UNIVERSITY OF MICHIGAN
POLICY ON RESEARCH WITH HUMAN PLURIPOTENT STEM CELLS
HUMAN EMBRYONIC STEM CELLS AND INDUCED PLURIPOTENT STEM CELLS

This University of Michigan (U-M) policy for research involving both the derivation and use of human pluripotent stem cells is based on the principles of the "NIH Guidelines for Research Using Human Pluripotent Stem Cells" (2000, 2009), Office for Human Research Protections (OHRP) guidelines, and the recommendations of the Committee on Guidelines for Human Embryonic Stem Cell Research, National Research Council, National Academy of Sciences (2005; amendments 2007, 2008).

Human pluripotent stem cells are derived either from embryos, resulting in human embryonic stem cells (hESC), or from other sources which result in induced pluripotent stem cells (iPSC).

Michigan Statute (MCLA 333.2688), effective December 19, 2008, permits the use of an embryo for non-therapeutic research and also the use of a deceased embryo with maternal consent. MCLA 333.16274 and 750.430a prohibits "human cloning" but does not prohibit other scientific research or cell-based therapies.

The University of Michigan has established the Human Pluripotent Stem Cell Research Oversight (HPSCRO) Committee to review all research at the University involving these cells. The policy below and related procedures are divided into sections applicable to hESC derivation and research use, and to human iPSC derivation and research use.

I. Human Embryonic Stem Cells (hESC)

A. Derivation

When a stem cell line is to be derived from a human embryo, or when research at U-M involves a stem cell line derived elsewhere from human embryos, the **U-M will ensure that the following conditions apply to the derivation**:

1. Embryos may be secured only from fertility clinics and must have been freely donated when no longer suitable or no longer needed for reproductive purposes;
2. Embryos must not be purchased;
3. There must be no financial or other incentives to create embryos solely for the purposes of research or to donate embryos for research;
4. Informed consent must have been obtained for donation of the embryo;
5. Provisions to protect the donor's privacy and confidentiality must be in place before any research can take place;
6. No federally-funded salaries, equipment, space, or supplies can be used **to derive** a new stem cell line from a human embryo (Federal funds may be used **for research** involving human embryonic stem cell lines, according to federal policy);
7. Derivation of new human embryonic stem cell lines by somatic cell nuclear transfer is not permitted.

B. hESC Research Restrictions

The following research uses are *not permitted*:

1. Research involving in vitro culture of any intact human embryo 14 days or older;
2. Research in which hESC lines are introduced into non-human primate blastocysts or in which any hESC lines are introduced into human blastocysts;
3. Research that involves breeding of any animal into which hESC lines have been introduced (at any stage of development).

II. Human Induced Pluripotent Stem Cells (iPSC)

A. Derivation

When human induced pluripotent stem cells are to be derived from human tissue, or when research at U-M involves human induced pluripotent stem cells derived outside the University from human tissue, the **U-M will ensure that the following conditions apply to the derivation**:

1. Informed consent must have been obtained from the donor for donation of the tissue unless an IRB waiver of informed consent is allowed;
2. Provisions to protect the donor's privacy and confidentiality must be in place.

B. iPSC Research Restrictions

The following research uses are *not permitted*:

1. Research in which human iPSC lines are introduced into non-human primate blastocysts or introduced into human blastocysts;
2. Research that involves breeding of any animal into which human iPSC lines have been introduced such that they could contribute to the germline.

III. Procedure for Obtaining Approval for hESC Research

A Derivation of an hESC line at U-M

The IRB will review the consent process for the donation of embryos from which new human embryonic stem cell (hESC) lines will be derived at U-M. The HPSCRO Office will receive notice of the submission of the application through eResearch and may provide consultation. The HPSCRO Office will request that the PI complete the HPSCRO application regarding the derivation and any subsequent research use of the hESC line. When the IRB application including the derivation of an hESC line has been approved by the IRB, and the HPSCRO Committee has all of the information it needs, HPSCRO will place that line on an internal registry of approved hES cell lines.

The HPSCRO Committee will work with investigators as needed to apply for acceptance on the NIH Registry of hESC lines derived at U-M.

B Obtaining hESC Lines Derived Outside the University

1. Material Transfer Agreements

All hESC lines obtained from outside the University must be accompanied by a Materials Transfer Agreement (MTA). When an hESC line that was obtained through the MTA process are shared with other investigators at the University, a Memorandum of Understanding (MOU) is required.

