

## HUMAN STEM CELL RESEARCH OVERSIGHT PROGRAM POLICY AND STANDARD OPERATING PROCEDURES

SECTION: **Definitions and References**  
ORIGINAL CREATION DATE: January 5, 2006  
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### Definitions:

1. **Adult Stem Cell:** An undifferentiated cell found in a differentiated tissue that can renew itself and (with certain limitations) differentiate to yield specialized cell types of the tissue from which it originated.
2. **Blastocyst:** A very early pre-uterine implantation 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.
3. **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.
4. **Human Stem Cell Research Oversight (hSCRO) Committee:** University appointed committee providing oversight of all issues related to the procurement and experimental use of human stem cells and stem cell lines and to facilitate education of investigators involved in human stem cell research.
5. **Embryonic Germ Cells:** Cells found in a specific part of the embryo/fetus called the gonadal ridge that normally develops into mature gametes (i.e., sperm and egg).
6. **Fetal Stem Cells:** Stem cells taken from aborted fetal tissue. Federal regulations treat fetal stem cells as adult stem cells.
7. **Fetus:** A developing human from usually two months after conception to birth.
8. **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.
9. **Human Embryonic Stem Cells (hESC):** 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 hESC may be derived from embryos, such stem cells are not themselves embryos.
10. **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.
11. **Human Subjects Research:** Any research or clinical investigation that involves human subjects.
12. **Institutional Animal Care and Use Committee (IACUC):** Committee charged with reviewing the use of animals in research, testing, teaching and related activities.
13. **Institutional Biosafety Committee (IBC):** Committee charged with reviewing research involving use of recombinant DNA molecules, infectious agents and select agents.
14. **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.
15. **In Vitro:** Literally, "in glass"; in a laboratory dish or test tube; an artificial environment.
16. **In Vitro Fertilization (IVF):** An assisted reproduction technique in which fertilization is accomplished outside the body.
17. **Non-Registered Human Embryonic Stem Cell Lines:** hESC lines excluded from the NIH registry because they do not meet the President's criteria.
18. **Permissible Expenses:** Necessary and reasonable costs directly incurred as a result of donation or participation in research activities. Permissible expenses may include but are

- not limited to costs associated with travel, housing, childcare, medical care, health insurance and actual lost wages.
19. **Pluripotent Stem Cell:** A single stem cell that has the capability of developing cells of all germ layers (endoderm, ectoderm, and mesoderm).
  20. **Registered Human Embryonic Stem Cell Lines:** hESC lines included on the National Institutes of Health (NIH) Human Embryonic Stem Cell Registry, which confirms that the stem cell lines comply with the Presidents' criteria as, stated on August 9, 2001.
  21. **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.
  22. **Somatic Cell:** Any cell of a plant or animal other than germ cell or germ cell precursor.
  23. **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 newly nucleated egg is then 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.
  24. **Stem Cells:** Cells with the ability to divide for indefinite periods in culture and to give rise to specialized cells.
  25. **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.

#### References:

1. **National Bioethics Advisory Commission**, Ethical Issues in Human Stem Cell Research Report, 1999
2. **National Academies of Science-Institute of Medicine**, Guidelines for Human Embryonic Stem Cell Research, National Academies Press: 2005
3. **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
4. **California Stem Cell Research and Cures Bond Act of 2004**, CA Health and Safety Code Sections 125291.10 - 125291.85
5. **California Law Chapter 483**, approved by Governor and filed with Secretary of State September 26, 2006
6. **California Embryonic Stem Cell Guidelines**, CA Health and Safety Code Sections 125118 - 125119.5
7. **California Policy on Human Stem Cell Research**, CA Health and Safety Code Sections 125300 – 125320
8. **California Informed Consent Requirements for Oocyte Production**, CA Health and Safety Code Sections 125330 - 125355
9. **California Institute for Regenerative Medicine Medical and Ethical Standards Regulations**, Title 17 CA Code of Regulations, Sections 100010-100110
10. **California Health and Safety Code**, Sections 24170 - 24197.5, and other applicable state statutes pertaining to the protection of human subjects in research
11. **Department of Health and Human Services (DHHS) Regulations**, Policy for the Protection of Human Research Subjects, 45 CFR Part 46, Subparts A-D
12. **DHHS, Food and Drug Administration**, 21 CFR Part 50 Human Subjects Protections and 21 CFR Part 56 Institutional Review Boards

13. **University of California, Irvine Research Policy**, Section 484-1: Review of Human Stem Cell Activities
14. **University of California, Irvine Research Policy**, Section 485-1: Protection of Human Subjects in Research

SECTION: **Institutional Authority and Responsibilities**  
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**Procedure:**

This procedure outlines responsibilities for review and approval of human stem cell activities.

I. Vice Chancellor for Research Responsibilities

- A. The Vice Chancellor for Research (VCR), serving as the designated Institutional Official, has responsibility for the UCI Human Stem Cell Research Oversight Program.
- B. The VCR ensures institutional compliance with applicable federal regulations, state statutes and regulations, and University policies and procedures relating to human stem cell activities.
- C. The VCR selects and appoints members of the hSCRO committee.
- D. The VCR may recommend suspension or termination of hSCRO protocols, subject to the overriding responsibilities of the IRB.
- E. 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.
- F. The VCR ensures proper internal reporting to the Chancellor and other campus officials.

II. Human Stem Cell Research Oversight (hSCRO) Committee Responsibilities

- A. hSCRO assures human stem cell activities are:
  - 1. In accord with National Academies and California DHS guidelines and ethical guidelines (e.g., Belmont Report, Declaration of Helsinki), and
  - 2. In compliance with California statute and California Institute for Regenerative Medicine (CIRM) regulations and applicable campus policies and procedures for human stem cell activities.
- B. hSCRO considers the ethical and social issues presented by human stem cell activities.
- C. 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. 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. hSCRO assures documentation of compliance with any required regulatory reviews (e.g., IRB, IACUC and IBC).
- F. hSCRO approves, requires modifications in, or disapproves protocols involving human gametes, embryos and human stem cell activities, subject to the overriding responsibilities of the IRB and IACUC.

III. Institutional Review Board (IRB) Committee Responsibilities

- A. The IRB reviews and approves, requires modifications in, or disapproves human stem cell activities that meet the federal definitions of human subject research and/or clinical investigation.

- B. The IRB reviews and approves, requires modifications in, or disapproves the procurement of gametes, blastocysts (embryos), fetal tissue or somatic cells for the purpose of deriving 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.
  - C. 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.
  - D. The IRB reviews, approves, requires modifications in, or disapproves human stem cells activities to assure the privacy of donors in accordance with HIPAA and CMIA regulations for use of personal health information for research purposes.
  - E. The IRB requests periodic progress reports and oversees the conduct of ongoing human subject protocols involving human stem cell research.
  - F. The IRB reviews and approves, requires modifications in, or disapproves proposed modifications to approved human stem cell research.
  - G. The IRB may suspend or terminate approved human stem cell research under its jurisdiction.
  - H. The IRB reviews and reports human stem cell research noncompliance in accordance with campus policy for resolving allegations of regulatory noncompliance.
- IV. Institutional Animal Care and Use Committee (IACUC) Responsibilities
- A. The IACUC is a committee responsible for reviewing all animal use protocols, ensuring compliance with federal regulations, inspecting animal facilities and laboratories, and overseeing training and education programs.
  - B. The IACUC is charged to ensure the ethical and humane care and use of animals in research, testing, and teaching.
  - C. The IACUC must review and approve all human stem cell activities that involve animals prior to initiation of the study.
- V. Institutional Biosafety Committee (IBC) Responsibilities
- A. The IBC is a committee responsible for potentially hazardous biological agents including but not limited to infectious agents, human and non human primate materials (including established cell lines), CDC select agents, recombinant DNA and studies involving human gene transfer.
  - B. The IBC assures that research involving these agents is conducted in a manner that does not endanger the researcher, laboratory worker, human research subjects, the public or the environment.
  - C. The IBC must review and approve all IBC relevant human stem cell activities prior to initiation of the study.
- VI. Office of Research Administration Responsibilities
- A. The Office of Research Administration (ORA) serves as the office of record for the UCI Human Stem Cell Research Oversight Program. It maintains the official records of approved hSCRO activities and a database of investigators conducting human stem cell activities.

