University of California, Los Angeles

Embryonic Stem Cell Research Oversight (ESCRO) Committee

Policies and Procedures

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1.0 PURPOSE

The purpose of the UCLA Embryonic Stem Cell Research Oversight (ESCRO) committee is to provide oversight of human embryonic stem cell (hESC) research and other stem cell research covered by the California Institute for Regenerative Medicine (CIRM) and California Department of Public Health (CA DPH) regulations in order to ensure that UCLA research meets the highest scientific and ethical standards. The goals are achieved in collaboration with the UCLA administration, the UCLA Institutional Review Boards (IRBs), other applicable campus compliance committees, and the participation of the research community.

2.0 AUTHORITY

UCLA policy and California law requires the creation of an ESCRO to oversee hESC and research with other covered cells[1] (referred to in this document as "stem cells"). The policy is based in part on the recommendations of the National Bioethics Advisory Commission[2], the National Academies of Science-Institute of Medicine[3] guidelines, and standards created by CIRM[4] and CA DPH.

3.0 FUNCTION

The ESCRO reviews new protocols, modifications to currently approved research, and continuing research using or creating human pluripotent stem cells or stem cell lines, any proposed collection and use of germ or other cells designed to generate pluripotent stem cells, and any "covered cells"[1] as required by State or Federal law.

4.0 Review

The ESCRO is one of several committees that may be required to review stem cell research. The other committees include but are not limited to the IRB http://ohrpp.research.ucla.edu/, the Chancellor's Animal Research Committee (ARC) http://oaro.research.ucla.edu/applications, the Institutional Biosafety Committee (IBC) http://biosafety.ucla.edu , or other committees required by laws, regulations, or institutional policy.

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[1] The CIRM defines "covered cells" as *"…culture-derived, human pluripotent stem cell population that is capable of: 1) sustained propagation in culture; and (2) self-renewal to produce daughter cells with equivalent developmental potential. This definition includes both embryonic and non-embryonic human stem cell lines regardless of the tissue of origin. 'Pluripotent' means capable of differentiation into mesoderm, ectoderm, and endoderm."* Therefore, ESCRO review is required for research with human pluripotent stem cells and populations, regardless of their origin, capable of differentiation into multiple tissue types. Adult precursors that differentiate into cells of a single tissue type do not meet all three CIRM criteria and would not be subject to ESCRO review.

[2] National Bioethics Advisory Commission, Ethical Issues in Human Stem Cell Research, 1999: http://www.georgetown.edu/research/nrcbl/nbac/pubs.html .

[3] National Academies of Science-Institute of Medicine, Guidelines for Human Embryonic Stem Cell Research, National Academies Press: 2005, http://fermat.nap.edu/books/0309096537/html/ .

[4] California Institute for Regenerative Medicine, Standards Working Group: *http://www.cirm.ca.gov/reg/default.asp*

4.1 Review Procedures

The ESCRO will assess protocols according to Standard Operating Procedures.

4.2 Scope of review and responsibilities

- **4.2.1** All issues related to derivation, use, procurement, and disposal of covered cells
- **4.2.2** Scientific merit, including whether the cells are well-characterized and screened for safety
- **4.2.3** Ensure the conditions under which cells are maintained and stored meet current scientific standards
- **4.2.4** Ensure that the primary cells or resulting cell lines were obtained ethically and with informed consent as required by law or policy
- **4.2.5** Compliance with relevant regulations and guidelines
- **4.2.6** Consultation and collaboration with the IRBs and other relevant compliance committees
- **4.2.7** Maintain a registry of covered cells and lines derived or obtained by investigators
- **4.2.8** Maintain a registry of UCLA stem cell research
- **4.2.9** Adverse Events
- **4.2.10** Monitoring
- **4.2.11** Suspension and Termination
- **4.2.12** Maintenance of records
- **4.2.13** Education

4.3 Continuing Review

The ESCRO will review on-going research at a minimum of once every year.

