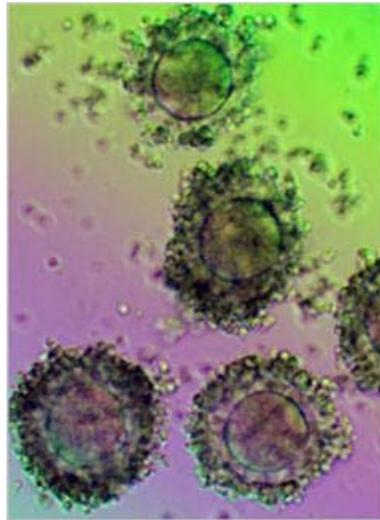


Human Stem Cell Compliance Tutorial



Stem Cell Research Oversight (SCRO) Committee

UConn

OFFICE OF THE VICE PRESIDENT FOR RESEARCH

There are five parts to this tutorial:

1. Role of the Stem Cell Research Oversight (SCRO) Committee in providing oversight of human embryonic stem cells (hESC) and human induced pluripotent stem cells (iPSC) research
2. Federal and State regulations
3. Responsibilities of the Principal Investigator (PI)
4. SCRO and Sponsored Program Services (SPS) Forms
5. Post-tutorial quiz

Additional information about SCRO policies can be found here: <http://research.uchc.edu/rcs/stem-cells/>

Terms and Acronyms Used in this Tutorial

human embryonic stem cells (hESCs): hESCs are pluripotent stem 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, stem cells are not themselves embryos.

human induced pluripotent stem cells (iPSCs): iPSCs are human pluripotent stem cells derived from non-embryonic sources through reverting somatic cells into an earlier stage of development.

hESC lines: A population of hESC that originated from a single hES cell.

hESC derivatives: Any partially differentiated cells obtained from hESC; DNA, RNA, proteins, or other products secreted or extracted from human embryonic stem cells.

Terms and Acronyms Continued

Stem Cell Research Oversight Committee (SCRO): Oversees all hESC research and some categories of iPSC research at UConn/UConn Health. SCRO review does not duplicate or replace any reviews by IRB, IACUC or IBC that are currently mandated by State and Federal regulations, or institutional policies.

UConn Storrs/UConn Health link: <http://research.uhc.edu/rcs/stem-cells/>

Sponsored Programs Services (SPS): Administers grants and contracts on behalf of the University, and reviews and negotiates agreements for obtaining hESC and iPSC lines from other institutions.

UConn Health link: <http://research.uhc.edu/sps-proposals/>,
<http://research.uhc.edu/sps-awards/>

UConn Storrs link: <http://research.uconn.edu/sps-proposals/>,
<http://research.uconn.edu/sps-awards/>

Terms and Acronyms Continued

Institutional Review Board (IRB): Reviews hESC and iPSC research protocols that involve the use of human material with donor identifiable information and oversees donations of cells, gametes, and embryos to UConn researchers.

UConn Health link: <http://research.uchc.edu/rcs/hspp/irb/>

UConn Storrs link: <http://research.uconn.edu/irb/>

Institutional Animal Care and Use Committee (IACUC): provides oversight of all research using animals. Review by the IACUC is required for Stem Cell Protocols that implant human stem cells or progenitors into any nonhuman animal at any stage of the animal's development or harvest any animal cells or gametes for use in human stem cell research. Each stem cell project that uses animals requires specific IACUC approval.

UConn Health link: <http://research.uchc.edu/animal/iacuc/>

UConn Storrs link: <http://research.uconn.edu/iacuc/>

Terms and Acronyms Continued

Institutional Biosafety Committee (IBC):

- At Storrs, this committee reviews research and teaching activities that involve biological materials including but not limited to: recombinant or synthetic nucleic acid molecules (rsNA), biological agents and toxins, bacteria and their phages and plasmids, viruses, fungi, mycoplasmas, prions, and parasites; human and non-human primate tissues, body fluids, blood, blood byproducts, and cell lines, animal remains and insects that may harbor zoonotic pathogens.

UConn Storrs link: <http://research.uconn.edu/ibc/>

- At UConn Health, the IBC reviews research involving recombinant or synthetic nucleic acid molecules (rsNA).

UConn Health link: <http://research.uchc.edu/rcs/ehs/biosafety/>

Role of the UConn Stem Cell Research Oversight (SCRO) Committee

- The SCRO Committee provides oversight of all ethical issues related to the derivation and research use of human embryonic stem cells and human induced pluripotent stem cells* at all schools, colleges, and research arms of the University of Connecticut/UConn Health regardless of the source of funding.
- The role of the SCRO Committee is to ensure that human embryonic stem cell (hESC) and human induced pluripotent stem cell (iPSC) research is well-justified and that inappropriate and/or unethical research is not conducted.
- The ethical mandate of the SCRO Committee is to ensure that appropriate respect is given to the value of human life.