- B. 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.
- C. The ORA coordinates the regulatory committee approval process and assures hSCRO review has been completed before human stem cell research is allowed to commence.
- D. The ORA develops policies (or revisions of policies) for the conduct of human stem cell research in consultation the hSCRO committee and IRBs.

SECTION: **Review and Oversight of Human Stem Cell Research**  
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**Policy:**

In order to undertake appropriate oversight and to comply with all applicable federal and state statutes, regulations, ethical guidelines; and 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 before such activities are initiated by or for UCI. This review requirement applies to the use of human gametes and blastocysts (embryos), the derivation and/or use of human embryonic stem cells (hESC), human embryonic or fetal germ cells, human adult and fetal stem cells and any other human pluripotent stem cells.

I. Activities that May be Permitted after Review by the UCI hSCRO

- A. Generation of new lines of human pluripotent stem cells from whatever source and by whatever means.
- B. Use of human gametes, embryos or human adult, fetal or embryonic stem cells.
- C. Activities involving the introduction of human adult, fetal or embryonic cell lines into nonhuman animals at any stage of embryonic, fetal, or postnatal development; provided that investigators evaluate the probable pattern and effects of differentiation and integration of the human cells into the nonhuman animal tissues.
- D. Activities in which the identity of the donors of blastocysts, gametes, or somatic cells from which human stem cells were derived is readily ascertainable or might become known to the investigator.

II. Other Regulatory Committee Reviews

Activities that are reviewed and approved by UCI hSCRO may require additional review by UCI IRB, IACUC, IBC and/or COI committees.

III. Activities Not Permitted

Activities that are not permitted at this time include and will not be approved by the UCI hSCRO include, but are not limited to, the following:

- A. In vitro culture of any intact human embryo, regardless of derivation method, after the appearance of the primitive streak or after 12 days whichever is earlier. The 12-day prohibition does not count any time during which the blastocysts and/or cells have been stored frozen.
- B. Introduction of hESC into nonhuman primate blastocysts and/or the introduction of any embryonic stem cells into human blastocysts.
- C. Introduction of hESC into a human uterus or equivalent, or any experiments attempting human reproductive cloning.
- D. Breeding of an animal into which hESC have been introduced at any stage of development.

IV. Protocol Submission Requirements

The electronic IRB Application and Appendix R- "Use of Human Gametes, Embryos or Derivation/Use of Human Stem Cells" are used for protocol submissions to the UCI hSCRO. Additional information to include with submissions for embryonic stem cell activities is as follows:

- A. Activities Involving Previously Derived hESC for In Vitro or Animal Use
1. hSCRO must receive documentation of:
    - (a) The provenance of the cell lines to determine they are acceptably derived;
    - (b) Appropriate informed consent in their derivation; and
    - (c) Evidence of compliance with any required review of the proposed research by an Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), or Institutional Biosafety Committee (IBC), or other mandated review.
  2. Exceptions for documentation:
    - (a) Human embryonic stem cell lines approved by the National Institutes of Health, deposited in the United Kingdom Stem Cell Bank, or derived by, or approved for use by, a licensee of the United Kingdom Human Fertilisation and Embryology Authority.
    - (b) Human embryonic stem cell lines 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,
    - (c) Human embryonic stem cell lines derived in accordance with the above organizations and approved by the California Independent Citizens' Oversight Committee.
  3. Acceptably derived cell lines have been:
    - (a) Approved by the National Institutes of Health, or
    - (b) Deposited in the United Kingdom Stem Cell Bank, or
    - (c) Derived by, or approved for use by, a licensee of the United Kingdom Human Fertilization and Embryology Authority, or
    - (d) 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
    - (e) Derived under the following conditions:
      - (i.) Donors of gametes, embryos, somatic cells or human tissue gave voluntary and informed consent.
      - (ii.) Donors of gametes, embryos, somatic cells or human tissue did not receive valuable consideration. This provision does not prohibit reimbursement for permissible expenses as determined by an IRB.
      - (iii.) Gametes, embryos, somatic cells, or human tissue were not purchased for research.
      - (iv.) Donation of gametes, embryos, somatic cells or human tissue was overseen by an IRB (or, in the case of foreign sources, an IRB-equivalent);
      - (v.) Individuals who consented to donate stored gametes, embryos, somatic cells or human tissue were not reimbursed for the cost of storage prior to the decision to donate.
- B. Activities Involving the Procurement or Derivation of New hESC Lines
1. The scientific rationale for the need to generate new hESC lines, by whatever means, shall be clearly presented and the basis for the numbers of blastocysts (embryos) needed shall be justified.

2. Research teams shall demonstrate appropriate expertise or training in derivation or culture of either human or nonhuman embryonic stem cells before approval to derive new lines is given.
  3. Documentation of compliance with any required review of the proposed research by an IRB, IACUC or other mandated review is required.
  4. When somatic cell nuclear transfer (SCNT) experiments involving either human or nonhuman oocytes are proposed as a route to generation of embryonic stem cells, the protocol shall have a strong scientific rationale.
  5. Blastocysts made using SCNT (whether produced with human or nonhuman oocytes) and parthenogenetic or androgenetic human embryos shall not be transferred to a human or nonhuman uterus and shall not be cultured as intact embryos in vitro after the appearance of the primitive streak or 12 days after cell division begins, whichever is earlier. The 12-day prohibition does not count any time during which the blastocysts and/or cell have been stored frozen.
  6. Clinical personnel who have a conscientious objection shall not be required to participate in providing donor information or securing donor consent for research use of gametes or embryos.
  7. Investigators shall document how they will characterize, validate, store, and distribute any new hESC lines and how they will maintain the confidentiality of any coded or identifiable information associated with the lines (Appendix M should be included with the IRB application submission).
  8. For research involving oocyte retrieval, the clinic retrieving oocytes shall be a member of the Society for Assisted Reproductive Technology.
- C. Activities Involving the Introduction of hESC into Living Individuals
1. The investigator must provide an acceptable scientific for rationale introducing stem cells into humans.
  2. The investigator must provide assurance that all covered stem cell lines have been acceptably derived.
  3. The investigator must evaluate the probable pattern and effects of differentiation and integration of the human cell into the human tissues.
  4. The investigator must provide documentation of compliance with any required review of the proposed activity by the IRB, IACUC, IBC or other mandated review.

V. Oversight and Monitoring of hESC Lines

- A. Once hESC lines have been derived, investigators, the UCI hSCRO and other relevant UC entities, such as regulatory oversight committees and other authorized UCI officials, shall monitor the use hESC lines.
- B. hSCRO shall require documentation of the provenance of all hESC lines, whether the cells were imported into the institution or generated locally, unless the requirement for such documentation has been waived under Section IV.A.2. 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. In vitro experiments involving the use of already derived and coded hESC lines shall not require full committee review (see hSCRO policy and procedure, "Review and Approval Process Human Embryonic Stem Cell Research.")

