Policy Number: 1
Title: Human Stem Cell Research Oversight Program Policy and Procedures
Date of Last Revision: 11/25/2024, 03/10/2025

Review and Oversight Policy:
All research or clinical investigations that involve the use of pluripotent human stem cells shall be reviewed and approved by the UCI Human Stem Cell Research Oversight Committee (hSCRO) before such activities are initiated by or for UCI.

I. The following activities require prospective UCI hSCRO review:

A. Generation of new lines of human pluripotent stem cells from whatever source and by whatever means.
B. Use or derivation of the following materials:
    1. human gametes
    2. blastocysts (embryos)
    3. human induced pluripotent stem cells (iPSC)
    4. human fetal tissue and/ or human fetal stem cells
    5. human embryonic stem cells (hESC)
C. Transplantation of neural stem cells into humans (not including mesenchymal or hematopoietic stem cells).
D. Activities involving the introduction of human adult pluripotent, human fetal tissue and/or fetal stem cells., human embryonic stem cells and/or their neural derivatives into nonhuman animals at any stage of embryonic, fetal, or postnatal development.
E. 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. The following hSCRO activities are prohibited in California:

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. Note: The 12-day prohibition does not count any time during which the blastocysts and/or cells have been stored frozen.
B. Introduction of human pluripotent stem cells into nonhuman primate blastocysts and/or the introduction of any embryonic stem cells into human blastocysts.
C. Introduction of pluripotent stem cells, whether human or nonhuman, into human embryos.
D. Breeding of an animal into which pluripotent stem cells have been introduced at any stage of animal's development.

III. hSCRO Protocol Submission Requirements:

The hSCRO New Protocol Application is used for protocol submissions. Additional documents provided with the application include the Informed Consent Document(s) (if applicable), and Provenance Documentation according to the UCI Provenance Policy (Table) (if applicable).

IV. Oversight and Monitoring of Stem Cell Lines:

A. hSCRO shall require documentation of the provenance of all stem cell lines, whether the cells were obtained from outside sources or generated locally. Notice to hSCRO may include evidence of written IRB-approval of the procurement process, evidence of and adherence to basic ethical and legal principles of procurement, and any other supporting documents. hSCRO approval of provenance will be determined on a case-by-case basis.

B. All protocols involving the combination of stem cells with nonhuman embryos, fetuses, or adult animals require IACUC review of animal welfare issues and require hSCRO review for consideration of the consequences of the human contributions to the resulting chimeras.

C. Experiments in which stem cells are introduced into nonhuman fetuses and allowed to develop into adult chimeras shall be reviewed, including consideration of any major functional contributions to the brain.

D. Introduction of pluripotent stem cells into nonhuman nonprimate mammalian blastocysts will be subject to serious scrutiny and stringent review.

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

Procedure Number: 1A
Title: Review and Oversight Procedures
Date of Last Revision: 11/25/2024, 03/10/2025

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) or designee, serving as the designated Institutional Official (IO), has responsibility for the UCI Human Stem Cell Research Oversight (hSCRO) Program.
B. The (VCR) or designee 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) or designee selects and appoints members of the Human Stem Cell Research Oversight (hSCRO) Committee.
D. The (VCR) or designee may recommend suspension or termination of hSCRO protocols, subject to the overriding responsibilities of the IRB.
E. The (VCR) or designee 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) or designee ensures proper internal reporting to the VCR (as appliable), the Chancellor and other campus officials.

II. Human Stem Cell Research Oversight Committee Responsibilities

A. hSCRO assures human stem cell activities are in accordance with applicable federal and state regulations as well as institutional requirements.
B. The UCI hSCRO abides by guidance and regulations cited in the following:
   1. National Academies Guidelines for Research on Human Embryonic Stem Cells,
   2. California Department of Public Health (CDPH, Health and Safety Code Sections 125118 - 125119.5),
   3. California Institute for Regenerative Medicine (CIRM, Title 17 CA Code of Regulations, Sections 100010-100110, and the
   4. National Institutes of Health (NIH Stem Cell Guidelines).
   5. In addition, the UCI hSCRO follows relevant and applicable campus policies and procedures for human stem cell activities.
C. hSCRO considers the ethical and social issues presented by human stem cell activities.
D. 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 question(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 will confirm active approval with other applicable institutional committees (e.g., IRB, IACUC and IBC).

F. hSCRO can approve, require amendments to, or disapprove protocols involving human gametes, embryos and human stem cell activities, subject to the overriding responsibilities of the IRB and IACUC.