*Specific types of human induced pluripotent stem cell use under the purview of the SCRO can be found on the slide titled “Areas of iPSC use where the SCRO has oversight”

Foundations of the SCRO Committee

- The review and approval of hESC research by a SCRO committee or its equivalent is required by the State of Connecticut.
- SCRO Committee review and approval of hESC research and some types of other pluripotent stem cell research is also required by the University of Connecticut's institutional policy.

Scope of SCRO Oversight and Review

- **SCRO** reviews all proposals funded by the State of Connecticut Regenerative Medicine Research Fund, including those not using hESC or iPSC lines.
- **SCRO** reviews all proposals to derive or use human embryonic stem cells.
- **SCRO** reviews induced pluripotent stem cell (iPSC) projects that transplant iPSCs or derivatives into prenatal animals or into the central nervous system of postnatal animals. It also reviews iPSC projects aimed at creating gametes.
- **SCRO** does not review derivation of new iPSC lines or *in vitro* iPSC research, unless funded by the State of Connecticut Regenerative Medicine Research Fund.
- Written **SCRO** approval is required before research within the scope of SCRO review may be conducted, and will be given only after documentation of other required approvals from the Institutional Biosafety Committee (IBC), Institutional Animal Care and Use Committee (IACUC), or Institutional Review Board (IRB) is received. IRB-approved consent forms may also be required.

Areas of hESC/iPSC use where the SCRO has oversight:

1. All research funded by the State of Connecticut Stem Cell Regenerative Medicine Research Fund (RMRF), including projects that do not use hESCs
2. All stem cell research using hESC lines and their derivatives
3. All stem cell research related to the creation and use of human embryos and gametes in hESC and iPSC research
4. in vivo research involving implantation of hESC and iPSC into prenatal animals or into the central nervous system of post-natal animals

Areas of iPSC use where the SCRO has oversight:

Activity	SCRO Committee iPSC Review
Any activity funded by the Regenerative Medicine Research Fund	Required
Derivation of new human iPS lines	Not required
in vitro research with no genesis of gametes or totipotent cells	Not required
in vitro research with genesis of totipotent cells, such as human gametes, embryos	Required
in vivo research involving implantation of human induced pluripotent stem cells into prenatal animals or into the central nervous system of post-natal animals	Required

Investigators with an approved SCRO protocol:

- Are authorized to use only the specified lines approved in their study.
- Must document procurement, culturing, storage, use, disposal, locations and user of hESCs in their possession.
- Should contact the SCRO before making any significant changes* including:
 - Change in Principal Investigator (PI) or other project personnel
 - Change in funding
 - Addition of human embryonic stem cell (hESC) lines to be used
 - Changes in the procurement of human embryos, gametes or somatic cells
 - Changes in experimental protocols in the use of hESC or derivatives, human gametes, or embryos; or changes in *in vivo* research involving implantation of human induced pluripotent stem cells (iPSCs) into prenatal animals or into the central nervous system of post-natal animals

*For questions, please contact the SCRO Office.

- Remember that any modifications in research that require Institutional Biosafety Committee (IBC), Institutional Animal Care and Use Committee (IACUC), or Institutional Review Board (IRB) approval must also be approved by the SCRO Committee.

The following research activities are prohibited:

- *In vitro* culture of intact human embryos for longer than 14 days or past the formation of the primitive streak, whichever occurs first.
- Introduction of hES cells into nonhuman primate blastocysts or any types of embryonic stem cells into human blastocysts
- Breeding of an animal into which hES cells have been introduced at any stage of development
- Implantation into any nonhuman animal, or human of any intact human embryo, or embryo-like entity created by nuclear transfer.

If any embryos are cultured *in vitro* past 14 days or the formation of the primitive streak, notify the SCRO Office and Research Compliance Services as soon as possible and follow standard disposal protocols immediately.

Federal Guidelines for hESC Research

In July 2009, the National Institutes of Health (NIH) adopted guidelines defining the eligibility of hESC lines for research with federal funding. These guidelines can be found at: <https://stemcells.nih.gov/policy/2009-guidelines.htm> Under the guidelines, hESC lines eligible for use with federal funding must meet the following conditions:

- Been derived from human embryos created for reproductive purposes that are no longer needed for this purpose;
- Donated by the individuals who sought reproductive treatment and gave voluntary written consent for their surplus embryos leftover from fertility treatment to be used for stem cell research;
- Documentation exists indicating that all options for future use of the surplus embryos were explained to the donors including donation for research, donation to another couple for reproductive use, storage of the embryos, and destruction of the surplus embryos.
- No payments, cash or in kind were offered for the donated embryos.
- The lines were reviewed and approved by the NIH Stem Cell Committee and placed on the NIH Human Embryonic Stem Cell Registry.

Restrictions on the Use of Federal Funds

Federal funds may be used **ONLY** for research using **eligible** hESC lines and their derivatives.

Eligible hESC lines are those which have been reviewed and placed on the NIH Human Embryonic Stem Cell Registry, found here:

https://grants.nih.gov/stem_cells/registry/current.htm

Ineligible hESC lines are those which have not been approved and placed on the NIH Human Embryonic Stem Cell Registry.

