Stem Cell Research Oversight Committee (SCRO) Standard Operating Procedures

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1 Stem Cell Research Oversight Committee (SCRO)

1.1 Policy

Research using human embryos and pluripotent or totipotent stem cells (hereafter refer to as hSCs) may be conducted at Stony Brook University, subject to the terms, conditions, and requirements of this Policy, and in conformance with all applicable federal and state regulations, as well as those of the University, and extra-mural research sponsors.

The Stem Cell Research Oversight Committee (SCRO) is a campus committee appointed by the Vice President for Research and charged with review and approval of human embryo and hSC research performed at SBU.

The University Standard Operating Procedures for the Stem Cell Research Oversight Committee (SCRO) detail the policies, procedures and regulations governing research with human embryos and stem cells and the requirements for submitting research proposals for review by the Stony Brook University SCRO. This is not a static document. The policies and procedures are regularly amended by the Vice President for Research, in consultation with applicable institutional entities (e.g., Office of Research Compliance staff, Stem Cell Research Oversight Committee, University Counsel, etc.).

The Vice President for Research will keep the University research community apprised of new information that affects the SCRO, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website and through campus electronic mailing lists. The policies and procedures will be available on the University's Office of Research Compliance website and copies will be available upon request.

1.2. Mission

The mission of the SCRO is to:

- Protect the safety of all subjects, employees, staff, and students
- Perform required reviews for the use of stem cells
- Educate investigators and research staff about their ethical responsibility to protect research subjects; and
- When appropriate, intervene in research and respond directly to concerns of research subjects.

1.3. Definitions

Term	Definition
Human Pluripotent Stem Cells (hPSC)	Human stem cells that can develop into cells of all three germ layers (endoderm, ectoderm, mesoderm) that form all organs of the body. hPSCs are defined as any human pluripotent stem cell including: human embryonic stem cell (hESC), human induced pluripotent stem cell (hiPSC), and human embryonic germ cell (hEGC). hPSCs do not give rise to the placenta and tissues needed for implantation.
Human Embryonic Stem Cells (hESC)	A subset of human pluripotent stem cells derived from pre-implantation embryos
Human adult stem cell/multipotent stem cell/lineage specific stem cell/progenitor cells/	Stem cells used by the human body for tissue repair and are capable of differentiating into one or a limited number of adult cell types.
Human stem cell	General term that refers to both human pluripotent and human adult stem cells.
Induced pluripotent stem cell	Adult somatic **cells** that have been **genetically reprogrammed** to an embryonic **stem cell**–like state by being forced to express genes and factors important for maintaining the defining properties of embryonic **stem cells**.
Extended pluripotent stem cells	Pluripotent stem cells that were manipulated in culture to be capable of generating all the cells/tissues of the embryo as well as the cells needed for implantation into the uterus (totipotent).
Totipotent cell	A cell that is isolated from a very early embryo or a stem cel that has been manipulated in culture such that they can give rise to all tissues needed for implantation of an embryo into the uterus and all tissues of the embryo.
Mesenchymal stem cells	Adult **stem cells** traditionally found in the bone marrow. Mesenchymal stem cells have the capacity to form fat, bone, and cartilage. Mesenchymal stem cells are distinct from the embryonic mesoderm which differentiates to form **hematopoietic stem cells** (form blood lineages).
Human embryonic germ cells:	Cells in the embryo that are reserved to form the gametes (egg and sperm)
Somatic Cells	Cells in the body that are not reproductive cells.
Somatic cell nuclear transfer (SCNT)	The transfer of a somatic cell nucleus into an enucleated oocyte (cloning)

1.4 SCRO Organization and Operation

Prior to beginning research using human embryos, or human pluripotent or totipotent stem cells regardless of source (not limited to embryos, adult tissues, amniotic fluid or fetal tissue) Stony Brook University investigators must have their research protocol approved by the campus Stem Cell Research Oversight Committee (SCRO).

- Approved research shall be reviewed by the SCRO Committee every year, or more frequently, as determined by the Committee on a case-by-case basis. The investigator will be reminded of expiration date(s), and s/he is responsible for submitting renewal applications in a timely manner.
- SCRO review does not preclude the necessity of review by other research oversight committees as applicable, e.g., Institutional Review Board (IRB), the Institutional Animal Care and Use Committee (IACUC), Institutional Biosafety Committee (IBC), etc. Such reviews may take place simultaneously with review by the SCRO committee. Approval from the SCRO must be completed prior to approval from the IRB.
- Annual protocol renewal reviews will confirm compliance with all applicable rules and regulations.