UCI Institutional Review Board (IRB) Committee Responsibilities

A. The IRB separately reviews, requires conditional and / or final approval for human subject research as defined under 45 CFR 46 and 21 CFR 56, where hSCRO review is also indicated.
B. The IRB may cede review to a commercial sponsor, as per Human Research Protections Policies.
C. The IRB, along with the IO has the authority to disapprove proposed human subject research at UCI.
D. The IRB, along with the IO has the authority to suspend or terminate approved human subject research at UCI.
E. When the human subject research involves a hSCRO approved protocol, and there is a reportable event that occurs under the IRB protocol, the UCI IRB will collaborate with the hSCRO committee to determine if hSCRO activities may continue to any degree at UCI.
F. If any IRB approved clinical trials involve hSCRO approved covered stem cells and their derivatives, a Data Safety Monitoring Board should be established to periodically review outcomes and safety of the trial and provide a monitoring plan for the trial (CDPH Guidelines for Human Stem Cell Research Health and Safety Code §125118.9.c.3)
G. When a human subject research protocol also involves hSCRO, the following details the regulatory committees' review processes. When the source of materials to derive induced pluripotent stem cells (iPSC) originate from a UCI IRB protocol:
    1. The hSCRO Chair, Vice Chair or designee will review the IRB Consent Form and the scientific rationale of the hSCRO protocol prior to IRB review.
    2. The hSCRO Chair, Vice Chair or designee (e.g., hSCRO Administrator) confirms the IRB Consent Form includes requisite provenance specific language. This confirmation is shared with the IRB as part of the IRB review.
    3. Release of the IRB approval depends upon confirmation of final hSCRO committee approval.

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.
D. The IACUC may suspend or terminate approved human stem cell research under its jurisdiction.
E. hSCRO review and approval runs concurrent with IACUC review and approval.
F. When IACUC review is applicable to a hSCRO protocol, 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 the review of 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. hSCRO review and approval runs concurrent with IBC review and approval.
D. When IBC review is applicable to a hSCRO protocol, the IBC must review and approve the protocol prior to initiation of the study.

VI. Office of Research Administration Responsibilities

A. The Office of Research (OR) 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 OR supports and coordinates all 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 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.
D. The OR develops policies (or revisions of policies) for the conduct of human stem cell research, working as necessary with the IRBs.

Procedure Number: 1B
Title: Committee Composition, Member Responsibilities and Procedures
Date of Last Revision: 11/25/2024, 03/10/2025

Procedure:
This procedure provides guidance in forming the hSCRO Committee and defines its responsibilities.

I. Composition of the hSCRO Committee

A. The hSCRO Committee is an appointed University Committee. The hSCRO Committee shall be composed of:

1. A minimum of five voting members with varying backgrounds and expertise to promote complete and adequate review of human stem cell research activities at UCI and fulfill the membership requirements of the CIRM.
2. Members who are experts in developmental biology, stem cell research, molecular biology, assisted reproductive technologies, and ethical issues in human stem cell research.
3. In addition, hSCRO should include at least one non-scientist member of the public who is not employed by UCI and who is not part of the immediate family of a person who is affiliated with UCI.
4. At least one patient advocate.
    i. The patient advocate may be affiliated with UCI.
5. 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 at the meeting.
6. Alternate members serve the same function as other hSCRO members. Alternate members participate in the review, discussion and vote of protocols when a primary hSCRO member cannot attend a convened meeting. Alternate members may also attend a meeting when their unique expertise is required.

B. hSCRO will have a hSCRO Chair who is appointed by the VCR or designee. The hSCRO Chair serves as the official representative of the hSCRO Committee 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, other hSCRO members, or on a volunteer basis.

B. The Senior Director or Director of Human Research Protections appoints the hSCRO Chair and members to a three year renewable term and appoints the hSCRO Chair and Vice Chair to a two year renewable term.

C. If a member is unable to fulfill the responsibilities of hSCRO membership, they may resign before the conclusion of their term and / or asked to resign by the hSCRO Chair or designee.

III. Compensation

A. The hSCRO Chair receives a monthly research fund of $750 per month of appointment. The use of these funds is governed by UCI expense policies, Academic Personnel additional compensation policies, and/or faculty compensation plan policies.
B. The hSCRO Vice Chair receives a monthly research fund of $250 per month of appointment. The use of these funds is governed by UCI expense policies, Academic Personnel additional compensation policies, and/or faculty compensation plan policies.
C. Other 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 Administrative Staff so that alternate arrangements can be made as necessary.
3. Members serve as primary or secondary reviewers on protocols based upon expertise.
4. Members must disclose any potential conflict of interest to the hSCRO Administrative Staff or Chair as soon as it is recognized.
5. Members must maintain confidentiality of hSCRO meeting proceedings, and any information contained in protocol reviews.
6. Members must have knowledge of the regulations regarding human stem cell research and an understanding of UCI policy and procedures.

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. Members of the public provide unique insight to possible community response to human stem cell research and serve as patient advocates.
3. Non-scientific status members are not assigned as primary or secondary reviewers.

C. Duties of the hSCRO Members with Patient Advocate Status

1. Patient advocate members should effectively represent the interest of the patient community and foster clinical equipoise.
2. Patient advocate members are not assigned as primary or secondary reviewers.

D. Duties of the hSCRO Chair

1. Convenes hSCRO Committee meetings.
2. Relays concerns of the hSCRO members to OR Administration regarding issues in review procedures.
3. Facilitates communications and dissemination of information from the IO and OR staff to the hSCRO members and to researchers.
4. Calls special meetings when necessary.
5. Acts as an advisor in the institution's research community.
6. Attend IRB Working Group meetings with HRP staff.
7. May delegate any of their 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 education and training that includes the following materials prior to their first meeting:

1. hSCRO Committee member appointment letter
    i. Member standards document for signature
2. Schedule of Committee meetings and submission deadlines
3. hSCRO Standard Operating Policies and Procedures
4. Guidelines and Regulations: NIH Guidelines for Human Stem Cell Research, National Academies' hESC Guidelines, CDPH Guidelines, CIRM Regulations
5. Ethical Guidelines: Belmont Report Principles and Declaration of Helsinki Information on stem cell basics - the science of stem cells (for non-scientific members)

B. Ongoing Training will consist of relevant articles and discussions conducted at regular hSCRO meeting regarding new issues as they become relevant.

