



TECH UNIVERSITY HEALTH SCIENCES CENTER

Operating Policy and Procedure

HSC OP: 73.19, **Human Pluripotent Stem Cell Research**

PURPOSE: The purpose of this HSC OP is to detail the process available for formal review and approval of research activities that involve the use of human embryonic stem cells (hESC) or human pluripotent stem cells (hPSC) conducted by TTUHSC faculty. The policy includes procedures related to the function of an Embryonic Stem Cell Research Oversight (ESCRO) Committee. The criteria for projects to be considered by the Committee are specified herein as are the composition and functions of the ESCRO.

REVIEW: This HSC OP will be reviewed by June 1 of each even-numbered year (ENY) by the Assistant Vice President for Research Integrity and the Chairperson of the ESCRO, with recommendations for revision forwarded to the Senior Vice President for Research (SVPR).

POLICY/PROCEDURE:

1. Introduction

Texas Tech University Health Sciences Center (TTUHSC) is committed to the highest ethical standards and responsible use of human embryonic stem cells (hESC) or human Pluripotent Stem Cells (hPSC) in research. As part of that commitment, TTUHSC has established an Embryonic Stem Cell Research Oversight (ESCRO) Committee that provides local oversight of ethical issues related to deviation and research of these types of cells in experiments expected to yield gametes or with the intent to integrate these cells in the central nervous system of animals. This oversight is completed through review and approval of all proposed uses of human embryonic stem cells prior to their use in research conducted by TTUHSC Principal Investigators. The committee's review will be conducted in accordance with general principles expressed in the National Academies' [Guidelines for Human Embryonic Stem Cell Research](#) and the [NIH Guidelines on Human Stem Cell Research](#) that became effective July 7, 2009.

2. Applicability

This policy applies to all permissible research involving human embryonic stem cells and human pluripotent stem cells (defined below in Sections 6 and 7) that is conducted by TTUHSC Principal Investigators (as defined in TTUHSC OP 73.08). The policy and requirement for ESCRO review applies regardless of the source of funding for the research and applicability of federal regulations. The information in this HSC OP is not intended to cover all applicable parts of the federal regulations and state laws. TTUHSC Principal Investigators are expected to be familiar with and to comply with regulations and laws related to research with human stem cells. If information in this policy conflicts with federal regulations or state laws, those regulations/laws supersede this policy.

3. Definitions

Adult stem cell/somatic stem cell — Undifferentiated multipotent cells found throughout the body that have the capacity to self-renew and to differentiate into cell types within a particular organ.

Blastocyst — A preimplantation embryo of approximately 150 cells; consisting of a sphere made up of an outer layer of cells (trophectoderm), a fluid-filled cavity (blastocoel), and a cluster of cells on the interior (inner cell mass).

Chimera — An organism composed of cells derived from at least two genetically different cell types. The cells could be from the same or separate species.

Embryo — In humans, the developing organism from the time of fertilization until the end of the eighth week of gestation, when it becomes known as a fetus.

Embryonic stem (ES) cells — Pluripotent cells that are derived from early stage embryos, up to and including the blastocyst stage, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers.

Fertilization — The process whereby male and female gametes unite to form a zygote (fertilized egg).

Gamete — A mature male or female germ cell, that is, sperm or oocyte, respectively.

Human embryonic stem (hES) cell — A type of stem cell derived from a human embryo.

Human pluripotent stem (hPS) cell — Pluripotent stem cells derived either from a human embryo or from a somatic cell that has been reprogrammed into an induced pluripotent stem cell.

Induced pluripotent stem (iPS) cell — Somatic (embryonic, fetal, or adult) cells reprogrammed to enter an embryonic stem cell-like state by being forced to express factors important for maintaining the “stemness” of embryonic stem cells.

Institutional Animal Care and Use Committee (IACUC) — TTUHSC Research compliance committee charged with reviewing the use of animals in research, testing, teaching and related activities and compliance with federal regulations.

Institutional Biosafety Committee (IBC) – TTUHSC Research compliance committee charged with reviewing research that involves biological, chemical infectious, and select agents and dual use research of concern.

Institutional Review Board (IRB) – TTUHSC Research compliance committee charged with reviewing proposed research involving human subjects to ensure the protection of those subjects and compliance with federal regulations.

In vitro — Literally, “in glass,” in a laboratory dish or test tube; in an artificial environment.