4.4 Modifications to Approved Protocols

All modifications to approved protocols must be submitted prospectively to the ESCRO. No modifications, except in an emergency, if necessary to safeguard the well-being of animal or human subjects, may be implemented without prospective review and approval by the ESCRO and other applicable committees.

4.5 Approval

The ESCRO has the authority to approve, require modifications in a protocol in order to approve, or disapprove submitted research. The ESCRO will notify investigators in writing in a timely fashion of its decision. An ESCRO decision to require modifications or disapprove a submission will include a written statement to the investigator of the reasons for its decision and give the investigator an opportunity to respond in writing and if requested, in-person during a convened meeting.

4.6 Appeals

Appeals of ESCRO decisions must return to the ESCRO for additional review. Investigators may request to present responses to ESCRO decisions during a convened

meeting. Appeals must be in writing and submitted directly to the ESCRO prior to an investigator's personal presentation to the ESCRO.

4.7 Expedited Review

Expedited review means the chair or other qualified member(s) of the committee has the authority to review and approve a proposal or request modifications in order to approve a proposal without convening a quorum of the committee. A proposal under expedited review may be referred to the ESCRO for a full committee review at the discretion of the reviewer.

4.7.1 *Eligibility for Expedited Review*

The ESCRO may perform an expedited review of new research and renewals. Expedited review may also be conducted for amendments that do not substantively modify the currently approved research.[5]

4.7.2 *Expedited Review of New and Continuing Research*

New and renewal applications may undergo expedited review when the project is conducted by qualified investigators who request to utilize stem cell lines that are currently approved at UCLA and/or techniques for creating hPSC previously approved by the ESCRO. New and renewal protocols that include certain types of animal or human research studies may require convened committee review.

4.7.3 *Expedited Review of Amendments to Approved Research*

Amendments requesting the addition of research personnel, space, animals, and de-identified cell lines consistent with the initially approved study aims and design are eligible for expedited review. A convened committee review may be required when new grants, etc., include aims that are inconsistent with the approved research protocol.

4.7.4 *Limits to Expedited Review Decisions*

The ESCRO member(s) conducting expedited review will only have the authority to approve or recommend modifications to the proposal in order to achieve approval. Expedited review may not be used to disapprove a proposal. Only the convened ESCRO may disapprove an application.

4.7.5 *Reporting Expedited Review to the ESCRO*

The ESCRO will be notified of all expedited approvals with a short description of the approved proposal.

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[5] Modifications may include the addition of non-human animal subjects with ESCRO approved cells so long as the changes will not result in any major functional contributions to the brain. Other modifications may include minor proposed changes that do not significantly modify the scientific design of the protocol, such as, changes in investigators, replacement of equivalent proven laboratory techniques, laboratory relocation, etc.

4.8 Monitoring

The ESCRO has the authority to observe or have a third party observe the research, monitor, and audit research under its jurisdiction.

4.9 Adverse Events

Adverse events may occur with human subjects, employees, or cellular material. Any adverse events that occur with human subjects that by UCLA policy require reporting to the IRB must also be reported to the ESCRO.

4.9.1 *Required Reporting of Events with Employees*

Any adverse events to employees or others that would be reported to the IBC/Environmental, Health, and Safety, will also be reported to the ESCRO.

4.9.2 *Required Reporting of Adverse Laboratory Events*

The investigator is responsible for documenting and reporting laboratory events to the ESCRO, such as but not limited to, the inability to expand cells due to contamination or contamination with pathogens. Such reports should include the reason for the contamination, the disposition of the cells, and any corrective actions.

4.10 IRB Review

IRB review is required when the research meets the federal or state threshold for human subjects research.[6]

4.10.1 *Collaboration with the IRBs*

When IRB review is required, the ESCRO and the IRBs will collaborate in order to ensure approved research meets the highest scientific and ethical standards.

When IRB review is required:

4.10.2 Ultimate ESCRO approvals will be contingent upon IRB approval of proposed research.

4.10.3 ESCRO review will occur prior to IRB review and serve to inform the IRB review.

4.10.4 ESCRO members are available to attend IRB meetings to discuss proposed research, as requested by the IRBs.

4.10.5 The IRBs and ESCRO will freely exchange information in order to facilitate and coordinate the review of proposed research.

