



<b>Policy Name: Research Using Human Stem Cells Policy</b>			
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### I. PURPOSE

Human pluripotent stem (hPS) cell research holds great promise for finding new treatment options for a wide range of diseases, conditions, and disabilities. MUSC encourages the use and derivation of hPS cells (including human embryonic stem (hES) cells, human pluripotent stem cells, human induced pluripotent stem cell lines, human neural and gonadal progenitor stem cells, and other human multipotent stem cells), provided the cells and cell lines are obtained and the research is conducted ethically, responsibly, and with appropriate oversight and in accordance with all applicable laws, rules, guidelines, and regulations.

This policy applies to all research involving the derivation or use of human pluripotent stem cells at MUSC, to help ensure that such research is conducted with the highest ethical and scientific research standards, and in compliance with all applicable federal and state regulations, MUSC policies, and the requirements of extramural research sponsors. Since the field of human stem cell research is rapidly changing, not all conceivable research involving human stem cells can be foreseen. Therefore, it is the responsibility of those deriving or using hPS cells to adhere to the intent of this policy, as well as to its specifics.

MUSC's Stem Cell Research Advisory Committee (hereafter "Committee" or "SCRO Committee") provides a recommendation to the Vice President for Research regarding research involving hPSCs and materials related to their derivation and use. The SCRO Committee conducts itself in consideration of the 2010 Amendments to the National Academies' Guidelines for Human Embryonic Stem Cell Research and the latest version of the international voluntary standards written by the International Society for Stem Cell Research (ISSCR), as well as in compliance with federal, state, and local requirements (See Section X References).

In addition, the SCRO Committee facilitates greater understanding of hPS research in the local community and helps keep investigators apprised of evolving policies impacting hPS cell research.

## II. AUTHORITY

The SCRO Committee resides in the Office of Research Integrity and reviews the ethical justification of hPS cell research at MUSC. The Committee is delegated authority by the Vice President for Research to approve, require modifications, or disapprove proposed research, and to suspend or terminate approved research for serious non-compliance or unanticipated problems.

## III. DEFINITIONS

**Blastocyst:** A pre-implantation embryo of 50-250 cells consisting of a sphere made up of an outer layer of cells, a fluid-filled cavity, and a cluster of cells on the interior

**hESC:** Human embryonic stem cell

**hPSC:** Human pluripotent stem cell

**iPSC:** Induced pluripotent stem cell by genetically reprogramming the nuclei of differentiated adult cells into a pluripotent state

**Multipotent:** Capable of differentiation into a limited spectrum of differentiated cell types

**Pluripotent:** Capable of developing into cells of all germ layers (endoderm, ectoderm, and mesoderm)

## IV. REVIEW PROCESS

### A. Review Process

To initiate review of a protocol by the SCRO Committee, Principal Investigators (PIs) must submit an application to the Committee. The SCRO Administrator will also be notified of the intent to conduct research involving hPSCs if that box is selected on the Electronic Proposal Data Sheet. On receipt of the application, the SCRO Administrator screens the information provided for completeness. If deemed complete, the Administrator suggests the appropriate level of review and forwards the application to the SCRO Committee Chair or Designated Reviewer. The level of SCRO review is determined by the Chair of the Committee.

## B. Levels of Review

### IV.B.1. Expedited Review

a) Protocols involving purely *in vitro* research (**excluding** protocols for differentiation of hPS cells into gametes or other epiblast-derived cell types), which only involve any of the following:

- (1) Human adult stem cells or human cord blood stem cells (however, see Section IV.B.4)
- (2) hESC lines that have been “acceptably derived”<sup>1</sup>.
- (3) hPSC lines which have previously been approved for use at MUSC by the SCRO Committee unless there is new information that calls into question renewal or approval
- (4) existing human induced pluripotent stem cells (iPSC) (**excluding** research directed at creating an human iPSC with embryonic stem cell quality from a somatic cell), provided one of the following criteria has been met:
  - (i) The IRB approved the consent form and process for obtaining the somatic cells used for induction; or
  - (ii) The SCRO Committee receives written confirmation from a Stem Cell Oversight Committee, an Institutional (IRB), or equivalent oversight body at another institution, that the oversight body approved the process for obtaining the somatic cells used for induction; or
  - (iii) The process for obtaining the somatic cell used for induction was not “research involving human subjects” within the meaning of Title 45, Part 46 of the US Code of Federal Regulations (45 CFR Part 46).
  - (iv) The process for obtaining the somatic cells used for induction was exempt from the requirements of 45 CFR Part 46, under 45 CFR Part 46.101(b).
  - (v) Cells are linked to one or more protected Health Information identifiers by code and MUSC researchers cannot trace cells back to donor per written agreement or policy. However, the provider of the iPSCs can.

b) generation of human iPSC, where the process for obtaining the somatic cells used for pluripotency induction, whether *in vitro* or *in vivo*, satisfies the requirements of Section IV.B.1.a.4 (i-v), above.