In vitro fertilization (IVF) — An assisted reproductive technique in which fertilization is accomplished outside the body.

In vivo — In the living subject; in a natural environment.

Multipotent stem cell — Stem cells that can differentiate into multiple but limited cell types; for example, hematopoietic stem cells in the bone marrow that can give rise to several different blood cell types.

Non-registered human embryonic stem cell lines — hESC lines excluded from the National Institutes of Health (NIH) registry because they do not meet the current NIH Guidelines.

Nuclear transfer (NT) — Replacing the nucleus of one cell with the nucleus of another cell.

Oocyte — Developing egg; usually a large and immobile cell.

Pluripotent stem cell — A single stem cell that has the capability of developing cells of all germ layers (endoderm, ectoderm, and mesoderm) but not the trophoblast (the outermost cells of the blastocyst that become part of the placenta).

Primitive streak — The initial band of cells from which the embryo begins to develop. The primitive streak establishes and reveals the embryo’s head-tail and left-right orientations.

Provenance — The place or source of origin.

Recombinant DNA Biosafety Committee (RDBC) — TTUHSC Research compliance committee charged with reviewing research that involves recombinant or synthetic DNA molecules and compliance with federal regulations.

Registered human embryonic stem cell lines — hESC lines currently included on the NIH Human Embryonic Stem Cell Registry.

Reproductive Cloning — The process of using somatic cell nuclear transfer to produce a normal, fully-grown organism genetically identical to the organism that donated the somatic cell nucleus.

Somatic cells — Any cell of a plant or animal other than a germ cell or germ cell precursor.

Somatic cell nuclear transfer (SCNT) — The transfer of a cell nucleus from a somatic cell into an egg (oocyte) whose nucleus has been removed. The newly nucleated egg is then stimulated, prompting it to take on the genetic and molecular characteristics of a fertilized ovum.

Stem cell — A cell that can renew itself and give rise to a more committed progenitor.

Totipotent stem cell — A stem cell that can differentiate into all differentiated cells in an organism, including the three germ layers (endoderm, mesoderm, and ectoderm) and the trophoblast (the outermost cells of the blastocyst that become part of the placenta).

4. Institutional Oversight

The Senior Vice President for Research (SVPR) has responsibility for the TTUHSC Human Pluripotent Stem Cell Program. The SVPR, in conjunction with the Assistant Vice President for Research Integrity, oversees institutional compliance with applicable federal regulations, state laws and institutional policies and procedures related to human stem cell activities. The SVPR has created the Embryonic Stem Cell Research Oversight (ESCRO) Committee and appoints members to the ESCRO. The SVPR has the authority to suspend or terminate research involving human stem cell protocols, subject to the overriding responsibilities of the IRB and IACUC.

5. Charge to the Embryonic Stem Cell Research Oversight (ESCRO) Committee

TTUHSC has established an Embryonic Stem Cell Research Oversight (ESCRO) Committee. The ESCRO is charged with the following tasks:

- a. Review of all research conducted by TTUHSC Principal Investigators that involves:
 - i. the use of hESC lines or their derivatives;
 - ii. the introduction of hPSCs, or their derivatives, obtained from a non-embryonic source, into non-human animals (excluding primates) at any embryonic, fetal, or postnatal stage, if an expected effect is that human cells will be integrated into the central nervous system, testes, or ovaries of the animal; or
 - iii. the storage or disposition of human embryos or gametes obtained for the purposes of stem cell research.
- b. Ensure that the provenance of hES cells is documented. This includes confirming evidence that the procurement process was approved by an IRB to ensure adherence to the basic ethical and legal principles of informed consent and protection of confidentiality.
- c. Maintain a registry of hES cell lines in use, a list of investigators working in this field, and brief descriptive information on the types of hES cell research in which the investigators are engaged, as well as a method of tracking projects that have been reviewed by the ESCRO.

Research falling within the ESCRO's scope of review can only be initiated after an application has been submitted to, reviewed by, and approved by the ESCRO. Details of the application and review process can be found below in Section 9.

