

## UCI ADMINISTRATIVE POLICIES & PROCEDURES

### RESEARCH AND SPONSORED ACTIVITIES

#### Human Stem Cell Research Oversight Program

#### Section 484-1: Review of Human Stem Cell Activities

Responsible Office: Office of Research Administration

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#### Background and Purpose

It is the purpose of this policy to describe the specific requirements, roles and responsibilities for the review and approval of human stem cell activities at UCI. This policy is intended to ensure the derivation, procurement, banking, and use of human stem cell lines is conducted in a responsible and ethically sensitive manner, and in compliance with all applicable federal and state laws and regulations, ethical guidelines and applicable University policies and procedures that are referenced in this policy.

#### Applicability

Any human stem cell activity conducted by or for UCI is covered under this policy if it satisfies any of the following criteria:

- A. It is conducted by or under the direction of UCI personnel in connection with his or her UCI responsibilities.
- B. It uses UCI property, facilities, or resources to support or carry out the activity.
- C. The name of the University of California, Irvine is used in applying for funds (intra or extramural).
- D. The investigator plans to use his/her University of California, Irvine association in any dissemination, publication or public presentation resulting from the activity.
- E. The name of the University of California, Irvine is used in explanations and/or representations to subjects.
- F. UCI's non-public information will be used to identify or contact human research subjects or prospective subjects.

#### Definitions

**Adult Stem Cell:** An undifferentiated cell found in a differentiated tissue that can renew itself and (with certain limitations) differentiate to yield all the specialized cell types of the tissue from which it originated.

**Blastocyst:** A very early embryo consisting of approximately 30 to 150 cells. The blastocyst consists of a sphere made up of an outer layer of cells, a fluid-filled cavity, and a cluster of cells on the interior.

**Clinical Investigation:** Any experiment that involves a test article and one or more human subjects that is subject to the Federal Food, Drug, and Cosmetic Act.

**Human Stem Cell Research Oversight (hSCRO) Committee:** University appointed committee providing oversight of all issues related to the procurement and use of human stem cell lines and to facilitate education of investigators involved in human stem cell research.

**Embryonic Germ Cells:** Cells found in a specific part of the embryo/fetus called the gonadal ridge that normally develop into mature gametes (i.e., sperm and egg).

**Fetal Stem Cells:** Pluripotent stem cells taken from aborted fetal tissue. Federal regulations treat fetal stem cells as adult stem cells.

**Fetus:** A developing human from usually two months after conception to birth.

**Human Embryo:** The developing organism from the time of fertilization until the end of the eighth week of gestation, when it becomes known as a fetus.

**Human Embryonic Stem Cells (hESCs):** Pluripotent cells that are self-replicating derived from human embryos and are capable of developing into cells and tissues of three primary germ layers. Although hESCs may be derived from embryos, such stem cells are not themselves embryos.

**Human Subject:** A living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual; or (2) identifiable, private information.

**Human Subjects Research:** Any research or clinical investigation that involves human subjects.

**Institutional Animal Care and Use Committee (IACUC):** Committee charged with reviewing the use of animals in research, testing, teaching and related activities.

**Institutional Biosafety Committee (IBC):** Committee charged with reviewing research involving use of recombinant DNA molecules, infectious agents and select agents.

**Institutional Review Board (IRB):** A specifically constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research and clinical investigations.

**In Vitro:** Literally, “in glass”; in a laboratory dish or test tube; an artificial environment.

**In Vitro Fertilization (IVF):** An assisted reproduction technique in which fertilization is accomplished outside the body.

**Pluripotent Stem Cell:** A single stem cell that has the capability of developing cells of all germ layers (endoderm, ectoderm and mesoderm).

**Research:** Activities undertaken to develop or contribute to generalizable (scholarly) knowledge or to devise new applications for such knowledge, including, but not limited to, preclinical and clinical trials, pilot testing, research development, product testing, evaluation of programs and services, fieldwork, and all care and use of animals.