- D. hSCRO 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 hESC.
- E. All protocols involving the combination of hESC with nonhuman embryos, fetuses, or adult animals shall be submitted to the IACUC for review of animal welfare issues and to hSCRO for consideration of the consequences of the human contributions to the resulting chimeras.
- F. Experiments in which hESC, 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.
- G. Introduction of hESC into nonhuman nonprimate mammalian blastocysts will be subject to serious scrutiny and stringent review.

SECTION: **Committee Composition, Member Responsibilities and Training**  
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**Procedure:**

This procedure provides guidance in forming the UCI Human Stem Cell Research Oversight (hSCRO) Committee and defines its responsibilities.

I. Composition of the hSCRO Committee

- A. The hSCRO is an appointed University Committee. hSCRO provides an additional level of oversight to ensure that the issues raised by human embryonic stem cell (hESC) research are addressed. The hSCRO Committee shall be composed of:
  - 1. At least nine voting members with varying backgrounds and expertise to promote complete and adequate review of hESC research activities at UCI.
  - 2. Members who are experts in developmental biology, stem cell research, molecular biology, assisted reproductive technologies, ethical and legal issues in hESC research, at least one public member who serves as a non-scientist, and at least one patient advocate.
    - (a) When stem cell activities involve the procurement or use of human oocytes, a member of the committee with expertise in assisted reproduction shall be present.
    - (b) The patient advocate may be affiliated or unaffiliated. The patient advocate should effectively represent the interest of the patient community and foster clinical equipoise.
  - 3. Alternate members may be appointed to provide depth of available expertise. Alternate members will not vote unless needed for their special expertise or to make a quorum.
- B. hSCRO will have one hSCRO Chair who is appointed by the VCR. The hSCRO Chair serves as the official representative of the hSCRO and is responsible for leading hSCRO meetings.

II. hSCRO Member Appointment

- A. hSCRO members are sought based on expertise and availability through recommendation from Department Chairs, School Deans, from recommendation of other hSCRO members, or on a volunteer basis. The VCR appoints the hSCRO Chair and members.
- B. The VCR appoints hSCRO members to a three-year renewable term and appoints hSCRO Chairs to a two-year renewable term.
- C. If a member is unable to fulfill the responsibilities of hSCRO membership, s/he may resign before the conclusion of his/her term.

III. Compensation

- A. hSCRO members serve as volunteers (without compensation).

IV. Specific Duties

- A. Duties of hSCRO Members:

1. hSCRO members are expected to make every effort to attend hSCRO meetings so that protocols may be reviewed. Members are asked to attend at least 75% of Committee meetings.
  2. In the event that a member is unable to attend, sufficient advance notice must be provided to the hSCRO Administrator so that alternate arrangements can be made as necessary.
  3. Members serve as primary or secondary reviewers on protocols based upon expertise.
  4. Members are to disclose any potential conflict of interest to the hSCRO Administrator or Chair as soon as it is recognized.
  5. Members are to maintain confidentiality of hSCRO meeting proceedings and any information contained in protocol reviews.
  6. Members must have an understanding of UCI policy and procedures regarding human stem cell research.
- B. Duties of hSCRO Members with Non-Scientific Status:
1. Non-scientific status members provide insight to the legal, ethical, and social issues related to human stem cell research.
  2. Non-scientific status members review informed consent documents to ensure that the information provided to the subject or their legally authorized representative shall be in language understandable to the subject or the representative.
  3. Members of the public provide unique insight to possible community response to human stem cell research and serve as patient advocates.
  4. Non-scientific status members are not assigned as primary or secondary reviewers.
- C. Duties of the hSCRO Chair:
1. hSCRO Chair convenes hSCRO meetings.
  2. hSCRO Chair relays concerns of the hSCRO member to ORA administration regarding issues in review procedures.
  3. hSCRO Chair facilitates communications and dissemination of information from the IO and ORA staff to the hSCRO members and to researchers.
  4. hSCRO Chair calls special meetings when necessary.
  5. hSCRO Chair acts as an advisor in the institution's research community.
  6. hSCRO Chair may delegate any of his/her responsibilities as appropriate to other qualified and duly appointed members of hSCRO.

V. Orientation and Training

- A. New hSCRO Member Orientation: All new members will receive a packet that includes the following materials prior to their first meeting:
1. hSCRO Committee member appointment letter
  2. Member standards document for signature
  3. Schedule of Committee meetings and submission deadlines
  4. hSCRO Standard Operating Policies and Procedures
  5. Guidelines and Regulations: NAS hESC Guidelines, CIRM Regulations
  6. Ethical Guidelines: Belmont Report Principles and Declaration of Helsinki
  7. Information on stem cell basics - the science of stem cells (for non-scientific members)
- B. Ongoing Training will consist of relevant articles forwarded to members via email and discussions conducted at regular hSCRO meeting regarding new issues as they become relevant.

SECTION:

**Informed Consent Requirements for Gamete or Blastocyst Donors**

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**Policy:**

Any individual who elects to donate gametes or blastocysts (embryos) to be used to derive human pluripotent stem cells for research shall provide written informed consent.

I. Approaching Donors From In Vitro Fertilization Clinics

- A. A physician and surgeon or other health care provider delivering fertility treatment shall provide his or her patient with timely, relevant, and appropriate information to allow the individual to make an informed and voluntary choice regarding the disposition of any human gametes or embryos remaining following the fertility treatment.
- B. IVF Providers must assure the individual to whom information is provided shall be presented with the following options:
  - 1. Storing any unused gametes or embryos;
  - 2. Donating the unused gametes or embryos to another individual;
  - 3. Discarding the unused gametes or embryos; or
  - 4. Donating the remaining gametes or embryos for research.
- C. When providing fertility treatment, a physician and surgeon or other health care provider shall provide a form to the male and female partner, or the individual without a partner, as applicable, that sets forth advanced written directives regarding the disposition of gametes or embryos. This form shall indicate the time limit on storage of the gametes or embryos at the clinic or storage facility and shall provide, at a minimum, the choices for disposition of the gametes or embryos per State statute.

III. Procuring Gametes, Blastocysts or Cells for New hESC Generation

- A. The IRB must review the procurement of all gametes, blastocysts, or somatic cells that meet the definition of human subject research, including the procurement of blastocysts in excess of clinical need from infertility clinics, blastocysts made through IVF specifically for research purposes, and oocytes, sperm, and somatic cells donated for development of hESC lines derived through NT or by parthenogenesis or androgenesis.
- B. Consent for donation shall be obtained from each donor, including individuals who have given prior indication of their intent to donate to research any blastocysts that remain after clinical care, at the time of donation.
- C. Donors shall be informed that they retain the right to withdraw consent until the blastocysts are actually used in cell line derivation.
- D. When donor gametes have been used in the IVF process, resulting blastocysts shall not be used for research without consent of all gamete donors.
  - 1. No payments, cash or in-kind, may be provided for donating blastocysts in excess of clinical need for research purposes. People who elect to donate stored blastocysts for research shall not be reimbursed for the costs of storage prior to the decision to donate.
  - 2. Women who undergo hormonal induction to generate oocytes specifically for research purposes (such as for SCNT) shall be reimbursed only for

direct expenses incurred as a result of the procedure, as determined by an IRB.