4.11 Suspension and Termination of ESCRO Approval

The ESCRO has the authority to suspend or terminate its approval of research that is not being conducted in accordance with the ESCRO's requirements, regulatory agency requirements, or that has been associated with unexpected serious harm to subjects, or

[6] Vice Chancellor Roberto Peccei to Deans, Directors, Department Chairs, and Faculty. Memorandum: Change in Institutional Review Board (IRB) Requirements for Human Embryonic Stem Cell (hESC) Research, January 4, 2007;

others. Suspension or termination will be promptly reported to the investigator, other applicable campus compliance committees, the hESC Research Policy Board, and the chair of the investigator's department.

5.0 STRUCTURE

The ESCRO shall consist of a minimum of 5 members and a maximum of 12 members, including the Chair. Members are appointed by the Vice Chancellor-Research after broad consultation with the UCLA research community. A majority of the voting members must have expertise in relevant scientific and/or medical fields, e.g., molecular biology, developmental biology, stem cell research, assisted reproduction, legal and/or ethical issues in hPSC research as well as non-scientific members and patient advocates who are not affiliated with UCLA. There may be alternates and non-voting members.

5.1 Consultants

The ESCRO may, at its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the ESCRO. These individuals may not vote with the ESCRO.

5.2 Ad Hoc Committees

The ESCRO may, as necessary, create ad hoc subcommittees, composed of members of the parent Committee and, as appropriate, consultants with relevant expertise to perform specific functions within the ESCRO's jurisdiction. Subcommittee members may serve as a voting member on more than one subcommittee.

5.3 Membership Terms

Members shall be invited to serve for overlapping terms of 2 years, with terms of no more than 2 years contingent upon renewal of the Committee's Charter by appropriate action prior to its expiration.

5.4 hESC Research Policy Board

The Vice Chancellor for Research will convene the hESC Research Policy Board at least quarterly to discuss and promulgate campus policy for hESC research. The ESCRO chair will also serve as a member on the UCLA hESC Research Policy Board.

5.5 Support

Management and support services will be provided by the UCLA Broad Stem Cell Research Center.

6.0 MEETINGS

Meetings shall be held as often as necessary to provide timely review of submitted research. Meetings shall be conducted, and records of the proceedings kept, as indicated in other sections of this policy.

6.1 Quorum

The ESCRO may only review and act upon proposed research during a convened meeting with a majority of the members present, including at least one non-scientist, or in accordance with expedited review policy. In order for the research to be approved at a convened meeting, it shall receive the approval of a majority of those members present at the meeting.

6.2 Conflict of Interest

No member may participate in the ESCRO's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the ESCRO. Members with a conflict of interest must be recused from the discussion and the vote of the protocol except to answer questions of the Committee about the proposed research.

7.0 ESCRO MEETING DOCUMENTATION

The ESCRO shall maintain documentation sufficient to meet the requirements of this policy.

7.1 Research and Cell Registries

The ESCRO will maintain an auditable database of:

a. stem cell research conducted by UCLA investigators
b. stem cells and cell lines derived or obtained by UCLA investigators.

7.2 Meeting Documentation

The ESCRO will maintain minutes of the meetings and relevant correspondence with investigators, including approvals and disapprovals. The Minutes shall be in sufficient detail to document:

a. attendance at the meetings;
b. actions taken by the ESCRO;
c. the vote on these actions including the number of members voting for, against, and abstaining;
d. the basis for requiring changes in or disapproving research; and
e. a written summary of the discussion of controverted issues and their resolution.

7.3 Documentation Maintenance

The ESCRO will maintain copies of reviewed proposals, reports of adverse events, progress reports, continuing review applications, correspondence with investigators, IRB and other applicable compliance committee approvals, and a list of ESCRO members.

7.4 Documentation Retention

The ESCRO will maintain related stem cells records for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research.