The SCRO committee has established guidelines (Table 1) indicating when a convened meeting is required for application review, when a review can be done electronically with quorum approval and when a subcommittee electronic review is sufficient. In addition, the SCRO may establish guidelines and procedures for expedited review of renewal applications with no alterations in stem cell procedures such that review by the entire SCRO committee is not required.

Table 1: Guidelines for SCRO committee review of applications

Type of SCRO committee review	Is a myResearch Safety application required?	Other Safety Reviews required.	Type of stem cell research
No SCRO Review Required	NO		***In vitro*** research involving multipotent (non-pluripotent) stem cells such as hematopoietic, neural progenitor, or mesenchymal stem cells where cells or derivatives are NOT introduced into animals or humans
SCRO designated member review	YES		***In vitro*** research using established human pluripotent or NIH/NAS approved totipotent stem cells
SCRO designated member review	YES		***In vitro*** research using established approved human embryonic stem cells
SCRO Committee Review	YES	IRB & IBC	***In vitro*** research creating induced pluripotent or totipotent stem cells from somatic cells or existing cell lines
SCRO Committee Review	YES	IRB & IBC	***In vitro*** research creating human embryonic, pluripotent, or totipotent stem cells from human embryos, gametes, or tissues
SCRO Committee Review	YES	IRB & IACUC	***In vivo*** research involving introduction of human pluripotent, totipotent, or embryonic stem cells or their derivatives (such as neural progenitors) into animals or humans
SCRO Committee Review	YES	IRB	Research using Human gametes or human embryos/embryo tissues used for human stem cell research

1.5 SCRO Committee Membership and Functions

The SCRO Committee shall be composed of persons with expertise including, but not limited to, stem cell research, developmental biology, molecular biology, assisted reproduction, and ethical issues in stem cell research. The SCRO Committee shall include at least one nonscientist member of the public who is not employed by, appointed to or remunerated by Stony Brook University and is not in the immediate family of a person employed by Stony Brook University. Membership terms are currently open ended. All SCRO Committee members must take the CITI stem cell training prior to reviewing stem cell research.

The SCRO meetings shall be convened at a frequency to ensure timely review of applications. A quorum, consisting of more than 50% of the total membership must be present in order for the meeting to be held. A simply majority of those members present

is required in order for a decision (e.g., approval, modifications required, etc.) to be passed.

No SCRO member shall have a financial conflict of interest in the research under review. SCRO Committee members who are involved in a research project that is being considered by the Committee must recuse themselves from the review and approval of that research project.

1.6 Recordkeeping

The SCRO shall be responsible for maintaining records (e.g., SCRO applications and committee determinations, registry of embryonic cell lines, etc.) pertaining to all human pluripotent stem cell research conducted at SBU. All records related to the SCRO committee and the research conducted will be retained for a minimum of six years and longer if regulatory requirements demand.

1.7 SCRO Committee Review & Notification

The chair or one of his/her designees may make the determination of whether or not a study meets the requirements for SCRO review. If the study meets the requirements for SCRO review, a primary and secondary reviewer will be assigned. If the SCRO determines that the expertise needed for a review is not found in the current SCRO membership, a consultant may be requested. The consultant will be asked to submit the review in writing. The consultant review will be available to the SCRO during committee deliberation.

If it meets the guidelines for committee review, chair/designee will determine how the review is to be done.

- Full convened meeting – all new embryonic stem cells, pluripotent
- Full meeting held electronically - at the discretion of the chair, with a quorum responding electronically
- Expedited review performed electronically

Renewals, with no significant changes, can be done in an expedited manner electronically. The Chair (or designee) will be given the renewal for review. Approval is issued for one year.

Renewals, with significant changes, must be reviewed according to the guidelines in Table 1. Approval is issued for one year.