3. No payments, cash or in-kind, shall be provided for donating oocytes for research purposes. Similarly, no payments shall be made for donations of sperm for research purposes or for donations of somatic cells for use in SCNT.
- E. To facilitate autonomous choice, decisions related to the creation of embryos for infertility treatment shall be free of the influence of investigators who propose to derive or use hESC in research. Whenever it is practicable, the attending physician responsible for the infertility treatment and the investigator deriving or proposing to use hESC shall not be the same person.

### III. Consenting Donors of Gametes or Embryos for Research

- A. When a UCI researcher seeks to procure gametes or embryos that are not available for research, the informed consent document must include the following statements, unless it is determined by the hSCRO or IRB to be inapplicable:
1. The gametes or early human embryos will be used to derive human pluripotent stem cells for research.
  2. The gametes or early human embryos will not survive in the stem cell derivation process.
  3. Whether the identity(ies) identifiers of the donor(s) will be known to those who will work with the resulting cells or cell products.
  4. Derived cells or cell lines may be kept for many years.
  5. Researchers may use cell lines for future studies, some of which may not be predicable at this time.
  6. Derived cells or cell products may be used in research involving genetic manipulation.
  7. Derived cells or cell lines may be transplanted into humans or animals.
  8. Derived cell or cell products are not intended to provide direct medical benefit to the donor(s), except in cases of autologous donation.
  9. The donation is being made without restriction regarding who may be the recipient of transplanted cells, except in the case of autologous donations.
  10. Neither consenting nor refusing to donate materials for research will affect the quality of any future care provided to potential donors.
  11. Donors will not receive any information about subsequent testing on the gametes or embryos or the derived human pluripotent cells.
  12. The results of the research may be patentable or have commercial potential, and that the donor will not receive patent rights and will not receive financial or any other benefits from future commercial development.
- B. For UCI research involving oocyte retrieval, the IRB must also find that the risks are reasonable even if there is no anticipated benefit to the donor. The informed consent document must include these additional statements, unless it is determined by the hSCRO or IRB to be inapplicable:
1. Foreseeable risks shall include but not be limited to information regarding the risks of ovarian hyperstimulation syndrome, bleeding, infection, anesthesia and pregnancy.
  2. The physician must disclose his/her relationship to the research or researcher(s) to the egg donor.

3. Prospective donors shall be informed of their option to deliberate before deciding whether to give consent. If a deliberation period is chosen, the donor shall be informed of their right to determine the method of recontact. The donor must be informed that they have the option to initiate recontact. The investigators shall not initiate recontact unless the donor has consented, and this consent is documented in the research record.
4. The researcher shall ascertain that the donor has understood the essential aspects of the research. Essential aspects of the research include understanding at least that:
  - (a) Their eggs will not be used for reproductive purposes.
  - (b) There are medical risks in oocyte donation, including the risks of ovarian hyperstimulation syndrome, bleeding, infection, anesthesia, and pregnancy.
  - (c) The research is not intended to benefit them or any other individuals directly at this time.
  - (d) Whether stem cell lines will be derived from their oocytes through fertilization, SCNT, parthenogenesis, or some other method.
  - (e) Stem cell lines developed from their oocytes will be grown in the lab and shared with other researchers for studies in the future.
  - (f) If stem cells are to be transplanted into patients, researchers might recontact the donor to get additional health information.
  - (g) Donors receive no payment beyond reimbursement for permissible expenses.
  - (h) Stem cell lines derived as a result of their oocyte donation may be patented or commercialized, but donors will not share in patent rights or in any revenue or profit from the patents.

SECTION: **Committee Review and Approval Process of Human Stem Cell Research**  
ORIGINAL CREATION DATE: January 5, 2006  
REVISION DATES: March 28, 2006; January 11, 2007; May 15, 2007; January 10, 2008

**Policy:**

- I. All uses of human gametes and blastocysts (embryos), the derivation and/or use of human embryonic stem cells (hESC), human embryonic or fetal germ cells, human adult (including fetal) stem cells and any human pluripotent stem cells, require full committee hSCRO review, except for those activities that fall into one of the following Expedited Review categories:
  - A. Category 1: Purely in vitro uses of NIH registered and UK Stem Cell Bank human stem cell lines.
  - B. Category 2: In vitro and in vivo (animal) uses of human adult stem cells that are not pluripotent or do not involve attempts to establish pluripotency.
  - C. Category 3: Purely in vitro uses of acceptably derived hESC lines when the UCI hSCRO has on record documentation of the provenance of the cell lines.
  - D. Category 4: Continuing review of activities falling into categories 1 - 3 listed above.

**Procedure:**

This procedure provides guidance for the review and approval of protocols by the UCI human Stem Cell Research Oversight Committee (hSCRO).

- I. Administrative Screening and Review
  - A. Investigators submit to the hSCRO by completing the electronic IRB protocol application. IRB applications involving human gametes, embryos or human embryonic or fetal stem cells are forwarded to the hSCRO administrator for screening.
  - B. The hSCRO administrator in consultation with the hSCRO Chair screens all protocol submissions prior to hSCRO review.
  - C. Protocol submissions are entered into the hSCRO database to maintain a record of the hSCRO submission.
  - D. Submissions are checked for completeness. The hSCRO administrator ensures that all required documents are provided. If the submission is incomplete, or if any of the required documents cannot be reviewed due to deficiency of information, the hSCRO administrator will contact the Lead Researcher (LR) and provide guidance with completing the submission.
  - E. All hSCRO submissions are administratively reviewed.
  - F. The hSCRO administrator prepares reviewer checklists and includes questions and comments to the hSCRO Committee members.
- II. Expedited Review Procedures
  - A. Applications for expedited research are accepted on a rolling basis and are evaluated and approved by a hSCRO subcommittee, which may consist of the hSCRO Chair and/or one or more experienced reviewers from among members of the hSCRO Committee designated by the hSCRO Chair.

- B. When a new hSCRO application for expedited review is received, the hSCRO administrator performs an administrative review of the protocol to ensure that the submission is complete (see Administrative Screening and Review above) and confirms that the protocol falls within at least one of the categories for expedited review.
- C. If the protocol does not appear to meet any of the expedited categories, the hSCRO administrator consults with the hSCRO Chair to determine whether the proposed activities meet the definition of human subject research or requires Full committee review. The hSCRO Chair can require full Committee review of any research at his/her discretion, even if the research would otherwise qualify for expedited review status. If Full committee review (or no hSCRO review) is required, the hSCRO administrator communicates the hSCRO determinations to the LR and, when applicable, provides the LR assistance with submission requirements.
- D. If the protocol meets the expedited review criteria, the hSCRO administrator prepares a reviewer checklist for the subcommittee, including any administrative comments and noting any protocol irregularities, problems or concerns.
- E. The hSCRO Chair or an experienced hSCRO member designated by the hSCRO Chair is assigned to review expedited protocols by the hSCRO administrator. An experienced hSCRO member is a voting member or alternate voting member who has served on an hSCRO for at least one year and in the judgment of the hSCRO Chair possesses the scientific/scholarly expertise needed to review the proposed research. The hSCRO administrator designates experienced members on the hSCRO member roster.
- F. Documentation provided to the subcommittee members for review includes:
  - 1. UCI IRB Application including, Appendix R and Appendix M, when applicable
  - 2. UCI IRB or hSCRO Protocol Narrative
  - 3. A Reviewer checklist that includes the administrative comments
  - 4. Any additional materials, such as documents that establish the provenance of the gametes, embryos or cell lines
- G. Categories of Action for Expedited Research:
  - 1. Approval
    - (a) Action taken by hSCRO subcommittee if the submission qualifies under at least one of the defined expedited categories and if the subcommittee, by a majority, recommends approval (i.e., no revisions to the submission are required).
    - (b) The hSCRO prepares an approval letter and obtains the hSCRO Chair's signature or obtains approval from the Chair to use a signature stamp.
    - (c) Once the hSCRO approval letter is signed, the hSCRO administrator processes the approved documentation. The approval letter documents the specific permissible expedited categories under which the protocol qualifies.
  - 2. Minor Revisions Required
    - (a) Action taken if one or more hSCRO subcommittee members require minor specific changes to the submission. The LR is required to submit the requested revisions/items for further evaluation by the hSCRO Chair. Further review by the subcommittee is not required.