Further Information on Restrictions on the Use of Federal Funds

Investigators are responsible for reviewing the most current National Institutes of Health (NIH) guidelines which may be found at the following link: <https://stemcells.nih.gov/policy.htm>

State of Connecticut Legislation on hESC Research

- Connecticut is one of several states that funds hESC research, including on **ineligible** hESC lines (i.e., research for which federal funds may not be used), via the Regenerative Medicine Research Fund (RMRF), managed by Connecticut Innovations (CI). <http://ctinnovations.com/academia/regen/>
- Each Regenerative Medicine Research Fund (RMRF) awardee must complete and sign the Regenerative Medicine Research Fund Embryonic Stem Cell Research Verification Form which is to be filed with Connecticut Innovations.
- All hESC research conducted in the State of Connecticut must be reviewed and approved by a Stem Cell Research Oversight (SCRO) Committee that functions consistently with the National Academy of Sciences (NAS) Guidelines on human embryonic stem cell research as amended from time to time.

State of Connecticut Legislation on hESC Research (continued)

- Connecticut legislation does not allow payments to donors of human gametes and/or embryos for hESC research.
- A patient who donates embryos, gametes and/or embryonic stem cells for hESC research is required to provide a written consent for the donation under Connecticut law.
- Connecticut law indicates that no person shall knowingly engage in the cloning of an individual, implant human embryos created by nuclear transfer into a uterus, or facilitate human reproduction through clinical or other use of human embryos created by nuclear transfer.
- Derivation of hESC lines from embryos must occur before day 14 of embryo genesis or before gastrulation.

The Principal Investigator (PI) is required:

- to ensure all faculty, staff, post-doctoral scholars, students, visiting scholars, and other researchers involved in protocols working with hESC and iPSCs are properly trained and are following institutional, state, and federal regulations.
- to ensure that biosafety training and other trainings are completed as required.
- to ensure compliance with UConn federal and state policies, laws, regulations and guidelines.
- to submit the appropriate forms for review, continuation, amendments, or completion of SCRO protocols as required.
- to take measures taken to ensure security and tracking in lab.
- to ensure that all labs in which hESC is conducted comply at a minimum with BSL2 and blood-borne pathogen standards.

Related Responsibilities of the PI

- Complete this required SCRO Human Stem Cell Compliance Tutorial.
- Initiate SCRO Review and complete Sponsored Program Service (SPS) forms for all research projects that fall within the mandate of the SCRO Committee, and all proposals funded by the State of Connecticut Regenerative Medicine Research Fund.
- Initiate Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC) and Institutional Biosafety Committee (IBC) reviews as necessary.
- Complete a Material Transfer Agreement (MTA) for each hESC line requested.

To initiate SCRO review, provide the following documentation to the SCRO:

1. SCRO Initial Application (form found here: <http://research.uhc.edu/rcs/stem-cells/forms/>)
2. Grant application
3. Compliance tutorial certificates for the PI and other staff members
4. As applicable, approvals or evidence of applications to, the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC) and Institutional Biosafety Committee (IBC). IRB-approved consent forms may also be required.

SCRO Continuation and Completion Forms

- SCRO protocol approvals are valid for one year. Principal Investigators must renew their protocols each year in order to be compliant.
- At the time of re-approval, providing evidence of other *current* committee approvals, such as Institutional Biosafety Committee (IBC), Institutional Animal Care and Use Committee (IACUC), or Institutional Review Board (IRB) as appropriate, is required.
- Continuation, completion and amendment forms can be found here: <http://research.uchc.edu/rcs/stem-cells/forms/>

UConn's established policies for obtaining research materials

All hESC lines require a **Material Transfer Agreement (MTA)** or similar agreement in place between the provider and UConn before hESC lines or iPSC lines can be transferred to investigators.

1. Investigators requesting hESC lines from the UConn-Wesleyan Core should contact the Core to arrange for a Simple Letter of Agreement.
2. Investigators who wish to use hESC lines not obtained from the UConn-Wesleyan Core and who have received prior SCRO approval to use those cell lines should complete an MTA routing form and send it to Sponsored Program Services (SPS).

UConn's established policies for obtaining research materials (continued)

3. Sponsored Program Services (SPS) will review the providers agreement for transferring hESC lines to ensure compliance with UConn policy, negotiate necessary changes, sign the agreement on behalf of UConn, and return the signed agreement to the provider, with a copy to the investigator.
4. SPS will sign MTA agreements only after receipt of a copy of the SCRO conditional approval.
5. For hESC lines not obtained from the Core, investigators must forward a copy of the MTA to the SCRO.
6. Investigators may not give hESC lines to other investigators who do not have an MTA for those lines.

End of Tutorial

Please complete the Human Stem Cell Compliance Tutorial Quiz now and email answer sheet to SCRO Coordinator, Ellen Ciesielski (eciesielski@uchc.edu). For questions, please call 860-679-6004.

Additional information can be found in the SCRO Committee Policy Manual (<http://research.uchc.edu/rcs/stem-cells/policies-regulations-guidance/>).