During the course of the approval period, changes may need to occur to the research. These changes should be submitted for review by the SCRO Committee prior to implementation. Actions likely to be considered a change requiring prior approval from the SCRO Committee include, but are not limited to the following:

- Change in the specific aims
- Change in source or type of human pluripotent stem cells;
- Any change from the approved use of animals or human subjects, including the substitution of one animal model for another;
- Shift of the research emphasis from one disease area to another;
- Application of a new technology;
- Change in investigators listed on the approved ISCRO application, including change in PI and removal of members; and a
- Change in funding source to the lab or to the project.

The SCRO shall provide scientific and ethical review and approval of SBU research on human pluripotent stem cell lines as described in this policy. The SCRO shall ensure that human pluripotent stem cell research protocols conform to the research and ethics guidelines and regulations of the organization(s) funding the research.

SBU stem cell research of the types described below must be reviewed and approved by the SCRO Committee. Research may not begin without documented SCRO Committee approval. In all cases, the investigator must provide to the SCRO Committee documentation of compliance with any required review of the proposed research by IACUC, IBC, IRB or other mandated review. In cases where SCRO Committee review and approval are required, the committee shall notify investigators in writing of its decision to approve, require modifications, defer, or disapprove, the research activity. For decisions other than approval, SCRO Committee will include in its written notification a statement of the reasons for its decision.

The SCRO shall investigate and report as necessary to the Institution, sponsoring agency, and other entities as required, any instance of serious investigator noncompliance with the requirements or determinations of the SCRO committee.

1.8 Research Covered by the SCRO

The following types of research on or with human stem cells are prohibited at Stony Brook University:

- Research involving in vitro culture of any intact human embryo, regardless of derivation method, for longer than 14 days or until formation of the primitive streak begins
- Research in which hPSCs are introduced into human or non-human primate preimplantation embryos
- Research in which any products of research involving human totipotent or pluripotent stem cells are implanted into a human or non-human primate uterus.
- Breeding of animals that had hPSCs introduced into the germ line
- Research on a stem cell line derived from human embryos created for research purposes rather than reproductive purposes

- Research on a stem cell line derived from human somatic cell nuclear transfer (SCNT)
- Research on a line derived from human parthenogenesis

This list may be revised to reflect changes in prevailing ethical and policy guidance and applicable law.

Research that may be conducted at SBU, following review and approval by the SCRO Committee:

- Research involving NIH-approved established human embryonic stem cells.
- Research involving establishment of new hPSCs; or
- Research using established human pluripotent stem cells where the research involves:
  - *in vitro* culture and/or differentiation of hPSCs;
  - introduction/transplantation of hPSCs or their derivatives into any nonhuman recipient; or animal at any stage of embryonic, fetal or postnatal development;
  - Introduction of human pluripotent cells or embryonic stem cells into humans

Note: Only NIH-Approved human embryonic stem cell lines, listed on the NIH Human Pluripotent Stem Cell Registry, http://stemcells.nih.gov/research/registry/, or cell lines not listed in the registry that were reviewed and approved by NIH committee may be used at SBU.

1.9 Education and Training

All study personnel at Stony Brook University performing research involving the use of human embryonic stem cells or human pluripotent stem cells must complete the training. Study personnel include the principal investigator and any staff member directly involved with participants or the informed consent process. The table below lists training requirements. The requirements depend on what type of research is involved.

To complete the CITI program's Stem Cell Research Oversight modules, you must register a profile with CITI or login to an existing one. After registration and login, select "Add a Course" on the main menu. To enroll in the necessary courses, be sure to select the "Stem Cell Research Oversight" box.

Research involving	**Institutional Review required**	**Safety training required**
Establishing new human embryonic or pluripotent cell lines from human tissue	SCRO approval IBC approval IRB approval Stem cell personnel must be included on all other protocols and protocols must include	CITI – Human stem cell research CITI – Biosafety training/retraining CITI – Responsible Conduct of Res in the Biomed Sci CITI – Recombinant DNA guidelines ELS 002 – Lab Safety Chemical (once) ELS 003 – Biological hazards (annual) EOS 004 – Bloodborne pathogens (annual) ENV 001 – Hazardous Waste (annual & with changes) ENV 005 – Biological Hazard Waste (annual & with changes)