6. Types of hESC research that may be permissible following ESCRO approval:

- a. Research involving all established hES cell lines listed on the National Institutes of Health (NIH) Human Embryonic Stem Cell Research Registry
[NIH Human Embryonic Stem Cell Registry](#)
- b. Research with established hES cell lines that are not currently listed on the NIH Registry.
- c. Research with human pluripotent stem (hPS) cells designed to yield gametes or integrate cells into the CNS of animals.
- d. New hES cell lines derived from the following sources:
 - i. blastocysts made for reproductive purposes and later obtained for research from in vitro;
 - ii. fertilization (IVF) clinics, with consent of donor (refer to the [TTUHSC Human Research Protection Program Manual](#) for additional information).

Note that additional review by other TTUHSC Research Committees may also be required before initiation of an ESCRO-approved protocol. This may include the IRB, IACUC, IBC, RDBC, and/or Conflict of Interest in Research Committee (COIRC).

7. Prohibited research involving Human Embryonic Stem Cells

- a. Derivation of new hES cell lines by nuclear transfer [Note: this research is currently prohibited by the NIH].
- b. Research involving in vitro culture of any intact human embryo, regardless of the derivation method, for longer than 14 days or beyond formation of the primitive streak.
- c. Research in which hES cells are introduced into non-human primate blastocysts or in which any embryonic stem cells are introduced into human blastocysts.
- d. Research that involves breeding of any animal into which hES cells have been introduced (at any stage of development).
- e. Blastocysts made specifically for research using IVF [Note: this research is currently prohibited by the NIH].
- f. Somatic cell nuclear transfer (NT) into oocytes without intent to create a hES cell line.
- g. Reproductive cloning of human beings; this prohibition specifically includes any use of SCNT to produce a human being.
- h. The sale of hES cells. This prohibition does not limit TTUHSC from paying or charging the reasonable costs associated with the transfer of cell lines from one location to another, including license fees justified by such costs.

8. ESCRO Membership and Meeting process

- a. The ESCRO shall consist of at least six voting members to include:
 - i. A community member who is not affiliated with TTUHSC as a current or former employee

- ii. At least two TTUHSC faculty members familiar with hESC research
 - iii. One faculty member, preferably a clinician, from OB/GYN
 - iv. One faculty member with a knowledge of ethical, legal, and social issues involved in biomedical research
 - v. At least one Research Compliance Committee chairperson (IRB, IACUC, IBC, RDBC)
 - vi. Non-voting, ex-officio members of the ESCRO will include the Assistant Vice President for Research Integrity and a representative from the TTU System Office of General Counsel.
- b. Members will be appointed by the SVPR to a two-year term and may be reappointed to serve additional years. The Chair of the ESCRO will be appointed to a two-year term from the membership by the Senior Vice President for Research.
 - c. The ESCRO will convene meetings at least annually and more often if needed depending on the quantity of submissions requiring review by the full Committee. An ESCRO Coordinator will be assigned by the Assistant Vice President for Research Integrity, who will be responsible for scheduling and coordinating all meetings. The Committee may convene meetings via conference call and/or conduct project reviews and voting by email to facilitate efficiency.
 - d. The ESCRO can conduct business if at least half of the voting members are present. A majority of those voting must agree on the outcome.
 - e. Prior to each convened meeting of the ESCRO, members will be given materials sufficient for conducting the business of the meeting. Materials may be provided to members via secure email prior to the meeting.
 - f. Written minutes of each convened meeting will be in sufficient detail to document attendance and presence of a quorum; actions taken by the Committee and the vote on these actions including number of members voting for, against, or abstaining. Meeting minutes and materials shall be maintained for a minimum of 3 years after the meeting date. The ESCRO Coordinator will be present at each meeting and will be responsible for taking minutes and maintaining records.
 - g. The ESCRO and any sub-committees established under this policy shall be considered “medical committees” as defined under Texas Health and Safety code 161.031 and/or other applicable state and federal statutes. All documents generated by, submitted to, or used for the purposes of fulfilling ESCRO duties are confidential and privileged as “medical committee documents.”

9. ESCRO Review Process

TTUHSC Principal Investigators wishing to conduct research with hESC, hPSC, or embryos should complete an initial application (**Attachment A** to this policy) and submit it via email to the ESCRO Coordinator (ttuhscresearch@ttuhsc.edu). The coordinator will review the application for completeness before forwarding the application for Committee review.