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<sup>1</sup> For purposes of this document, pluripotent stem cell lines have been “acceptably derived” when they have been:

- (a) Approved by the National Institutes of Health (NIH); or
- (b) Deposited in the United Kingdom Stem Cell Bank; or
- (c) Derived by, or approved for use by, a licensee of the United Kingdom Human Fertilization and Embryology Authority; or
- (d) Derived in accordance with the Canadian Institutes of Health Research Guidelines for Human Pluripotent Stem Cell Research under an application approved by the National Stem Cell Oversight Committee, or;
- (e) Derived in accordance with the Japanese Guidelines for Derivation and Utilization of Human Embryonic Stem Cells, or;
- (f) Found to be “acceptably derived” by the California Institute for Regenerative Medicine, or;
- (g) derived from gametes or embryos for which (i) the donation protocol was reviewed and approved by an IRB or, in the case of donations taking place outside the United States, a substantially equivalent oversight body; (ii) consent to donate was voluntary and informed; (iii) donation was made with reimbursement policies consistent with the NAS Guidelines; and (iv) donation and derivation complied with the extant legal requirements of the relevant jurisdiction.

- c) Protocols involving the injection/transplantation of a stem cell line (described in Section IV.B.1.a) into non-human blastocysts, embryos or fetuses, or post-natal animals, **excluding** the following:
- (1) Protocols involving the introduction of cells suspected to be neural progenitor cells into non-human blastocysts, embryos or fetuses, or into the brain of post-natal non-human animals require full committee review;
  - (2) Protocols in which there is a significant possibility that the implanted human stem cells could give rise to functional neural or gametic cells and tissues require full committee review. In considering the likelihood of such an outcome, particular attention should be paid to at least three factors: (i) The extent to which the implanted cells are anticipated to colonize and integrate into the animal tissue, and; (ii) The degree of anticipated differentiation of the implanted cells, and; (iii) The possible effects of the implanted cells on the function of the animal tissue;  
NOTE: Use that is limited to teratoma formation to test for pluripotency does not require SCRO review.
- d) Protocols involving the use of human oocytes or embryos that are inadequate for reproductive purposes, would otherwise be discarded, and will not be used to create pluripotent stem cells; or
- e) Continuing Reviews (renewals) of previously approved protocols or requests for modifications that would not require Full Review, regardless of the initial level of review

#### IV.B.2. Full Committee Review

Review by the convened SCRO Committee is required for any protocol not described in Section IV.B.1, IV.B.3, and IV.B.4. For example:

- a) Use of human embryonic and iPSC lines not previously approved by the MUSC SCRO committee, irrespective of de-identification.
- b) Derivation of any pluripotent or multipotent stem cell lines by any means.
- c) Research involving processing of human adult stem cells that significantly modifies/alters their capabilities
- d) Human totipotent cells or pluripotent stem cells that are mixed with pre-implantation human embryos. In no case shall such experiments be allowed to progress for more than 14 days of development in vitro, or past the point of primitive streak formation, whichever is first.
- e) Clinical research in which cells of totipotent or pluripotent human origin are transplanted into living human subjects.  
NOTE: Transplantation of stem cells as part of recognized and accepted medical treatment for a disease or condition will not need SCRO review;
- g) Research involving the introduction of hPSCs into animals (other than humans or primates, see Prohibited Research) at any stage of embryonic, fetal, or postnatal development and in which there is a significant possibility that the implanted cells could give rise to neural or gametic cells and tissues.
- h) Introduction of human neural stem cells into the central nervous system of any non-

human animal (pre- or perinatal) if such progenitors are suspected or documented to have "transdifferentiative" potential *in vivo* (greater potency than anticipated *in vitro*).  
NOTE: this includes neural stem cells from any source, including but not limited to hES cells, non-embryonic hPSCs, fetal tissue, adult somatic cells, and other non-embryonic sources.

#### IV.B.3. Administrative Review of Changes to Approved Proposals

- a) Change of personnel named in the Application.
- b) Grammatical corrections or clarifications to the study documents.

NOTE: Change of PI requires Expedited Review.