- (b) The hSCRO administrator sends a memo to the LR on behalf of the subcommittee (usually within a week of subcommittee's review), which includes the subcommittee's requested specific changes and instructions on how to resubmit the protocol.
  - (c) When the LR responds, the hSCRO administrator checks the LR's response to ascertain whether all of the requested revisions were made.
  - (d) The hSCRO administrator presents any remaining administrative questions and concerns to the hSCRO Chair at a weekly meeting.
  - (e) If the hSCRO Chair determines that the LR did not adequately address the subcommittee's concerns, the hSCRO administrator sends a memo to the LR on behalf of the hSCRO Chair (usually within a week of hSCRO Chair's review), which includes the requested changes and instructions on how to resubmit the protocol.
  - (f) This process repeats until the hSCRO Chair determines that the protocol can be approved (i.e., no further revisions are necessary).
  - (g) Once the hSCRO Chair signs the approval letter or authorizes use of the signature stamp, the HRP staff processes the approved documentation.
3. Tabled for Re-review by Subcommittee
- (a) Action taken if substantial modifications and/or clarifications are required to meet specific criteria for hSCRO approval per UCI policy, guidelines and regulations, or if insufficient information is at hand to judge the application adequately (e.g., the social or ethical issues posed by the research cannot be assessed with the information provided). The LR is informed of the reason(s) for the decision (usually within a week of subcommittee's last review) and is required to submit revised documents/requested items for further evaluation by the subcommittee.
  - (b) Upon receipt of the revised documentation, the hSCRO administrator prepares administrative review comments on a new set of reviewer checklists, noting any remaining protocol irregularities, problems or concerns on the reviewer checklist for the subcommittee. Whenever possible, the hSCRO administrator provides the revised submission and reviewer checklists to the same subcommittee members that participated in the initial review. If these reviewers are unavailable, other reviewers are selected from the same Committee based upon their experience and expertise and, when necessary, input from the hSCRO Chair).
  - (c) Upon approval by a majority of subcommittee members, the hSCRO administrator presents the subcommittee's findings to the hSCRO Chair at a weekly meeting for final approval. Once the hSCRO Chair signs the approval letter or authorizes use of the signature stamp, the hSCRO administrator processes the approved documentation.
4. Tabled for Re-review by Full Committee
- (a) Action taken if:
    - i. The subcommittee determines that the protocol does not qualify for expedited review;

- ii. Agreement to approve the expedited research submission is not reached by a majority among the subcommittee (with the exception of minor administrative changes); or
    - iii. The subcommittee recommends disapproval of a protocol. This is only done after multiple attempts have been made to resolve the issues (i.e., Tabling the protocol for Re-review) including, at the discretion of the hSCRO Chair, inviting the Investigator to the Committee meeting (i.e., the subcommittee determines that the criteria for approval cannot be fulfilled, even with revisions to the protocol).
  - (b) Under these circumstances, the study is forwarded to the full Committee for further evaluation at the next convened hSCRO meeting.
  - (c) The LR is informed of the reason(s) for the subcommittee's actions by the hSCRO administrator as soon as possible (usually within 5 working days of subcommittee review, to provide the LR sufficient time to submit any required documentation to the next full Committee deadline) and, if necessary, is provided assistance with submission requirements.
- H. If researchers disagree with any hSCRO comments and/or requests for revisions, the researcher should provide written justification for his/her position for review by the original hSCRO subcommittee. If after review, the subcommittee determines that the revisions/clarifications are required per regulations, guidelines, state laws and UC/UCI policies and procedures, the changes will be required prior to granting hSCRO approval.
- J. Approval Period for Expedited Research
  - 1. For research approved by the expedited procedure, the approval period starts on the date of the approval. The end of the approval period is the day before the approval date plus the approval period. (For example, if the hSCRO approves the research on April 12, 2006 for one year, the approval period is April 12, 2006 - April 11, 2007.)
  - 2. In all cases, the expiration date (the last day the research is approved) is the last day of the approval period. Research may be conducted on the expiration date, but may not be conducted after the expiration date without continuing review. (For example, if the approval period is April 12, 2006 - April 11, 2007, the expiration date is April 11, 2007.)

### III. Full Committee Review Procedures

- A. Research is evaluated by the full Committee at a convened hSCRO meeting if the protocol:
  - 1. Does not qualify for expedited review and/or;
  - 2. Could not be approved by the subcommittee or the hSCRO Chair.
- B. Before the hSCRO Meeting:
  - 1. Submissions are reviewed at a scheduled convened meeting, which generally occurs on the second Thursday of each month from 9:00 am to 11:00 am. Submissions are accepted prior to posted submission deadlines for scheduled hSCRO meetings.
  - 2. Upon receipt of a submission, the hSCRO administrator screens the submission to ensure completeness. If the submission is acceptable, the protocol is added to the hSCRO meeting agenda on a first come, first serve basis.

3. If the submission is unacceptable, the hSCRO administrator will consult with the hSCRO Chair. The hSCRO Chair can accept the submission “as is” or deem the submission incomplete and unacceptable. If unacceptable, the hSCRO administrator contacts the LR to provide assistance with correcting the submission.
4. Once the hSCRO administrator has established the hSCRO meeting agenda, administrative review of each submission begins. The hSCRO administrator documents any administrative questions and comments on the reviewer checklist for the Committee’s consideration, noting any protocol irregularities, problems, or concerns.
5. The hSCRO administrator provides the hSCRO Committee members with any supplemental materials that may assist them with their review.
6. After reviewing the submission, the hSCRO administrator assigns two reviewers (primary and secondary) to each new submission. The reviewers are selected from the hSCRO Committee. The hSCRO administrator assigns reviewers based upon expertise in the area of the research adequate to the scope and complexity of the research.
7. The primary and secondary reviewers are required to review the proposed research, consents and applicable document to determine whether the study is permissible.
8. Each hSCRO member will receive the following materials one week in advance of the hSCRO meeting:
  - (a) hSCRO meeting agenda, which includes the topics of discussion, reviewer assignments and the order of protocols to be reviewed.
  - (b) hSCRO submissions signed by LR including:
    - i. UCI IRB Application including, Appendix R and Appendix M, when applicable
    - ii. UCI IRB or hSCRO Protocol Narrative
    - iii. UCI Informed Consent document, when applicable
    - iii. A reviewer checklist that includes the administrative comments
    - iv. Any additional materials, such as documents that establish the provenance of the gametes, embryos or cell lines

C. At the hSCRO Meeting:

1. The hSCRO Chair begins the meeting once a quorum has been attained including at least one member whose primary concerns are in nonscientific areas. Quorum is defined as the presence of the majority of hSCRO members.
2. The hSCRO Chair leads the meeting and facilitates the discussion of agenda items and protocol reviews.
3. The hSCRO administrator records the Committee’s deliberations, motions and votes, noting the number of hSCRO members voting for and against hSCRO actions as well as the number of abstentions.
4. Only regular or alternate members who are in attendance at the hSCRO meeting may vote. If an hSCRO member has a potential conflict of interest, he/she is recused during the protocol review and is not included in the vote.
5. The hSCRO administrator also documents if an hSCRO member was recused during a protocol review due to a conflict of interest. The hSCRO administrator’s notes are detailed so that the meeting minutes can be

written in sufficient detail to document the activities of the hSCRO meeting.