- a. **Designated/Expedited review:** The ESCRO Chairperson or designee may review and approve applications protocols that meet the following criteria:
- i. Research projects only involve in vitro experiments with federally approved hES cell lines (those found on the current [NIH Human Embryonic Stem Cell Registry](#)) human iPS cells or hPS cells.
 - ii. Research projects only involve in vitro experiments with derived and coded hES cell lines. Documentation must include provenance of all hES cell lines, evidence of IRB approval of the procurement process and of adherence to basic ethical and legal principles of procurement. In the case of hES cell lines being imported from another institution, documentation that these criteria were met at the time of derivation will suffice.
 - iii. Minor changes or additions were made, as requested by hPSCC members, to a previously reviewed ESCRO application.
 - iv. Minor amendments that are requested to a previously approved registration document that do not change the design or scope of the project.
 - v. Projects that have been reviewed by the designated/expedited procedure will be included on the meeting minutes for the next convened meeting of the ESCRO for review by all members.
- b. **Review at convened meetings.** Full ESCRO review and approval is required for protocols that meet the following criteria:
- i. Research involving the introduction of any human iPS cells or hPS cells, including hES cells, into non-human animals; consideration will be given to the contribution of human cells to the resulting chimeras.
 - ii. Research in which personally identifiable information about the donors is linked to the hES cell line. An experienced IRB member may be invited as a non-voting consultant to the meeting to assist with these reviews.
 - iii. Research using non-federally approved hES cell lines.
 - iv. Derivation of new hES cell lines from donated blastocysts from in vitro fertilized oocytes.
 - v. Research involving the use of hPS cells expected to yield gametes or with the intent or potential to integrate these cells into the CNS, testes or ovaries of animals. An experienced IACUC member may be invited as a non-voting consultant to the meeting to assist with these types of reviews.
- c. **Considerations during review.** Before making determinations regarding the approvability of proposed research, the ESCRO will consider the following:
- i. Conformity with all applicable state and federal laws, regulations, and guidelines and all applicable institutional policies;
 - ii. The anticipated risks, benefits and significance of the knowledge to be gained, and,
 - iii. The qualifications and training of the investigator and key personnel to conduct the research.
 - iv. Consideration of other TTUHSC committees (IRB, IACUC, IBC, RDBC, COIRC) which may require additional review of the project before it is initiated.
 - v. Whether ongoing ESCRO review of the project is required, and, if so, the review cycle and method of review (expedited or convened meeting) for those reviews.

- d. **Annual review of approved projects.** All projects approved by the ESCRO Committee will require at least an annual review. More frequent reviews may be required by the Committee if warranted. The annual review may be conducted by designated/expressed review or by the full Committee.
- e. **Authority of the ESCRO.** The ESCRO shall have the authority to review, approve, require modifications in, or deny approval of all research activities involving hES cells engaged in by TTUHSC Principal Investigators. The Committee shall also have the authority to require ongoing review of the status of each project at a specified time frame determined by the Committee. The ESCRO shall have the authority to observe or have a third party observe the conduct of any research activity subject to ESCRO oversight and has the authority to request and review all records associated with the conduct of the research.

10. **Breach of Policy**

Alleged deviations from this policy must be reported by anyone who becomes aware of the violation in accordance with the TTUHSC Institutional Compliance Plan, [HSC OP 52.01](#). Alleged deviations or violations may be reported to the Chairperson of the ESCRO, the Assistant Vice President for Research Integrity, the Research Compliance Officer, or through the system-wide EthicsPoint hotline number (1-866-294-9352). Allegations of non-compliance will be investigated by the ESCRO with assistance from any compliance authorities at TTUHSC. Allegations may be shared as appropriate with other institutional committees/personnel with shared jurisdiction (IRB, IACUC, IBC, Research Integrity Officer, etc.). Confirmed breaches of this policy, state laws, or federal regulations will be reported to the SVPR and other institutional offices or external funding sources. The ESCRO may also recommend additional sanctions to the SVPR. These sanctions may include, but are not limited to:

- A letter of reprimand to the employee with a copy to the employee's manager, chairperson, dean, and personnel file;
- Temporary or permanent suspension of the individual to submit new applications for external funding and/or research involving human subjects or animals;
- Temporary or permanent suspension of research privileges;
- Other discipline up to and including dismissal or termination.

The SVPR shall make the final determination regarding which sanctions, if any, shall be imposed on the investigator or research personnel.

11. **Amendments and Termination**

TTUHSC reserves the right to modify, amend or terminate this policy at any time. Nothing in this policy should be construed as a contract between TTUHSC and its employees or agents.