**Somatic Cell:** Any cell of a plant or animal other than germ cell or germ cell precursor.

**Somatic Cell Nuclear Transfer (SCNT):** A technique in which the nucleus of any cell of the body (somatic cell) – other than sperm or egg (germ cell) – is injected into an egg that has had its nucleus removed. The nucleated egg is then electrically stimulated, prompting it to take on the genetic and molecular characteristics of a fertilized ovum. The embryonic stem cell taken from the embryo in the culture dish will be genetically identical to the body cell from which the nucleus was derived.

**Stem Cells:** Cells with the ability to divide for indefinite periods in culture and to give rise to specialized cells.

**Test Article:** Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act.

### **Policy Statement**

In order to provide appropriate oversight and to comply with all applicable federal and state laws and regulations, ethical guidelines and applicable University policies and procedures, all activities, including research or clinical investigations, that involve the use of human stem cells shall be reviewed and approved by the UCI hSCRO Committee before such activities are initiated. This review requirement applies to the use of human gametes and blastocysts (embryos), the derivation and/or use of human embryonic stem cells, human embryonic or fetal germ cells, human adult and fetal stem cells and any other human pluripotent stem cells.

The UCI hSCRO Committee has the authority to approve, require modifications (to secure approval), or disapprove all human stem cell activities that are covered by this policy, or are performed at or in collaboration with offsite locations. All other applicable regulatory committee approvals (e.g., Institutional Review Board, Institutional Animal Care and Use Committee), University approvals, and completion and/or receipt of all other necessary documentation (e.g., provenance of gametes, blastocysts, or cell lines from collaborating locations) are required prior to the initiation of any human stem cell activity. No other UCI officials may approve a human stem cell activity that has not been approved by the UCI hSCRO Committee.

Activities funded by outside entities, such as biotechnology companies, require an agreement between the University and the company. If UCI will receive compensation for conducting or directing a research activity, a contract must be established through UCI Office of Research Administration, Sponsored Projects. When contracts or other agreements are required, the language is to be developed and negotiated by Sponsored Projects staff to document UCI's responsibilities for the conduct of the specific activity.

### **Oversight and Monitoring of Human Embryonic Stem Cell (hESC) Lines**

- A. Once hESC lines have been derived, investigators, the UCI hSCRO Committee and other relevant UC entities, such as regulatory oversight committees and other authorized UCI officials, shall monitor the use hESC lines.

- B. The hSCRO Committee shall require documentation of the provenance of all hESC lines, whether the cells were imported into the University or generated locally, unless the requirement for such documentation has been waived. Notice to hSCRO shall include evidence of written IRB-approval of the procurement process, evidence of and adherence to basic ethical and legal principles of procurement. In the case of lines imported from another institution, documentation that these criteria were met at the time of derivation will suffice.
- C. The hSCRO Committee shall maintain a registry of its investigators who are conducting hESC activities and ensure that all registered users are kept up to date with changes in guidelines and regulations regarding the use of hESCs.
- D. All protocols involving the combination of hESCs with nonhuman embryos, fetuses, or adult animals shall be submitted to the UCI IACUC for review of animal welfare issues and to the hSCRO for consideration of the consequences of the human contributions to the resulting chimeras.
- E. Experiments in which hESCs, their derivatives, or other pluripotent cells are introduced into nonhuman fetuses and allowed to develop into adult chimeras shall be carefully reviewed, including consideration of any major functional contributions to the brain.
- F. Introduction of hESCs into nonhuman nonprimate mammalian blastocysts will be subject to serious scrutiny and stringent review.

### **Authority and Responsibility**

#### **Vice Chancellor for Research Responsibilities**

The Vice Chancellor for Research (VCR), serving as the designated Institutional Official, has responsibility for the UCI Human Stem Cell Research Oversight Program.

- A. The VCR ensures institutional compliance with applicable federal and state statutes and regulations, and University policies and procedures relating to human stem cell activities.
- B. The VCR selects and appoints members of the hSCRO Committee.
- C. The VCR may recommend suspension or termination of hSCRO protocols, subject to the overriding responsibilities of the IRB.
- D. The VCR provides adequate resources in support of the hSCRO and communicates regularly with the hSCRO Chair on issues related to human stem cell activities.
- E. The VCR ensures proper internal reporting to the Chancellor and other campus officials.