Policy Number: 2
Title: Informed Consent Requirements for Gamete or Blastocyst Donors
Date of Last Revision: 11/25/2024, 03/10/2025

Review and Oversight 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.

II. 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 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) 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 predictable at this time.
6. Donated embryos, 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 <u>oocyte retrieval</u>, 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 their 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) 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 directly benefit the donor or any other individual.
    (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.

Policy Number: 3
Title: Committee Review and Approval Process of New Human Stem Cell Research Protocols
Date of Last Revision:
Review and Oversight Policy:

I. All research or clinical investigations that require hSCRO review (Policy 1) shall be reviewed and approved by the UCI Human Stem Cell Research Oversight (hSCRO) Committee before such activities are initiated by or for UCI.

Adult tissue-specific stem cells such as hematopoietic cells, cord blood stem cells or mesenchymal cells do not require hSCRO review and approval unless such cells have been shown to or are being induced to pluripotency as shown by the capacity to differentiate into the three major germ lines.

All new research protocol submissions must be reviewed by the hSCRO Full Committee.

Procedure Number: 3A
Title: Committee Review and Approval Process of New Human Stem Cell Research Protocols
Date of Last Revision: 11/25/2024, 03/10/2025

Procedure:
This procedure provides guidance for the review and approval of New Protocols by the UCI hSCRO Committee.

I. Administrative Screening and Review

A. Investigators submit to the hSCRO by completing the hSCRO New Protocol Application.

B. The hSCRO Administrative Staff screens all protocol submissions prior to hSCRO Full Committee 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 Administrative Staff ensure 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 Administrative Staff will contact the Lead Researcher (LR) and provide guidance with completing the submission.

II. Full Committee Review Procedures

A. All new research protocols are evaluated by the Full Committee at a convened hSCRO meeting.

B. Before the hSCRO Meeting:

1. Once the hSCRO Administrative Staff have established the hSCRO meeting agenda, each submission is administratively reviewed. The hSCRO Administrative Staff document any administrative questions and comments for the Committee's consideration, noting any protocol irregularities, problems, or concerns.
2. The hSCRO Administrative Staff provide the hSCRO Committee members with any supplemental materials that may assist them with their review.
3. After reviewing the submission, the hSCRO Administrative Staff assign two reviewers (primary and secondary) to each new submission. The hSCRO Administrative Staff assign reviewers based upon expertise in the area of the research adequate to the scope and complexity of the research.
4. The primary and secondary reviewers are required to conduct an in-depth review of all pertinent documentation.
5. Each hSCRO member receives access to the following information 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 including:
      i. hSCRO New Protocol Application
      iii. IRB Informed Consent document, when applicable
      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, including review and approval of the prior meeting's minutes, and protocol reviews.
   3. The hSCRO Administrative Staff record 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 attend the hSCRO meeting may vote. If an hSCRO member has a potential conflict of interest, they are recused during the protocol review and are not included in the discussion or the vote.
   5. The hSCRO Administrative Staff also document if a hSCRO member was recused during a protocol review due to a conflict of interest. The hSCRO Administrative Staff notes are detailed so that the meeting minutes can be written in sufficient detail to document the activities and deliberations of the hSCRO Committee during the meeting.

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

A. hSCRO Chair:
   1. hSCRO Chair opens protocol discussion.
   2. hSCRO Chair guides discussion and formally proposes final motion.
   3. hSCRO Chair calls for a vote by the Committee.
   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 new research 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 Amendments, 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 Reviewer:
      (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 Administrative Staff processes the approval letter and releases it to the LR.

2. Minor Revisions Required:
   (a) Action taken if a 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 or designee. Further review by the full Committee is not required.
   (b) The hSCRO Administrative Staff drafts and forwards a memo to the LR on behalf of the Committee, usually within 5 working days of the hSCRO Committee review. The memo includes the Committee's requested specific changes.
   (c) The hSCRO Chair reviews the responses. If the Chair determines that the LR did not adequately address the Subcommittee's concerns, the hSCRO Administrative Staff send a memo to the LR on behalf of the hSCRO Chair (usually within a week of the hSCRO Chair's review), reiterating the Committee's requested changes.
   (d) When the hSCRO Chair determines the protocol can be approved, the hSCRO Administrative Staff processes the approval letter and releases it to the LR.

3. Tabled for Re-review by the Full Committee:
   (a) Action taken if a majority of the Committee determines that substantial Amendments 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 Full Committee.
   (b) The hSCRO Administrative Staff forward 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.
   (d) The hSCRO Administrative Staff provide all hSCRO members who will be attending the meeting the LR's responses. 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 Administrative Staff processes the approval letter and releases 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 is approved or disapproved.