IV. Responsibilities of hSCRO Members for New Protocol Reviews at the Meeting

- A. hSCRO Chair:
  - 1. hSCRO Chair opens protocol debate.
  - 2. hSCRO Chair guides debate and formally proposes final motion.
  - 3. hSCRO Chair calls for a vote by the Committee by a show of hands.
  - 4. hSCRO Chair states whether a motion carries.
  - 5. If a motion does not carry, hSCRO Chair reopens discussion and proposes a new motion.
- B. Each protocol is assigned a primary and secondary reviewer. The reviewers will conduct an in depth review of all pertinent documentation to determine whether the study is consistent with sound research design, the study design can be reasonably expected to answer the proposed questions, the importance of the knowledge expected to result from the research known and whether it is permissible consistent with hSCRO policy.
  - 1. Primary Reviewer:
    - (a) Primary Reviewer (PR) functions as the chief reviewer of the protocol. PR presents the study in summary form to the Committee highlighting any controverted issues and recommending modifications, if applicable.
    - (b) PR provides the Committee with an overview of the study scope, rationale and relevance.
    - (c) PR articulates and discusses scientific, legal and ethical issues that require attention and discussion.
    - (d) PR proposes a motion.
  - 2. Secondary Review:
    - (a) Secondary Reviewer (SR) presents additional protocol issues not mentioned by the primary reviewer.
    - (b) SR agrees with the primary review's motion, modifies it or proposes a different motion.
- C. Categories of Voting Actions Following Protocol Reviews
  - 1. Approval Recommendation:
    - (a) Action taken by the Committee if a majority of the Committee members present at the meeting votes for approval (i.e., no revisions to the submission are required).
    - (b) The hSCRO administrator processes the approval letter for the hSCRO Chair's signature and forwards it to the LR.
  - 2. Minor Revisions Required:
    - (a) Action taken if the majority of the Committee determines that the submission requires specific minor changes. The required revisions are agreed upon at the meeting. The LR is required to submit the requested revisions for further evaluation by the hSCRO Chair. Further review by the full Committee is not required.
    - (b) The hSCRO administrator forwards a memo to the LR on behalf of the Committee, which is usually sent within 10 working days of the hSCRO review. The memo includes the Committee's requested specific changes and instructions on how to resubmit the protocol.

- (c) If the hSCRO Chair determines that the LR did not adequately address the Subcommittee's concerns, the hSCRO administrator sends a memo to the LR on behalf of the hSCRO Chair (usually within a week of the hSCRO Chair's review), which includes the requested changes and instructions on how to resubmit the protocol.
  - (d) This process repeats until the hSCRO Chair determines that the protocol can be approved (i.e., no further revisions are necessary).
  - (e) Once the hSCRO Chair determines the protocol can be approved, the hSCRO administrator processes the approval letter for the hSCRO Chair's signature (or signature stamp, when authorized) and forwards it to the LR.
3. Tabled for Re-review by the Full Committee:
- (a) Action taken if the majority of the Committee determines that substantial modifications and/or clarifications are required or if insufficient information is at hand to assess the protocol adequately. The LR is required to submit revised documents/requested items for further evaluation by the Committee.
  - (b) The hSCRO administrator forwards a memo to the LR on behalf of the Committee, which is usually sent within 5 working days of the hSCRO review so the LR may resubmit the protocol to the next full Committee deadline. The memo includes the reasons for the Committee's action as well as the requested changes and instructions on how to resubmit the protocol.
  - (c) The hSCRO administrator prepares administrative review comments on a new set of reviewer checklists, noting any remaining protocol irregularities, problems or concerns for the Committee.
  - (d) The hSCRO administrator provides all hSCRO members who will be attending the meeting the revised documentation. The primary and secondary reviewers also receive a copy of the researcher's memo explaining the revisions. When possible, the same reviewers that initially reviewed the protocol are assigned as primary and secondary reviewers. If they are unavailable, other reviewers who were present at the initial review are selected based upon their experience and expertise and, when necessary, with input from the hSCRO Chair.
  - (e) If a majority of the Committee approves the revised submission, the hSCRO administrator processes the approval letter for the hSCRO Chair's signature (or signature stamp, when authorized) and forwards it to the LR.
  - (f) If the Committee does not approve the revised submission, the procedures described in "If the Committee determines that a protocol requires minor revisions" or "If the Committee tables the protocol for resubmission to full Committee" are repeated until the protocol can be approved.
4. Disapproval:
- (a) Action taken by the Committee if a majority of the Committee votes for disapproval.

- (b) Disapproval of a protocol is only considered after multiple attempts have been made to resolve the issues (i.e., Tabling the protocol for Re-review) including, at the discretion of the hSCRO, inviting the Investigator to the Committee meeting.
- (c) The hSCRO administrator notifies (via e-mail) the LR of the Committee's decision in a memo, which is usually sent within 10 working days of the hSCRO review. The memo includes the rationale for the Committee's decision to disapprove and give the LR an opportunity to respond in writing. The LR is responsible for communicating the hSCRO Committee's decision to the Sponsor of the research, if applicable.

SECTION:

**Other hSCRO Reviews and Approvals of Human Stem Cell Research**

ORIGINAL CREATION DATE:

January 11, 2007; May 15, 2007

REVISION DATES:

**Policy:**

I. Continuing Review of Approved Protocols

- A. The hSCRO shall conduct continuing review of minimal expedited and full Committee not less than once per year.
- B. Once a protocol has been approved by the hSCRO, it is the LR's responsibility to maintain hSCRO approval until all uses of gametes, blastocysts and cell lines have concluded.
- C. There is no grace period extending the conduct of the research beyond the expiration date of hSCRO approval period.
- D. Since failure to maintain current approval of protocols is contrary to UCI policy, LRs are encouraged to submit their applications for continuing review at least 30 days prior to the expiration of hSCRO protocol approval for protocols qualifying for continuing expedited review, or at least 60 days prior to the expiration of hSCRO protocol approval for protocols that require full committee review.
- E. As a courtesy, all researchers and their administrative contacts are sent automated e-mail memos 90 days prior to expiration of approval for full committee protocols and 60 days prior to expiration for expedited protocols reminding them to submit for continuing review prior to expiration or close the protocol.
- F. In order for the hSCRO to determine whether the research continues to meet the requirements for continuing approval, the researcher must submit detailed information and documentation regarding the status of the research.

II. Amendments/Modifications to Approved Research

- A. Once a protocol has received hSCRO approval (initial or continuing), any subsequent change(s) to the study (e.g., addition or deletion of study procedures, research personnel, or research performance sites; revisions to the protocol narrative, consent, or other approved documents, etc.) must be reviewed and approved by the hSCRO prior to their implementation.
- B. The researcher may submit requests for approval of protocol modifications at any time during the protocol's approval period. Modifications are reviewed by either the subcommittee or the full Committee based on whether the proposed change is considered "minor" or "significant." Minor changes do not significantly affect the assessment of the ethical and social issues, such as the provenance or derivation of the gametes, embryos or cell lines of the study, and do not substantially change the specific aims or design of the study. Minor changes qualify for expedited review by the hSCRO Chair or designee. Any change not considered a "minor" change is considered a "significant" change.