#### **hSCRO Committee Responsibilities**

The hSCRO Committee reviews and approves, requires modifications in, or disapproves all human stem cell activities defined in this policy.

- A. The hSCRO ensures human stem cell activities are:
  - 1. In accord with National Academies and California embryonic stem cell guidelines and ethical principles (e.g., Belmont Report, Declaration of Helsinki), and
  - 2. In compliance with California statute and California Institute for Regenerative Medicine regulations and applicable University and campus policies and procedures for human stem cell activities.
- B. The hSCRO considers the ethical and social issues presented by human stem cell activities.

- C. The hSCRO reviews the scientific/scholarly merit of human stem cell activities to assure procedures are consistent with sound research design, the study design can be reasonably expected to answer the proposed questions(s), and the importance of the knowledge expected to result is known.
- D. The hSCRO assures that the provenance (origin) of gametes, blastocysts, fetal tissue and the derivation of human stem cells are documented. Documentation should sufficiently establish that procurement of the cell lines complies with standard clinical care consenting procedures and/or human stem cell and research regulations, as applicable.
- E. The hSCRO assures documentation of compliance with any required regulatory reviews (e.g., IRB, IACUC and IBC).
- F. The hSCRO approves, requires modifications in, or disapproves protocols and amendments of approved protocols involving human gametes, embryos and human stem cell activities, subject to the overriding responsibilities of the IRB and IACUC.
- G. The hSCRO reviews and reports human stem cell research noncompliance in accordance with campus policy for resolving allegations of regulatory noncompliance.

#### **Institutional Review Board (IRB) Committees Responsibilities**

The IRB reviews and approves, requires modifications in, or disapproves all human stem cell activities that meet the federal definition of human subjects research. The IRB must review and approve such activities prior to initiation.

- A. The IRB reviews and approves, requires modifications in, or disapproves the procurement and derivation of gametes, blastocysts (embryos), fetal tissue or somatic cells for the purpose of generating new stem cell lines, including the procurement of blastocysts in excess of clinical need from infertility clinics, blastocysts made through in vitro fertilization specifically for research purposes, and oocytes, sperm and somatic cells donated for development of human embryonic cell lines through nuclear transfer.
- B. The IRB reviews, approves, requires modifications in, or disapproves human stem cell activities to ensure proper consent from the donors of sperm, oocytes, or somatic cells used to make blastocysts for research.
- C. The IRB reviews, approves, requires modifications in, or disapproves human stem cells activities to ensure the privacy of donors in accordance with privacy regulations for use of personal health information for research purposes.
- D. The IRB may suspend or terminate approved human stem cell research.
- E. The IRB reviews and reports human stem cell research noncompliance in accordance with campus policy for resolving allegations of regulatory noncompliance.

#### **Institutional Animal Care and Use Committee (IACUC) Responsibilities**

The IACUC reviews and approves, requires modifications in, or disapproves all human stem cell activities that involve the use of live, vertebrate animals. The IACUC ensures the ethical and humane care and use of animals in research, testing, and teaching. The IACUC must review and approve such activities prior to initiation.

#### **Institutional Biosafety Committee (IBC) Responsibilities**

The IBC reviews and approves, requires modifications in, or disapproves all human stem cell activities that involve the use of recombinant DNA (rDNA) molecules, risk group pathogens and select agents. The IBC ensures the safe conduct of research by requiring

appropriate containment levels and decontamination practices. The IBC must review and approve such activities prior to initiation.

### **Office of Research Administration Responsibilities**

The Office of Research Administration (ORA) serves as the office of record for the UCI Human Stem Cell Research Oversight Program and maintains a database of investigators conducting human stem cell activities.