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 attend a committee meeting.
   (c) The hSCRO Administrative Staff notifies 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. The LR is responsible for communicating the hSCRO Committee's decision to the Sponsor of the research, if applicable.

Policy Number: 4
Title: Other hSCRO Reviews and Approvals of Human Stem Cell Research
Date of Last Revision: 11/25/2024, 03/10/2025

Review and Oversight Policy:

I. Renewal of Approved Protocols

A. The hSCRO Committee shall conduct Renewal Review of ongoing hSCRO approved studies not less than once per year. Unless determined otherwise, the UCI hSCRO will grant a one-year approval for research that:
- uses human gametes
- uses human embryos
- uses human fetal tissue
- uses or generates new human fetal stem cell lines
- uses or generates brain organoids, iBlastoids
- generates new human embryonic stem cell lines
- transplants hSCRO covered materials into animals / humans

B. The hSCRO Committee may provide a three-year approval for purely in-vitro research:
- using or creating materials from non-identifiable cells, or
- cell lines recognized by an “authorized authority” like NIH, or
- in which the provenance is approved by the UCI hSCRO Committee

C. All research approved by the hSCRO Full Committee qualifies for Expedited Renewal Review unless the research has had any instance of noncompliance or unanticipated problems during the previous year of approval.

D. Personnel updates (removal or addition of personnel, including lead researcher changes) are allowed at the time of Renewal review.

E. For protocols that include continuous generation of stem cells, new stem cell lines can be added at the time of Renewal review if the source material used to create these new lines has been collected at UCI using an active UCI IRB-approved Consent or whose provenance documentation has already been reviewed for this protocol.

F. It is the Lead Researcher's responsibility to ensure all applicable Ancillary Committee approvals, such as Institutional Review Board (IRB), Institutional Biosafety Committee (IBC) and Institutional Animal Care and Use Committee (IACUC) approvals are up to date in the hSCRO protocol.

G. Once a protocol has been approved by the hSCRO Committee, it is the LR’s responsibility to maintain hSCRO approval until all procurement and use of gametes, blastocysts, pluripotent stem cells or fetal tissue and hSCRO approved cell lines have concluded.

H. There is no grace period extending the conduct of the research beyond the expiration date of hSCRO approval period.

I. Since failure to maintain current approval of protocols is contrary to UCI policy and CDPH regulations, LRs must submit their Renewal Application at least 30 days prior to the expiration of hSCRO protocol approval.

J. As a courtesy, all LRs and their administrative contacts are sent emails via the hSCRO Database at 30, 60 and 90 days prior to expiration of approval for protocols reminding them to either submit a renewal for Renewal review prior to study expiration or submit a closing report if the research is completed.

K. As a courtesy, for studies issued a three year approval, all LRs and their administrative contacts are sent annual emails via the hSCRO Database

reminding them that, should a planned amendment make the study ineligible for three year approval, a Renewal & Amendment must be submitted. The hSCRO Committee will review the study's progress and reset the approval period to an annual review cycle.

L. In order for the hSCRO Committee to confirm compliance with all applicable rules and regulations, the researcher must submit detailed information and documentation regarding the status of the research. Please see the UCI hSCRO Policy related to non-compliance.

M. Expired protocols will be closed out within 6 months of expiration.

II. Amendments to Approved Research

A. Once a protocol has received hSCRO approval (Initial or Renewal), any subsequent change(s) to the study (e.g., addition or deletion of study procedures, research personnel, or research performance sites; or other approved documents, etc.) must be reviewed and approved by the hSCRO Committee or the hSCRO Administrative Staff prior to implementation.

B. The researcher LR may submit changes to the study for review and approval any time during the protocol's approval period. Amendments are reviewed by either the Subcommittee, the Full Committee, or Administratively based on the following criteria:

1. Administrative review
    (a) Addition or deletion of personnel if key research personnel are not deleted from the study team.
    (b) Updates in study locations and cell storage locations.
    (c) Deletions of cell lines.
    (d) Additions of registered cell lines, cell lines/ materials that have been previously approved by UCI hSCRO or cell lines obtained from source material that has previously been verified by UCI hSCRO including standard fluorescent reporter lines (such as GFP). *Note: federally/state-funded cell repositories are considered already verified sources, e.g., NIGMS and NIMDS Repositories at Coriell.*
2. Subcommittee review
    (a) Proposed changes in research related to activities that do not significantly affect the assessment of the ethical and social issues, and do not substantially change the specific aims or design of the study.
3. Full committee review
    (a) Addition of new cell lines (hESC, iPSC, fetal, neural, per Section III.I) if documentation of registry or previous UCI approval is not available and provenance must be reviewed.
    (b) Amendments containing substantial changes to the specific aims or design of the study.
    (c) In vivo transplantation of pluripotent stem cells, cells of fetal origin or neural stem cells (except for the addition of teratoma assays which qualify for expedited review).
    (d) In vivo transplantation of genetically modified pluripotent, fetal, or neural cell lines will also require hSCRO Full Committee review.

C. The LR may request Renewal Review concurrent with review of an Amendment. If so, the LR is required to submit a Renewal and Amendment Application and all required materials.