III. Closing Reports

- A. LRs are required to submit a Closing report to the hSCRO once all human subjects research activities are complete and uses of gametes, embryos and cell lines for described activity have concluded.
- B. If a study is canceled without any activity, LRs are still required to submit a Closing Report to the hSCRO.

**Procedure:**

This procedure provides guidance for the continuing review and approval of protocols by the UCI human Stem Cell Research Oversight Committee (hSCRO).

I. Administrative Screening and Review

- A. Investigators submit to the hSCRO by completing the hSCRO continuing review application.
- B. The hSCRO administrator in consultation with the hSCRO Chair screens all protocol submissions prior to hSCRO review.
- C. Protocol submissions are entered into the hSCRO database to maintain a record of the hSCRO submission.
- D. Submissions are checked for completeness. The hSCRO administrator ensures that all required documents are provided. If the submission is incomplete, or if any of the required documents cannot be reviewed due to deficiency of information, the hSCRO administrator will contact the Lead Researcher (LR) and provide guidance with completing the submission.
- E. All hSCRO submissions are administratively reviewed.
- F. The hSCRO administrator prepares the reviewer checklist and includes questions and comments for the hSCRO Committee members.

II. Documentation Provided to Reviewers of Expedited and Full Committee Continuing Review Protocols

- A. hSCRO Continuing Review Application
  - 1. Status report on the progress of the research,
  - 2. Number of gametes, embryos or cell lines used and the number of new cell lines derived from these materials,
  - 3. Current, approved Protocol Narrative,
  - 4. Current, approved Consent form(s), if applicable,
  - 5. A reviewer checklist that includes the administrative comments.
- B. hSCRO members may request access to the complete hSCRO protocol file and relevant hSCRO minutes, if applicable, with at least 12 hours advance notice to the hSCRO administrator.
- C. hSCRO members may request access to the complete IRB or IACUC protocol files and relevant minutes, if applicable, with at least 12 hours advance notice to the hSCRO administrator.
- D. If the hSCRO determines that verification from sources other than the researcher is required to confirm that no material changes have occurred since the previous hSCRO review, the hSCRO will request an independent assessment of information or data provided in the continuing review application. The scope and extent of such an independent assessment is determined on a case-by-case basis.
- E. In general, the focus of continuing reviews is to evaluate the collection of gametes, embryos and cell lines (as applicable), the derivation of new cell lines and their use, and to ensure that the protocol remains in compliance with all applicable regulations, guidelines, state laws and UC/UCI policies and procedures.
- F. If a protocol lapses in approval the researcher is required to stop all research activities.

### III. Expedited Review Process for Continuing Review

#### A. hSCRO Review Procedures:

1. Expedited continuing protocol applications are accepted on a rolling basis and are reviewed weekly by the hSCRO Chair or hSCRO member designee.
2. Continuing review of research previously approved by a hSCRO subcommittee may be reviewed using the expedited review process if it continues to fall into the Expedited Review categories.

#### NOTES:

- For details of how the hSCRO administrator and hSCRO subcommittee review an Expedited Continuing Protocol Application, see “Review Procedures for Expedited Research” under “Review and Approval Process Human Embryonic Stem Cell Research” policy and procedure.
- For Categories of Action for Continuing Expedited Research, see “Categories of Action for Expedited Research” under “Review and Approval Process Human Embryonic Stem Cell Research” policy and procedure.

### IV. Full Committee Review Process for Continuing Review

#### A. Before the hSCRO Meeting:

1. Similar to initial hSCRO applications that require full committee review, Continuing Protocol applications are accepted prior to posted submission deadlines for scheduled hSCRO meetings.
2. Upon receipt of an application for full committee continuing review, the hSCRO administrator screens the submission to ensure that it is complete (see Administrative Screening and Review policy).
3. If the submission can be accepted for review (i.e., all required documents and signatures are provided, appropriate institutional clearances are obtained, etc.), the protocol is added to the meeting agenda on a first come, first serve basis.
4. After administratively reviewing the protocols, the hSCRO administrator assigns one reviewer to each Continuing Protocol submission.
  - (a) If necessary, the hSCRO administrator may assign more than one reviewer to protocols that require additional expertise.
  - (b) The reviewer(s) are selected from voting members of the Committee or alternate members who will attend the hSCRO meeting and vote.
  - (c) Although they cannot vote, special consultants may also be designated as reviewers when if warranted.
  - (d) The hSCRO administrator makes an effort to assign the same reviewer to the protocol as the protocol’s previous review. If that reviewer is not available, the hSCRO administrator selects another reviewer based upon his/her type of expertise and sensitivity to particular human subject protection concerns.
  - (e) When necessary, the hSCRO administrator consults with the hSCRO Chair when unsure about who to assign to a continuing review.
5. In addition to the documentation listed above per Continuing Protocol submission, each hSCRO member who will be in attendance at the hSCRO meeting receives prerequisite meeting documentation one week in advance of the hSCRO meeting.

## NOTES:

- For Procedures at the convened hSCRO Meeting, see Full Committee Research – “At the Meeting” and “After the Meeting.”
- For Categories of Action for Continuing Full Committee Research see, “Categories of Action for Full Committee Research.”

## **Procedure:**

This procedure provides guidance for the amendment or modification of protocols approved by the UCI Human Stem Cell Research Oversight Committee (hSCRO).

### I. Submission of Modification Requests

Researchers seeking hSCRO approval for protocol modifications send a hSCRO Protocol Modification Request form, available on the Office of Research Administration (ORA) website. If a modification request also is required for IRB review, the IRB-e-modification request form may be used in lieu of the hSCRO form.

- A. Upon receipt of a modification request, the hSCRO administrator enters the submission into the hSCRO database, prints the documents and performs an administrative review to ensure that the submission is complete.
- B. Required documentation for hSCRO review of minor and significant protocol modifications include:
  1. hSCRO Protocol Modification Request form
  2. Any new documents or any updated documents that were previously approved by the hSCRO, which includes all of the new changes (e.g., revised protocol narrative, revised consent forms)
  3. New Investigator’s Assurance document signed by the LR (if the modification request includes a change in LR)
  4. New Disclosure of Investigators’ Financial Interest form signed by LR (if a new conflict of interest arises due to changes in study team membership or status).
  5. Any other documents that may be required to assist with hSCRO review.
- C. For modification requests that require full Committee review, Committee Members also receive a Modification checklist, which includes the hSCRO administrator comments.

**NOTE:** For a complete list of documents provided to hSCRO members at the convened hSCRO Meeting, see Full Committee Research – “Before the hSCRO Meeting.”

- D. If a submission is incomplete, the hSCRO administrator contacts the LR and provides assistance with submission requirements.
- E. Once the modification request is approved, the amendments are appended to the protocol and given the same expiration of approval date as the study.
- F. In general, modification requests for expired protocols are not accepted unless the protocol is in the continuing review process or unless the modification was requested by the hSCRO.