- A. The ORA supports and coordinates all of the activities of the program and serves as the liaison between the hSCRO, other regulatory oversight committees, and the UCI research community, specifically:
  - 1. Facilitates the protocol review process.
  - 2. Communicates to investigators in writing, on behalf of hSCRO, all Committee actions.
  - 3. Provides training, education, and consultative services on human stem cell research review requirements.
  - 4. Communicates to the Institutional Official (IO) any study-related issues that are likely to present risks or other concerns for the institution.
  - 5. Communicates with other UCI administrative units and regulatory committees conducting administrative audits of alleged occurrences of regulatory noncompliance in collaboration with the IRBs in accordance with campus policy.
  - 6. Assists with the conduct of regulatory committee reviews in accordance with campus policy.
  - 7. Reports to the IO and governmental agencies any significant problems or violations of federal regulations, hSCRO or IRB requirements, or suspension or termination of IRB approval.
- B. The ORA coordinates required regulatory committee approval process and ensures hSCRO review has been completed before human stem cell research is allowed to commence.
- C. The ORA develops policies (or revisions of policies) for the conduct of human stem cell research in consultation with the hSCRO Committee and IRBs.

### **Lead Researcher Responsibilities**

The Lead Researcher (LR) of a human stem cell protocol is responsible for:

- A. Fully complying with all federal and state statutes and regulations, policies and guidelines, and applicable University policies and procedures, and regulatory requirements concerning human stem cell activities.
- B. Ensuring that all co-researchers and personnel engaged in human stem cell activities have been educated about stem cell requirements and have read and understand the approved protocol and all procedures to be performed.
- C. Ensuring hSCRO approval is in place prior to the commencement of any human stem cell activity.
- D. Understanding that hSCRO approval, in and of itself, does not necessarily constitute permission for implementation of human stem cell activities. Accordingly, the activity should not begin until all required approvals have been obtained.
- E. Assuring no changes to approved studies are initiated without first having submitted those changes for review and approval by the hSCRO.
- F. Providing the hSCRO with any information requested relative to the conduct of human stem cell activities.

- G. Complying with a VCR decision to suspend or withdraw approval of a human stem cell activity.
- H. Obtaining continuing hSCRO approval prior to the expiration date approval of the study and recognizing such activities must cease until current hSCRO approval is obtained.
- I. Filing a closing report with the hSCRO at the conclusion of the study.
- J. Maintaining and making available for inspection by the hSCRO, authorized University officials and outside entities, all hSCRO protocol and study records.

## **References**

- A. National Bioethics Advisory Commission, Ethical Issues in Human Stem Cell Research Report, 1999
- B. National Academies of Science-Institute of Medicine, Guidelines for Human Embryonic Stem Cell Research, National Academies Press: 2005
- C. Ethical codes of conduct for research involving human subjects: Belmont Report of the National Commission for the Protection of Human Subjects in Behavioral and Biomedical Research; Declaration of Helsinki; Nuremberg Code
- D. California Stem Cell Research and Cures Bond Act of 2004, CA Health and Safety Code Sections 125291.10 - 125291.85
- E. California Law Chapter 483, approved by Governor and filed with Secretary of State September 26, 2006
- F. California Embryonic Stem Cell Guidelines, CA Health and Safety Code Sections 125118 - 125119.5
- G. California Policy on Human Stem Cell Research, CA Health and Safety Code Sections 125300 – 125320
- H. California Informed Consent Requirements for Oocyte Production, CA Health and Safety Code Sections 125330 - 125355
- I. California Institute for Regenerative Medicine Medical and Ethical Standards Regulations, Title 17 CA Code of Regulations, Sections 100010-100110
- J. California Health and Safety Code, Sections 24170 - 24197.5, and other applicable state statues pertaining to the protection of human subjects in research
- K. Department of Health and Human Services (DHHS) Regulations, Policy for the Protection of Human Research Subjects, 45 CFR Part 46, Subparts A-D, effective July 27, 1981 in accordance with Public Law 93-348 and all subsequent amendments thereto
- L. DHHS, Food and Drug Administration, 21 CFR Part 50 Human Subjects Protections and 21 CFR Part 56 Institutional Review Boards, effective July 27, 1981, and all subsequent amendments thereto
- M. University of California Policy on the Protection of Human Subjects in Research, issued September 2, 1981
- N. UCI Research Policies: Responsibilities for Conduct and Administration of Research, issued January 31, 1998, amended December 1, 2004; May 23, 2005