III. Closing Reports

A. Once all hSCRO related activities are complete, and procurement / use of gametes, embryos and cell lines for described activities have concluded the LR should submit a Closing Report

Procedure Number: 4A
Title: Other hSCRO Reviews and Approvals of Human Stem Cell Research
Date of Last Revision: 11/25/2024, 03/10/2025

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

I. **Administrative Screening and Review**
- A. LRs submit for renewal approval to the hSCRO by completing the requisite hSCRO Application.
- B. The hSCRO Administrative Staff in consultation with the hSCRO Chair screen all protocol submissions prior to hSCRO review.
- C. Submissions are checked for completeness. The hSCRO Administrative Staff ensure 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 Administrative Staff will contact the LR and provide guidance with completing the submission.
- D. All hSCRO submissions are administratively reviewed.
- E. The hSCRO Administrative Staff prepare any questions and comments for the hSCRO Committee members.

II. Documentation Provided to Reviewers of Expedited and Full Committee Renewal Reviews
- A. hSCRO Application for Renewal review
  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,
- B. hSCRO members have access to the complete hSCRO protocol and relevant hSCRO minutes.
- C. In general, the focus of renewal 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 hSCRO approval, the LR is required to stop all hSCRO related research activities.

III. Expedited Review Process for Renewals
- A. hSCRO Review Procedures:
  1. Expedited Renewal applications are reviewed weekly by the hSCRO Chair or designee.
  2. Renewal review of research previously approved by the hSCRO Committee may be reviewed using the expedited review process unless the protocol meets one of the above exception criteria.

Procedure Number: 4B
Title: Other hSCRO Reviews and Approvals of Human Stem Cell Research
Date of Last Revision: 11/25/2024, 03/10/2025

Procedure:
This procedure provides guidance for the seeking changes or Amendment to protocols approved by the UCI Human Stem Cell Research Oversight Committee (hSCRO).

I. Submission of Amendment Requests

Researchers seeking hSCRO approval for protocol amendments complete a hSCRO Protocol Amendment Request.

A. A separate amendment submission will not be required to add new cell lines and revisions may be submitted at the time of renewal review if:
    1. the protocol includes continuous collection of source materials and generation of stem cells, and the source material used to create new lines has been collected at UCI using an active UCI IRB-approved Consent, or
    2. added of cell lines are obtained from source materials that have previously been verified by UCI hSCRO. This includes standard fluorescent reporter lines (such as GFP). *Note:* federally/state-funded cell repositories are considered already verified sources.

B. Upon receipt of an amendment request, the hSCRO Administrative Staff enters the submission into the hSCRO database and performs an administrative review to ensure that the submission is complete.

C. Required documentation for hSCRO review of minor and significant protocol amendments include:
    1. hSCRO Protocol Amendment Request
    2. Any new documents or any updated documents that were previously approved by the hSCRO, which includes all the new changes
    3. Lead Researcher's Assurance statement completed by the LR (if the amendment request includes a change in LR) in the hSCRO database.
    4. Any other documents that may be required to assist with hSCRO review.

Note: For a complete list of documents provided to hSCRO members at the convened hSCRO Meeting, see section 3A II. Full Committee Research – “Before the hSCRO Meeting”.

D. If a submission is incomplete, the hSCRO Administrative Staff contacts the LR and aids with submission requirements.

E. Once an Amendment request is approved, the Amendment is appended to the protocol and given the same expiration of approval date as the study.
    1. If a Renewal Application was also reviewed at the time of Full Committee Amendment Request, the assigned approval period starts on the day of approval and ends one year from the day of approval minus one day (365 days - 1 day). For example, if the hSCRO approves the research on April 12, 2011, for one year, the approval period is April 12, 2011 – April 11, 2012.

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

A. The hSCRO Committee 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 Amendments that include minor changes are reviewed weekly by the hSCRO Chair. Examples of minor changes to a protocol include, but are not limited to, the following:
   1. 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.
   2. Removal of research procedures that do not affect the assessment above.

C. When unsure about whether the proposed changes may be considered minor, the hSCRO Administrative Staff consults with an hSCRO Chair to determine the appropriate level of review.

   a. Review Amendment Requests that involve administrative changes to the Research
   b. The hSCRO Committee may use the administrative review procedure to review administrative changes in previously approved research during the period (of one year or less) for which approval is authorized.
   c. Protocol Amendments that include administrative changes are reviewed weekly by the hSCRO Administrative Staff.
   d. Administrative Amendments are limited to the following:
      i. Addition and/or deletion of study team members when those members being added and/or deleted are not the Lead Research or Co-researchers
      ii. Administrative changes to the approved documents (e.g., correction of typographical error)
      iii. Location changes or updates
      iv. Deletions of cell lines
      v. Additions of registered cell lines or materials that have been previously approved by UCI hSCRO.
      vi. Additions of cell lines obtained from source materials that have previously been verified by UCI hSCRO including standard fluorescent reporter lines (such as GFP). *Note: federally/state-funded cell repositories are considered already verified sources.*

III. Review Process for Amendment Requests that Require Full Committee Review

A. Amendments that involve significant changes to the research require review by the Full Committee at a convened meeting. The hSCRO Chair can also refer an expedited Amendment request to the Full Committee for further evaluation.