### II. Review Process Modification Requests that involve Minor Changes to the Research

- A. The hSCRO may use the expedited review procedure to review minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

- B. Protocol modifications that include minor changes are accepted on a rolling basis and are reviewed weekly by an hSCRO Chair. Examples of minor changes to a protocol include, but are not limited to, the following:
  1. Addition or deletion of study team members.
  2. Addition of procedures that do not significantly affect the assessment of the ethical and social issues, such as the provenance or derivation of the gametes, embryos or cell lines of the study, and do not substantially change the specific aims or design of the study.
  3. Removal of research procedures that do not affect the assessment above.
  4. Administrative changes to the approved documents (e.g., correction of typographical errors).
- C. Minor modification submissions are reviewed by the hSCRO Chair.
- D. When unsure about whether the proposed changes may be considered minor, the hSCRO administrator consults with an hSCRO Chair to determine the appropriate level of review.

NOTE: See Subcommittee Actions under Expedited Review for details about the review process and the action options.

### III. Review Process for Modification Requests that Require Full Committee Review

- A. Modifications that involve significant changes to the research require review by the full Committee at a convened meeting. The hSCRO Chair can also refer an expeditable modification request to the full Committee for further evaluation.
- B. Modification requests that require full committee review are evaluated at a scheduled convened hSCRO meeting, which occur once a month. Modification requests are accepted prior to the posted submission deadlines for scheduled full Committee hSCRO meetings.
- C. Examples of significant changes to a protocol include, but are not limited to, the following:
  1. Addition of a new and/or separate source of gametes, embryos or cell lines.
  2. Addition of new research procedures that significantly affect the assessment of the ethical and social issues, such as the provenance or derivation of the gametes, embryos or cell lines of the study.

NOTE: See Full Committee Review for Procedures Before, During, and After the hSCRO Meeting and Actions.

### IV. Administrative Protocol Preparation Procedures

Upon receipt of a Modification Request, the hSCRO administrator screens the submission to ensure that it is complete.

- A. If the submission can be accepted for review (i.e., the submission is complete, all required documents are provided), the modification request is added to the hSCRO meeting agenda on a first come, first serve basis.
- B. Following the administrative review, the hSCRO administrator assigns one reviewer to each modification request.
- C. If necessary, more than one reviewer may be assigned to modifications that require additional expertise.
- D. The reviewer(s) are selected from voting members of the hSCRO or alternate members who will attend the hSCRO meeting and vote.

- E. Although they cannot vote, special consultants may also be designated as reviewers when if warranted.
- F. When appropriate, the hSCRO administrator makes an effort to assign the same reviewer to the modification request as the protocol's previous review. If that reviewer is not available, the hSCRO administrator selects another reviewer based upon his/her type of expertise.
- G. When necessary, the HRP staff consults with the hSCRO Chair when unsure about whom to assign to a review.

**Procedure:**

This procedure provides guidance for the closing of protocols approved by the UCI human Stem Cell Research Oversight Committee (hSCRO).

I. Closing Reports

- A. An electronic Closing report (E-Closing Report) is available on the ORA website. The E-Closing Report is completed on-line and submitted electronically by the LR to the hSCRO and the IRB, when applicable.
- B. Although not required, additional items relating to the study, such as the sponsor's completion summary or adverse events occurring at other sites (i.e., multi-site study), are accepted for the protocol file even after the study has been closed.
- C. Upon receipt the hSCRO administrator retrieves a copy of the closing report and all attachments from HPS, checks the report for accuracy and completeness and arranges for hSCRO Chair review to verify that the protocol can be closed.
- D. The official retention period for UCI's hSCRO records begins on the date a closing report is submitted to the hSCRO by the LR or 30 days after protocol expiration, whichever comes first.

SECTION: **Program Records Maintenance and Retention**  
ORIGINAL CREATION DATE: January 5, 2006  
REVISION DATES: March 28, 2006; January 11, 2007

**Policy:**

The hSCRO administrator prepares and maintains adequate documentation of hSCRO activities. All documents supporting hSCRO submissions will be maintained in the hSCRO files.

I. hSCRO Minutes

- A. The minutes of all hSCRO Committee meetings must be sufficiently detailed to demonstrate:
  - 1. Attendance at the meeting;
  - 2. For each protocol reviewed, the minutes should detail:
    - (a) The assigned reviewers and their scientific or non-scientific status as indicated on the roster;
    - (b) If a consultant is used and attends the meeting in person, the key information provided by the consultant;
    - (c) If a member is excused from the meeting discussion and vote of the study due to a conflict of interest;
    - (d) Actions taken by the hSCRO Committee;
    - (e) Discussion of any controverted issues and resolutions;
    - (f) The vote on these actions including the number for voting “for,” “against,” or “abstaining.”
    - (g) Attendance for the meeting.
  - 3. A copy of the meeting’s agenda and any documents distributed to the members during the meeting should be included with the minutes.
- B. The minutes are retained in the hSCRO Committee meeting binder.

II. Members Roster

- A. The information contained on the member roster should include the following: Name, Title, Department and Area of Expertise, Address, Phone, email; and Term of Appointment.

III. Protocol Files

- A. New Submission – All available documents related to the submission of a research protocol including but not limited to:
  - 1. Protocol Narrative;
  - 2. hSCRO Application;
  - 3. Consent Documents;
  - 4. Documentation regarding provenance of cell lines;
  - 5. Scientific evaluations.
- B. Continuing Review – Records of continuing review activities including but not limited to:
  - 1. Continuing Review Application;
  - 2. Current Protocol Narrative;
  - 3. Current Consent Forms.
- C. hSCRO administrator is to maintain copies of all correspondence (reviews, letters, e-mail) between hSCRO and researchers and place them in the hSCRO protocol file.

IV. Retention of Records

- A. All records are kept accessible for inspection and copying by authorized UCI entities and regulatory agencies at reasonable times and in a reasonable manner.
- B. To remain compliant with the UC records retention policy, UCI keeps and maintains protocol records for at least three years after completion of the research.
- C. Administrative records (e.g., minutes, member roster, etc.) are maintained indefinitely.

SECTION: **Funding for Human Embryonic Stem Cell Research**  
ORIGINAL CREATION DATE: January 5, 2006  
REVISION DATES: March 28, 2006; December 14, 2006; May 15, 2007

**Policy:**

All UCI research activities involving the derivation or use of human embryonic stem cells (hESC) shall be in accordance with the applicable State and Federal regulations and funding governing such research, including any restrictions on the use of Federal funds for such research. Individuals conducting research deriving or using non-registered hESC lines must financially separate the direct and indirect costs of the research and charge the costs to a non-Federal funding source.

- I. Research Funding for Registered Human Embryonic Stem Cell Lines
  - A. Federal funds may not be used for research using hESC lines unless the stem cells were derived from an embryo that was created for reproductive purposes and was no longer needed; informed consent was obtained for the donation of the embryo, and the donation did not involve financial inducement; and the process of derivation was begun prior to 9 pm EDT on August 9, 2001.
  
- II. Research Funding for Non-Registered Human Embryonic Stem Cell Lines
  - A. Federal funds may not be used directly or indirectly for research using non-registered hESC lines or their derivatives.
  - B. Precautionary measures must be taken in managing resources used for non-registered hESC related research to ensure that no federal funds are spent directly or indirectly to support non-registered hESC research.

**Procedures:**

On March 24, 2006, UCI issued guidance for the expenditure of funds for stem cell research, which can be found at [http://www.rgs.uci.edu/ora/Guidance\\_Charging\\_Costs\\_Stem\\_Cell.pdf](http://www.rgs.uci.edu/ora/Guidance_Charging_Costs_Stem_Cell.pdf).