	description of how stem cells will be used.	
Establishing new human embryonic or pluripotent cell lines from established human cell lines	SCRO approval IBC approval IRB approval may be needed for new use of the cell lines (depending upon the source of starting cell line) Stem cell personnel must be included on all other protocols and protocols must include description of how stem cells will be used.	CITI – Human stem cell research CITI – Biosafety training/retraining CITI – Responsible Conduct of Res in the Biomed Sci ELS 002 – Lab Safety Chemical (once) ELS 003 – Biological hazards (annual) EOS 004 – Bloodborne pathogens (annual) ENV 001 – Hazardous Waste (annual & with changes) ENV 005 – Biological Hazard Waste (annual & with changes)
Utilizing already established human embryonic or pluripotent cell lines	The original cell line should have IRB approval or be listed on approved registry list. If not on the approval list, MTA from originating institution may be required. Stem cell personnel must be included on all other protocols and protocols must include description of how stem cells will be used.	CITI – Human stem cell research CITI – Biosafety training/retraining CITI – Responsible Conduct of Res in the Biomed Sci ELS 002 – Lab Safety Chemical (once) ELS 003 – Biological hazards (annual) EOS 004 – Bloodborne pathogens (annual) ENV 001 – Hazardous Waste (annual & with changes) ENV 005 – Biological Hazard Waste (annual & with changes)
If Stem Cell Research also involves:	**Add the following Safety Reviews:**	**Add the following Safety Training:**
Introducing genes into human cell lines	IBC approval – personnel must be listed under IBC Stem cell personnel must be included on protocols, and protocols must include description of how stem cells will be used.	CITI – Recombinant DNA guidelines
Introducing human cell lines into vertebrate animals	IACUC Stem cell personnel must be included on protocols and protocols must include description of how stem cells will be used.	CITI – Relevant animal training depending upon use of stem cells in animals
Introducing human cell lines into humans	IRB Stem cell personnel must be included on protocols and protocols must include description of how stem cells will be used	CITI – Human stem cell research
Fixing human cell lines or derivatives of cells with		ELS 009 – Lab Safety Formaldehyde (annual)

formaldehyde or related fixatives		
Shipping human cell lines or cell lines fixed in formaldehyde		EOS 016 – Signing a regulated medical waste manifest

1.10 Informed Consent Requirements

The SBU Institutional Review Board (IRB), is responsible for managing the informed consent approval process. Review of informed consent documents can take place simultaneously with review of the research protocol by the SCRO Committee. When the IRB approves the consent process for a given project, it will notify both the principal investigator and the SCRO Committee.

Research may not violate the documented preferences of subjects with regard to the use of their donated materials. In addition to the general requirements for informed consent, to ensure that subjects are fully informed of the potential uses of donated materials:

- Researchers must inform the subject that derived cells or cell products may be kept for many years.
- Researchers must disclose in the consent document whether the identity of the subject will be ascertainable to those who work with the resulting cells or cell products. If the identity of the subject is retained (including coded), the consent document must address plans for re-contacting subjects (for purposes of, e.g., providing information about research findings, obtaining additional health information, etc.), and must obtain specific consent for re-contact. Subjects may be re-contacted in the future only if they consent to re-contact at the time of donation.
- Researchers must inform subjects that cell lines may be used for future studies, some of which may not be predicted at this time, will undergo further ethics review to assess the need for further consent and to ensure that the subjects' research rights remain protected.
- Researchers must inform subjects that derived cells or cell products may be used in research involving genetic manipulation.
- Researchers must inform subjects that derived cells or cell products may be transplanted into humans or animals.
- Researchers must inform subjects that derived cells or cell products are not intended to provide direct medical benefit to the subject(s), except in the case of autologous donation.
- Researchers must inform subjects that the donation is being made without restriction regarding who may be the recipient of transplanted cells, except in the case of autologous donations.
- Researchers must inform subjects that neither consenting nor refusing to donate materials for research will affect the quality of any future care provided to potential subjects.

- Researchers must inform subjects that the results of research may be patentable or have commercial potential, and that the subject will not receive patent rights and will not receive financial or any other benefits from future commercial development.
- Researchers shall offer subjects an opportunity to document their preferences regarding future uses of their donated materials. Researchers may choose to use materials only from subjects who agree to all future uses.
- For research involving the donation of the umbilical cord, cord blood or the placenta, consent shall be obtained from the birth mother.