#### IV.B.4. Prohibited Research

Research not allowed to be conducted at MUSC at this time, **regardless of funding source**:

- a) Research involving *in vitro* culture of any intact human embryo, regardless of method of creation, for longer than 14 days or until formation of the primitive streak begins, whichever occurs first.
- b) Experiments that involve transplantation of human pluripotent stem cells into human blastocysts.
- c) Transfer into a human or non-human uterus of experimentally created human or cybrid (a cell with a human nucleus and the cytoplasm of another species) embryos made by any method.
- d) the following categories of research unless there is strong scientific rationale and ethical basis for the proposal:
  - 1. research in which human pluripotent stem cells are introduced into mammalian (including non-human primate) blastocysts
  - 2. breeding of animals into which human pluripotent stem cells have been introduced
  - 3. human stem cell research deemed ineligible by the National Institutes of Health

### C. Review Procedures

1. Administrative reviews may be carried out by the SCRO Administrator. All administrative review approvals are formally reported monthly in writing to the SCRO Committee and the Director of the Office of Research Integrity. Reports include the name of the PI, title of the protocol, and a short description of the protocol.

2. Expedited reviews may be carried out by the SCRO Chair and by one or more reviewers (Designated Reviewer) selected from among members of the SCRO Committee. The SCRO Administrator assigns the Application to the Chair and

Designated Reviewer who will recommend whether the protocol should be approved or should go to the full Committee for review. Approved Expedited protocols will be presented to the full Committee at the next Committee meeting. An inclusive list of Expedited approved protocols will be made available to Committee Members upon request. Reviewers of Expedited applications may not disapprove protocols (requires review by the full Committee). All expedited review approvals are formally reported monthly in writing to the Director of the Office of Research Integrity and the Vice President for Research.

3. Full Committee Review: The SCRO Administrator designates two Committee members as lead reviewers to review the protocols that require full review: one with scientific expertise pertinent to the protocol and one with ethics expertise or a non-affiliated SCRO Committee member. The applications are made available to all SCRO Committee members. At a Committee meeting, the two lead reviewers present the protocol and their analysis to the Committee. After deliberation, a quorum of Committee members votes on the outcome of the application. All Full Committee review approvals and disapprovals are formally reported monthly in writing to the Director of the Office of Research Integrity and the Vice President for Research.

4. Additional Information: At any stage in the review process, the Chair or lead reviewer may require the applicant to submit additional information or documentation to the SCRO Committee in support of the Application. Requests will be facilitated through the SCRO Administrator.

5. Additional Review: If the Chair or the Vice President for Research determines that a protocol requires an additional review, he or she may forward the application to an *ad hoc* reviewer or to one or more additional Committee members. If either the Chair or designated reviewer has concerns about an expedited Application, he or she must forward the Application to the Committee for full review.

#### **D. Continuing Review (Renewal) of Protocol**

SCRO Committee approvals are issued for no more than one year. Researchers may not conduct any research covered by that application either before activation or after the approval expiration date. The SCRO Committee must receive a renewal application at least 2 months prior to the expiration date in order to assure continuity of the research. Newly established or acquired hPSCs lines need to be registered as part of the Continuing Review, unless they were already registered prior. After three years, the PI must submit a new protocol for a *de novo* review by the SCRO committee.

#### **E. Modifications or Amendments**

Modifications approved to an active protocol do not change the expiration date, unless the modification is submitted as part of a complete application for Continuing Review (Renewal). Modifications may be submitted at the same time as requests for regularly scheduled Continuing Review.

#### **F. Restrictions, Suspension, and Termination of Covered Activities**

1. The SCRO Committee may advise the Vice President for Research to place restrictions on any aspect of studies involving hPSCs at MUSC.
2. The SCRO Committee may recommend suspension or termination of activities involving hPS cells that are not being performed in compliance with the terms of the approved protocol, its policies, or applicable laws or regulations. Such recommendations shall be made in writing by the SCRO Chair to the Vice President for Research, who will take any appropriate action as he/she deems necessary.
3. The Principal Investigator must immediately notify the SCRO Committee in writing if a sponsor or any MUSC committee or non-MUSC institution or agency initiates an inquiry into research involving human stem cells, or into ethical concerns involving human stem cells, or suspends or terminates a study involving human stem cells.

#### **G. Post-Approval Monitoring of Covered Activities**

The SCRO Committee may observe or have a third party observe the conduct of any activities under its jurisdiction, including a review of all records associated with the activities.

### **V. OBLIGATIONS OF INVESTIGATORS**

All scientific investigators, regardless of their field, bear the ultimate responsibility for ensuring that they conduct themselves in accordance with professional standards and with integrity. In particular, people whose research involves hESCs should work closely with oversight bodies, demonstrate respect for the autonomy and privacy of those who donate gametes, morulae, blastocysts, or somatic cells and be sensitive to public concerns about research that involves human embryos.

All MUSC activities involving human stem cell research shall be in accordance with the applicable federal, state and funding agency regulations governing such research, including any restrictions on the use of federal funds for such research as issued under the NIH Stem Cell Guidelines. It is the responsibility of the PI and all research personnel involved in human stem cell research to understand and adhere to these Federal restrictions.