B. Amendment requests that require Full Committee review are evaluated at a scheduled convened hSCRO meeting, which occur once a month. Amendment 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 that have not been previously approved by the UCI hSCRO.
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.

IV. Administrative Protocol Preparation Procedures

Upon receipt of an Amendment Request, the hSCRO Administrative Staff screen 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 Amendment request is added to the hSCRO meeting agenda on a first come, first serve basis.
B. Following the administrative review, the hSCRO Administrative Staff assigns one reviewer to each Amendment request.
C. If necessary, more than one reviewer may be assigned to Amendments 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 if warranted.
F. When appropriate, the hSCRO Administrative Staff make an effort to assign the same reviewer to the Amendment request as the protocol's previous review. If that reviewer is not available, the hSCRO Administrative Staff selects another reviewer based upon their type of expertise.
G. When necessary, the hSCRO staff consults with the hSCRO Chair regarding review assignments.

Procedure Number: 4C
Title: Other hSCRO Reviews and Approvals of Human Stem Cell Research
Date of Last Revision: 11/25/2024, 03/10/2025

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. A Closing Report is submitted electronically by the LR via the hSCRO database.

B. Upon submission, the hSCRO Administrative Staff reviews the closing report and all attachments, checks the report for accuracy and completeness and arranges for hSCRO Chair review to verify that the protocol can be closed.

C. The official retention period for UCI's hSCRO records begins on the date a closing report is submitted to the hSCRO Committee by the LR or 30 days after protocol expiration, whichever comes first.

Policy Number: 5
Title: Review of Non-Compliance
Date of Last Revision: 11/25/2024, 03/10/2025

Review and Oversight Policy:
It is the policy of the UC Irvine (UCI) hSCRO to uphold its role in assuring prompt reporting of any serious or Renewal non-compliance with CA Health and Safety Code Sections 125291.10 - 125291.85 and California Embryonic Stem Cell Guidelines, CA Health, and Safety Code Sections 125118 - 125119.5 or the requirements or determinations of the hSCRO.

I. Definitions of Terms:

A. **Non-Compliance:** Failure to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects, embryonic, fetal, or any research activity under the purview of hSCRO as it relates to the ethical procurement of materials, requirements of the approved protocol, and/or with the requirements or determinations of the hSCRO Committee.

B. **Serious Non-Compliance:** Failure to comply with applicable laws, regulations, or institutional policies pertaining to research requiring hSCRO review and/or with the requirements or determinations of the hSCRO Committee that has a significant adverse impact either on the rights or welfare of research participants (if applicable) or on the integrity of the data.

C. **Continuing Non-Compliance:** A pattern of noncompliance that indicates an inability or unwillingness to comply with applicable laws, regulations, or institutional policies pertaining to the protection of research participants (if applicable) and/or with the requirements or determinations of the hSCRO Committee.

F. **Research Misconduct:** Defined by federal law and University policy as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

1. Fabrication is making up data or results and recording or reporting them.
2. Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research records.
3. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

Improper practices that are not defined as research misconduct may be considered misconduct under other University policies including, but not limited to, conflict of interest, intellectual property, biosafety, use of human and animal subjects, financial management, use of university facilities, outside professional activities, employee relations and faculty-student relations.

Disputes related to research but that do not involve research misconduct or other misconduct should be resolved within the appropriate research group, center, or department. Such disputes might relate to authorship, attribution of credit, confidentiality, access to or interpretations of data, simple negligence, differences of opinion, or honest error.

II. Goals of the hSCRO Committee, in general, in investigating and managing issues of potential noncompliance include:

A. Assuring protection of human participants as it relates to ethical procurement of materials;
B. Developing action plans to prevent reoccurrence, and promote future compliance;
C. Educating research staff to assure the understanding of applicable guidelines and regulations, and UCI hSCRO Policy.

III. Review Procedures and Possible Actions

A. All reports of alleged non-compliance or inappropriate involvement of humans in research that involves activities under hSCRO purview are investigated. Such reports may come from any source such as an hSCRO Committee Member, an Investigator, institutional personnel, other institutional Committees, UCI Health Affairs Compliance Officer, the media, anonymous sources, or the public.

B. The hSCRO Chair reviews the potential noncompliance at a Subcommittee to assess whether:
    1. There is no issue of noncompliance
    2. There is noncompliance which is neither Serious nor Continuing noncompliance;
    3. There is Serious or Continuing noncompliance;
    4. There is insufficient information to make a determination.

C. If the hSCRO Chair reviews the noncompliance and determines the information to be Serious or Continuing, the hSCRO Chair forwards the noncompliance issue to convened hSCRO Committee for further review and determination.

D. If the hSCRO Full Committee confirms the issue constitutes Serious or Continuing non-compliance, the Committee may require the following:
    1. Require amendment to existing protocol to ensure compliance!
    2. Require a corrective action plan from the LR
    3. Suspension of the research
    4. Termination of the research
    5. Dismiss the allegation

E. In addition, the hSCRO Committee may consider additional actions (optional):
    1. Monitoring of the research, which may include:
        a. Modify the Renewal review cycle;
        b. Request additional LR and research personnel education focused on hSCRO from available sources (e.g., CITI, CIRM, etc.)