2. NIH Registry hESC Lines

The NIH maintains a registry of hESC lines that have been approved by NIH through review of the provenance. NIH Registry lines can be used by an investigator at U-M after approval from the HPSCRO Committee. An expedited HPSCRO review process may be available for *in vitro* research with NIH Registry lines.

3. hESC Lines Not on the NIH Registry

The HPSCRO Committee will review the provenance of hESC lines that are not on the NIH Registry when a U-M investigator wishes to obtain such a cell line for research. In conjunction with the HPSCRO review, the U-M IRB may conduct an independent review of the consent process. The IRB may place reasonable reliance on reviews of the consent process approved by other IRBs.

When the provenance of a non-NIH Registry hESC line derived elsewhere has been found to be acceptable by the HPSCRO Committee, the committee will place that line on an internal registry of approved hESC lines.

C Research Use of hESC Lines

Once the HPSCRO application has been completed and submitted to the HPSCRO Committee by the Principal Investigator (PI) for derivation of a new hESC line, or for obtaining an hESC line derived outside the university, this application is also reviewed by the HPSCRO Committee for the proposed research uses of the hESC line. The HPSCRO Committee will issue approval of the proposed research uses.

The **research use** categories for hESC lines are listed below. Depending upon the category of research use proposed, oversight bodies in addition to the HPSCRO Committee may also review the proposed research, as indicated:

1. *In vitro* hESC research with pre-existing hESC lines that are on the NIH Registry (approved by NIH for federal funding)
2. *In vitro* hESC research with pre-existing hESC lines that are not on the NIH Registry (not approved by NIH for federal funding)
3. Research involving the introduction of hESC lines or their derivatives into non-human animals at any stage of embryonic, fetal, or postnatal development (IACUC review also required)
4. Research involving the introduction of hESC lines or their derivatives into humans (FDA and IRB review also required)

5. Research in which personally identifiable information about the donors of the blastocysts, gametes, or somatic cells from which the hESC liens were derived is linked to the cell lines (IRB review also required)

IV. Procedure for Obtaining Approval for Derivation of Human iPSC Lines

A Obtaining Human Tissue

1. Tissue from U-M patients

The IRB will review the consent process for the donation of tissue from which iPSC lines will be derived. The HPSCRO Office will be notified of the review and may provide consultation. The U-M IRB may place reasonable reliance on reviews of derivation protocols approved by other IRBs. The HPSCRO Committee will review the plan for derivation of the iPSC line.

2. Tissue from outside the University

When the tissue for derivation of an iPSC line is to be obtained from outside the University, a Material Transfer Agreement (MTA) is required. The IRB may review the consent process for the donation of tissue and may place reasonable reliance on reviews of derivation protocols approved by other IRBs. The HPSCRO Committee will review the plan for derivation of the iPSC line.

When the tissue procurement has been approved by the IRB, and the derivation has been reviewed by the HPSCRO Committee, the resulting iPSC line will be placed on an internal registry of approved iPS cell lines.

B Obtaining an Induced Pluripotent Stem Cell Line Derived Outside the University

1. Material Transfer Agreements

iPSC lines obtained from outside the University must be accompanied with a Materials Transfer Agreement (MTA). When iPSC lines obtained through the MTA process are shared with other investigators at the University, a Memorandum of Understanding (MOU) is required.

2. Provenance

The HPSCRO Committee must review (with IRB consultation as needed) the adequacy of the consent process for an iPSC line derived outside the University.

When the provenance of an iPSC line derived elsewhere has been found to be acceptable by the HPSCRO Committee, the HPSCRO Office will place that line on an internal registry of approved iPSC lines.

C Research Use of Human iPSC Lines

A HPSCRO application that is completed by the PI for derivation of a new iPSC line or for obtaining an iPSC line derived outside the University will also cover the proposed research uses of the iPS cell line. The HPSCRO Committee will review and issue approval of the proposed research uses.

The **research use** categories for iPSC lines are listed below. Depending upon the category of research use proposed, oversight bodies in addition to the HPSCRO Committee may also review the work, as indicated:

1. *In vitro* iPSC research.
2. Research involving the introduction of iPSC lines into non-human gametes or into non-human primates or other animals at any stage of embryonic, fetal, or postnatal development (IACUC review also required)
3. Research involving the introduction of iPSC lines into humans (FDA and IRB review also required)
4. Research in which personally identifiable information about the donors of the somatic cells from which the iPSC lines were derived is linked to the cell lines (IRB review also required)