**With respect to research using human stem cell lines not approved by the NIH, it is essential that all supplies and personnel supporting these projects are segregated from other research activities, supplies and equipment.**

Investigators are required to be familiar with applicable MUSC and other compliance policies, rules, and regulations governing such activity. See Section VII. Training.

It is the responsibility of the PI to register all human pluripotent stem cell lines, derived or imported, with the MUSC Human Stem Cell Registry. See Section VI MUSC Human Stem Cell Registry.

It is the responsibility of the PI to make sure an MTA is in place prior to transferring human stem cell materials to other individuals or corporate entities, both on and off MUSC campus. See Section VIII Transfer of Materials.

### **VI. TRAINING OF PI, CO-INVESTIGATORS AND SUPPORT STAFF**

All individuals involved in hPSCs studies are required to be familiar with applicable MUSC and other compliance policies, rules, and regulations governing such activity. All individuals involved in hPSCs studies must complete the Stem Cell Research Oversight training program from the Collaborative Institutional Training Initiative (CITI Program) at the University of Miami, prior to conducting hPSCs studies.

## **VII. TRANSFER OF MATERIALS**

A fully executed Material Transfer Agreement is required for all exchanges of human stem cell materials, incoming and outgoing. The Office of Sponsored Research Projects handles negotiation of such agreements. It is the PI responsibility to comply with SCRO requirements for assuring prior approval and providing information for campus tracking of such transactions, as appropriate.

**Principal Investigators intending to transfer any human stem cell materials to other researchers within MUSC must notify the SCRO Administrator at least one week prior to transfer, to assure the recipient has appropriate prior approval and to provide information for campus tracking of such transactions.**

## **IX. SCRO COMMITTEE**

### **A. Membership**

The SCRO Committee shall consist of at least five members appointed by the Vice President for Research. Members shall serve for staggered, renewable terms of three years each. Appointments to the SCRO Committee shall be made to persons from a variety of academic and professional fields in order to reflect the scientific, medical and ethical expertise necessary to carry out the committee's responsibilities. The SCRO Committee shall consist of the following:

- a) Members with pertinent scientific and clinical expertise
  - (1) Principal Investigators
  
- b) Members with expertise in research ethics, law and human subjects protection, e.g.
  - (1) Ethicist
  - (2) IRB Program Manager
  
- c) Non-scientist unaffiliated member, e.g.
  - (1) Patient Advocate
  - (2) Community Representative
  
- d) Ex officio nonvoting members, e.g.
  - (1) Vice President for Research
  - (2) Representative from Legal

### **B. Quorum**

A quorum of the membership of the SCRO Committee, including at least one member with relevant scientific expertise and at least one member whose primary concerns are in

nonscientific areas, must be met before a meeting can be convened. The MUSC SCRO Committee deems quorum as the presence of at least one-half the voting membership plus one. In the event a member must participate by teleconference, the member will have access to the review materials prior to the meeting and the minutes of the convened SCRO committee meeting will reflect that the member participated by teleconference.

### **C. Coordination with other regulatory oversight committees**

The SCRO Chair and Administrator will communicate outcomes of the committee's deliberations to other regulatory oversight committees (IRB, IACUC, IBC) as needed, in a timely manner. Review and approval by the SCRO Committee is in addition to and is not a replacement for approval by or adherence to other University policies, federal regulations, and state and local laws governing research. Other policies that need to be considered include, but are not limited to, review by the Institutional Animal Care and Use Committee (IACUC), the Institutional Review Board (IRB), or the Institutional Biosafety Committee (IBC).

No research subject to this Human Stem Cells Policy may be initiated until all regulatory oversight approvals have been obtained. For projects that involve more than one institution, review of the scientific merit, justification, and compliance status of the research may be carried out by a single SCRO committee if all participating institutions agree. At MUSC, the Vice President for Research shall make this decision.

### **D. Standard of Review**

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

In circumstances where a funding organization does not have established ethics guidelines and regulations, the MUSC SCRO Committee will follow the major recommendations outlined in the 2012 Amendments to the National Academies' Guidelines for Human Embryonic Stem Cell Research and the international voluntary standards written by the International Society for Stem Cell Research (ISSCR).

## **X. REFERENCES**

2009 National Institutes of Health Guidelines on Human Stem Cell Research (<http://stemcells.nih.gov/policy/pages/2009guidelines.aspx>)

2010 Amendments to the National Academies' Guidelines for Human Embryonic Stem Cell Research ([http://www.nap.edu/catalog.php?record\\_id=11278](http://www.nap.edu/catalog.php?record_id=11278) )

International Society for Stem Cell Research Guidelines for the Conduct of Human Embryonic Stem Cell Research (ISSCR; <http://www.isscr.org/home/publications/guide-clintrans>)