IV. Reporting Serious or Continuing Noncompliance

A. Serious and / or continuing non-compliance involving studies using embryonic stem cells will be reported to the Vice Chancellor for Research.
    1. The report will be included in the annual report submitted to California Department of Public health (CDPH).

B. Instances that may meet the definition of research/scientific misconduct will be initially reported to the Research Integrity Officer at 949-824-5796.

1. Attempts to unduly influence an hSCRO Committee Member or hSCRO staff may be considered research misconduct.
2. In addition, the Whistleblower Office may be an appropriate reporting agency.

Policy Number: 6
Title: Program Records Maintenance and Retention
Date of Last Revision: 11/25/24, 03/10/2025

Review and Oversight Policy:
The hSCRO Administrative Staff 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.

B. The final version of the hSCRO minutes is maintained electronically. The Institutional Official has access to all final version of the minutes in UCI's electronic hSCRO Database.

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. hSCRO Application;
   2. Consent Documents if applicable;
   3. Documentation regarding provenance of cell lines.

B. Renewal Review – Records of Renewal review activities including but not limited to:
   1. Renewal Application;
   2. Current Consent Forms if applicable.

C. All correspondence (reviews, letters, emails) between hSCRO Staff and researchers can be found within UCI's electronic hSCRO Database.

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 Office of Research keeps and maintains hSCRO protocol records for at least five years after completion of the research for consistency with UCOP policy.

C. Administrative records (e.g., minutes, member roster, etc.) are maintained indefinitely.

Policy Number: 7
Title: Funding for Human Embryonic Stem Cell Research
Date of Last Revision: 11/25/2024

Review and Oversight 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 lines.

Policy Number: 8
Title: Provenance Policy (Table)
Date of Last Revision: 11/25/2024

Proposed Material	Information, Examples, etc.	Provenance Documents Required
Registered Pluripotent Cell Lines	• NIH Registered • CIRM Registered • UK Stem Cell Bank • UK Human Fertilization & Embryology Authority • Canadian National Stem Cell Oversight Committee • Japanese Guidelines for Derivation & Utilization of Human Embryonic Stem Cells	Appropriate registry name and registry number for each line. Some lines may require approval documentation from the registry.
Non-Registered Embryonic Pluripotent Cell Lines	Cell lines provided by a company, institution, or collaborator that do not appear on one of the above registration lists	1. A sample Consent Document 2. IRB (or equivalent) Approval Letter appropriate to the Consent document
Induced Pluripotent Cells (iPSC)	Source Material: • **See Fresh Somatic Cells** • **See Archived Somatic Cells**	Please provide the appropriate documentation based on the source material.
Fresh Somatic Cells for the purpose of generating: a) induced or re-programmed pluripotent cells, or b) neural stem cells (NSC) that will be used for in vivo transplantation	Usually in the form of tissue (e.g., punch biopsy, foreskin, residual tissue from surgical procedure, etc.)	**Provenance involves a non-UCI IRB:** • A sample Consent Document • IRB (or equivalent) Approval Letter • *In some instances*, a statement from the providing company or institution indicating specimens are de-identified, no access to the key code will be granted, and appropriate IRB (or equivalent) oversight was in place at the time of donation is acceptable. **Provenance involves the UCI IRB:** • A sample Consent Document (See Section III) • IRB Approval Letter (if available).
Archived Somatic Cells for the purpose of generating: a) induced or re-programmed pluripotent cells, or b) NSC that can be used for in vivo transplantation	Usually obtained from a tissue bank	Please provide written acknowledgement from provider (i.e., Tissue bank, Institution, etc.,) indicating specimens are de-identified, and you will not receive access to the key code under any circumstance.
Fetal Tissue-derived multipotent stem cells	Usually obtained from a tissue bank or academic institution	See **Fresh Somatic Cells**
Fetal Tissue	Aborted pregnancy tissues, pathology samples	Provide the following statements as outlined in Code of California Regulations title 17 § 100085: Use of Fetal Tissue. • Statement signed by woman donating the material (can be in the form of a sample Informed Consent document) • Statement signed by attending physician (can be in the form of a sample Informed Consent document) • Statement related to use of Human Fetal Tissue signed by Principal Investigator

Embryos/Oocytes		1. Consent Document (either sample IRB-approved Consent or Consent document proposed for use) 2. In both instances (Embryos and Oocytes) IRB Approval is required

Policy Number: 9
Title: Use of Human Embryonic Stem Cells (HUES) by CIRM Grantees
Date of Last Revision: 11/25/2024

Policy:
The use of Human Embryonic Stem Cell (HUES)[1] Lines is allowed as defined below. The hSCRO Committee will review new and amendment submissions to help enforce the following.

I. CIRM Funded Research

A. The HUES lines are acceptable for use in CIRM funded research so long as the lines are used for "legitimate" non-commercial research purposes as defined in the Harvard University Material Transfer Agreement (MTA).

II. NIH Funded Research

A. Federal funds may only be used for embryonic development of endoderm with a focus on pancreatic formation when utilizing the HUES Cell lines.

