biological Safety Committee.

## **IV. Levels of Review**

There are three levels of review applied to research protocols submitted to the GESCR Committee for review; administrative review, expedited review, and full review.

### **A. Administrative Review**

The following protocols are eligible for administrative review:

1. Protocols involving purely in vitro research, excluding protocols for differentiation of human stem cells into gametes or totipotent cells, which use only:
  - (a) Human adult stem cells or human cord blood stem cells; or.
  - (b) Human pluripotent stem cell lines that have been "acceptably derived". For purposes of this document, pluripotent stem cell lines have been "acceptably derived" when they have been:
    - (i) Approved by the National Institutes of Health;

- (ii) Deposited in the United Kingdom Stem Cell Bank;
  - (iii) Derived by, or approved for use by, a licensee of the United Kingdom Human Fertilization and Embryology Authority;
  - (iv) Derived in accordance with the Canadian Institutes of Health Research Guidelines for Human Pluripotent Stem Cell Research under an application approved by the National Stem Cell Oversight Committee, or;
  - (v) Derived in accordance with the Japanese Guidelines for Derivation and Utilization of Human Embryonic Stem Cells, or;
  - (vi) Derived prior to November 22, 2006, and been found to be “acceptably derived”, within the meaning of Title 17, Section 10080 of the California Code of Regulations, by the Independent Citizens’ Oversight Committee, which is the governing board of the California Institute for Regenerative Medicine, or
- (c) Human stem cell lines which have been previously been approved for use by the GESCR Committee, or;
  - (d) Non-pluripotent human stem cells derived from a stem cell line listed in Section IV.A.1(a), (b) or (c), above, or;
  - (e) Induced pluripotent (iPS) cells, excluding protocols directed at creating a totipotent human cell from an iPS cell, which satisfy at least one of the following requirements:
    - (i) The GESCR Committee approved the consent form and process for obtaining the somatic cells used for induction.
    - (ii) The GESCR Committee receives written confirmation from a Stem Cell Research Oversight Committee, an Institutional Research Board (IRB)<sup>1</sup> or, if the iPS cells were derived at an institution outside of the United States, a substantially equivalent oversight body, that the oversight body approved the process for obtaining the somatic cells used for induction.
    - (iii) The process for obtaining the somatic cells used for induction was not “research involving human subjects” within the meaning of Title 45, Part 46 of the US Code of Federal Regulations (45 CFR Part 46).
    - (iv) The process for obtaining the somatic cells used for induction was exempt from the requirements of 45 CFR Part 46, under 45 CFR Part 46.101(b).
- 2. Protocols for human iPS cell induction, where the process for obtaining the somatic cells used for induction satisfies the requirements of Section IV.A.1(e)(i), (ii), (iii) or (iv), above.
  - 3. Protocols involving the injection of human stem cells into post-natal non-human animals, which use a stem cell line that is described in Section A.1 above, excluding:
    - (a) Protocols involving the introduction of neural progenitor cells into the brains of post-natal non-human animals, and;
    - (b) Protocols involving the introduction of human pluripotent stem cells into post-natal non-human animals; and
    - (c) Protocols in which there is a significant possibility that the implanted human stem cells could give rise to neural or gametic cells and tissues. In considering the likelihood of such an outcome, particular attention should be paid to at least three factors:
      - (i) The extent to which the implanted cells colonize and integrate into the animal tissue, and;

- (ii) The degree of differentiation of the implanted cells, and;
  - (iii) The possible effects of the implanted cells on the function of the animal tissue.
4. Renewals of approvals for protocols and requests for modifications to protocols which have been previously approved by the GESCR Committee, where no modifications to the protocol require expedited or full review, regardless of the initial level of review.

#### **B. Expedited Review**

The following protocols are eligible for expedited review:

1. Protocols involving the injection of human stem cells into non-human blastocysts, embryos or fetuses, which use a stem cell line that is described in Section IV.A.1, above, excluding:
  - (a) Protocols involving the introduction of human pluripotent stem cells into non-human blastocysts, embryos or fetuses, and;
  - (b) Protocols involving the introduction of neural progenitor cells into a non-human blastocyst, embryo or fetus, and;
  - (c) Protocols in which there is a significant possibility that the implanted human stem cells could give rise to neural or gametic cells and tissues. In considering the likelihood of such an outcome, particular attention should be paid to at least the three factors listed in Section IV.A.3(c), above.
2. Protocols involving the injection of human stem cells into non-human post-natal animals that:
  - (a) Use a stem cell line that is described in Section IV.A.1, above, and;
  - (b) Do not qualify for administrative review under Section IV.A.3, above, but excluding: (i) protocols involving the introduction of human pluripotent stem cells into post-natal non-human primates or (ii) protocols involving the introduction of neural progenitor cells into the brains of post-natal non-human primates.

#### **C. Full Review**

Full review by the GESCR Committee is required for any other protocols, outside of those described in Section IV.A and Section IV.B above, which require review by the GESCR Committee.

#### **V. Other Resources**

California Code of Regulations, Title 17, Section [100080](#) (Acceptable Research Materials)

California Department of Public Health Guidelines for Human Stem Cell Research, as recommended by the Human Stem Cell Research Advisory Committee pursuant to Health and Safety Code 125118, [Section 6](#)

[National Academies Guidelines for Human Embryonic Stem Cell Research \(2005\)](#)

[Amendments to the National Academies Guidelines for Human Embryonic Stem Cell Research \(2007\)](#)

“Establishing Procedures for Institutional Oversight of Stem Cell Research”, Patricia Zettler, Leslie E. Wolf, JD, MPH, and Bernard Lo, MD, *Academic Medicine*, Vol. 82, No. 1, January 2007

<sup>1</sup> “IRB” has the same meaning as the term defined in Title 17, California Code of Regulations, Section 100020(g): an entity established in accordance with the Code of Federal Regulations, Title 45, Section 46.107.