[1] Harvard's naming convention for the hESC lines it has developed is to identify the lines with the acronym HUES, which stands for Human Embryonic Stem Cells, and then to number the lines sequentially (HUES 1-28).

Policy Number: 10
Title: Definitions of Terms and References
Date of Last Revision: 11/25/2024

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. **Continuing Non-Compliance:** A pattern of noncompliance that indicates an inability or unwillingness to comply with applicable laws, regulations, or institutional policies pertaining to human stem cell research oversight and/or with the requirements or determinations of the hSCRO Committee.
5. **Human Stem Cell Research Oversight (hSCRO) Committee:** University appointed committee providing oversight of all issues related to the procurement and experimental use of human pluripotent stem cells and stem cell lines and to facilitate education of investigators involved in human stem cell research.
6. **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).
7. **Fetal Stem Cells**: Stem cells taken from fetal tissue. Federal regulations treat fetal stem cells as adult stem cells.
8. **Fetus**: A developing human from usually two months after conception to birth.
9. **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.
10. **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.
11. **Human Subject:** Human subject means a living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
12. **Human Subjects Research**: Any research or clinical investigation that involves human subjects.
13. **Induced Pluripotent Stem Cells (iPSC):** Pluripotent cells that are self-replicating derived from somatic cells via genetic reprogramming and are capable of developing into cells and tissues of three primary germ layers.
14. **Institutional Animal Care and Use Committee (IACUC)**: Committee charged with reviewing the use of animals in research, testing, teaching, and related activities.
15. **Institutional Biosafety Committee (IBC)**: Committee charged with reviewing research involving use of recombinant DNA molecules, infectious agents and select agents.
16. **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.
17. **In Vitro**: Literally “in glass”; in a laboratory dish or test tube; an artificial environment.
18. **In Vitro Fertilization (IVF)**: An assisted reproduction technique in which fertilization is accomplished outside the body.

19. **Non-Compliance:** Failure to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects, embryonic, fetal, or any research activity under the purview of hSCRO as it relates to the ethical procurement of materials, requirements of the approved protocol, and/or with the requirements or determinations of the hSCRO Committee.
20. **Non-Registered Human Embryonic Stem Cell Lines**: hESC lines excluded from the NIH registry, California Institute of Regenerative Medicine (CIRM) registry or other recognized lists of acceptably derived lines.
21. **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.
22. **Pluripotent Stem Cell**: A single stem cell that has the capability of developing cells of all germ layers (endoderm, ectoderm, and mesoderm).
23. **Registered Human Embryonic Stem Cell Lines**: hESC lines included on the National Institutes of Health (NIH) Human Embryonic Stem Cell Registry, or another acceptable registry such as the CIRM Registry.
24. **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.
25. **Research Misconduct:** Defined by federal law and University policy as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.
26. **Serious Non-Compliance:** Failure to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects, embryonic, fetal, or any research activity under the purview of hSCRO as it relates to the ethical procurement of materials, requirements of the approved protocol, and/or with the requirements or determinations of the hSCRO Committee that has a significant adverse impact on the integrity of the research.
27. **Somatic Cell**: Any cell of a plant or animal other than germ cell or germ cell precursor.
28. **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.
29. **Stem Cells**: Cells with the ability to divide for indefinite periods in culture and to give rise to specialized cells.
30. **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. **California Stem Cell Research and Cures Bond Act of 2004**, CA Health and Safety Code Sections 125291.10 - 125291.85
2. **California Law Chapter 483**, approved by Governor and filed with Secretary of State September 26, 2006
3. **California Embryonic Stem Cell Guidelines**, CA Health and Safety Code Sections 125118 - 125119.5
4. **California Policy on Human Stem Cell Research**, CA Health and Safety Code Sections 125300 – 125320
5. **California Informed Consent Requirements for Oocyte Production**, CA Health and Safety Code Sections 125330 - 125355
6. **California Institute for Regenerative Medicine Medical and Ethical Standards Regulations**, Title 17 CA Code of Regulations, Sections 100010-100110
7. **California Health and Safety Code**, Sections 24170 - 24197.5, and other applicable state statues pertaining to the protection of human subjects in research
8. **Department of Health and Human Services (DHHS) Regulations**, Policy for the Protection of Human Research Subjects, 45 CFR Part 46, Subparts A-D
9. **DHHS, Food and Drug Administration**, 21 CFR Part 50 Human Subjects Protections and 21 CFR Part 56 Institutional Review Boards
10. **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
11. **International Society for Stem Cell Research (ISSCR)** Guidelines for Stem Cell Research and Clinical Translation
12. **National Bioethics Advisory Commission**, Ethical Issues in Human Stem Cell Research Report, 1999
13. **National Academies of Science-Institute of Medicine**, Guidelines for Human Embryonic Stem Cell Research, National Academies Press: 2005
14. **NIH Grants Policy Statement** Section 4.1.14 Human Fetal Tissue Research
15. **University of California, Irvine Research Policy**, Section 484-1: Review of Human Stem Cell Activities
16. **University of California, Irvine Research Policy**, Section 485-1: Protection of Human Subjects in Research