

# National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells

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## I. Scope of Guidelines

These Guidelines apply to the expenditure of National Institutes of Health (NIH) funds for research using human pluripotent stem cells derived from human embryos (technically known as human embryonic stem cells) or human fetal tissue (technically known as human embryonic germ cells). For purposes of these Guidelines, "human pluripotent stem cells" are cells that are self-replicating, are derived from human embryos or human fetal tissue, and are known to develop into cells and tissues of the three primary germ layers. Although human pluripotent stem cells may be derived from embryos or fetal tissue, such stem cells are not themselves embryos. NIH research funded under these Guidelines will involve human pluripotent stem cells derived 1) from human fetal tissue; or 2) from human embryos that are the result of in vitro fertilization, are in excess of clinical need, and have not reached the stage at which the mesoderm is formed.

In accordance with 42 Code of Federal Regulations (CFR) §52.4, these Guidelines prescribe the documentation and assurances that must accompany requests for NIH funding for research using human pluripotent stem cells from: (1) awardees who want to use existing funds; (2) awardees requesting an administrative or competing supplement; and (3) applicants or intramural researchers submitting applications or proposals. NIH funds may be used to derive human pluripotent stem cells from fetal tissue. NIH funds may not be used to derive human pluripotent stem cells from human embryos. These Guidelines also designate certain areas of human pluripotent stem cell research as ineligible for NIH funding.

## II. Guidelines for Research Using Human Pluripotent Stem Cells that is Eligible for NIH Funding

### A. Utilization of Human Pluripotent Stem Cells Derived from Human Embryos

#### 1. Submission to NIH

Intramural or extramural investigators who are intending to use existing funds, are requesting an administrative supplement, or are applying for new NIH funding for research using human pluripotent stem cells derived from human embryos must submit to NIH the following:

- a. An assurance signed by the responsible institutional official that the pluripotent stem cells were derived from human embryos in accordance with the conditions set forth in Section II.A.2 of these Guidelines and that the institution will maintain documentation in support of the assurance;
- b. A sample informed consent document (with patient identifier information removed) and a description of the informed consent process that meet the criteria for informed consent set forth in Section II.A.2.e of these Guidelines;
- c. An abstract of the scientific protocol used to derive human pluripotent stem cells from an embryo;
- d. Documentation of Institutional Review Board (IRB) approval of the derivation protocol;
- e. An assurance that the stem cells to be used in the research were or will be obtained through a donation or through a payment that does not exceed the reasonable costs associated with the transportation, processing, preservation, quality control and storage of the stem cells;
- f. The title of the research proposal or specific subproject that proposes the use of human pluripotent stem cells;
- g. An assurance that the proposed research using human pluripotent stem cells is not a class of research that is ineligible for NIH funding as set forth in Section III of these Guidelines; and

h. The Principal Investigator's written consent to the disclosure of all material submitted under Paragraph A.1 of this Section, as necessary to carry out the public review and other oversight procedures set forth in Section IV of these Guidelines.

## 2. Conditions for the Utilization of Human Pluripotent Stem Cells Derived From Human Embryos

Studies utilizing pluripotent stem cells derived from human embryos may be conducted using NIH funds only if the cells were derived ( without Federal funds ) from human embryos that were created for the purposes of fertility treatment and were in excess of the clinical need of the individuals seeking such treatment.

- a. To ensure that the donation of human embryos in excess of the clinical need is voluntary, no inducements, monetary or otherwise, should have been offered for the donation of human embryos for research purposes. Fertility clinics and/or their affiliated laboratories should have implemented specific written policies and practices to ensure that no such inducements are made available.
- b. There should have been a clear separation between the decision to create embryos for fertility treatment and the decision to donate human embryos in excess of clinical need for research purposes to derive pluripotent stem cells. Decisions related to the creation of embryos for fertility treatment should have been made free from the influence of researchers or investigators proposing to derive or utilize human pluripotent stem cells in research. To this end, the attending physician responsible for the fertility treatment and the researcher or investigator deriving and/or proposing to utilize human pluripotent stem cells should not have been one and the same person.
- c. To ensure that human embryos donated for research were in excess of the clinical need of the individuals seeking fertility treatment and to allow potential donors time between the creation of the embryos for fertility treatment and the decision to donate for research purposes, only frozen human embryos should have been used to derive human pluripotent stem cells. In addition, individuals undergoing fertility treatment should have been approached about consent for donation of human embryos to derive pluripotent stem cells only at the time of deciding the disposition of embryos in excess of the clinical need.
- d. Donation of human embryos should have been made without any restriction or direction regarding the individual ( s ) who may be the recipients of transplantation of the cells derived from the embryo.
- e. Informed Consent Informed consent should have been obtained from individuals who have sought fertility treatment and who elect to donate human embryos in excess of clinical need for human pluripotent stem cell research purposes. The informed consent process should have included discussion of the following information with potential donors, pertinent to making the decision whether or not to donate their embryos for research purposes.

Informed consent should have included:

- ( i ) A statement that the embryos will be used to derive human pluripotent stem cells for research that may include human transplantation research;
- ( ii ) A statement that the donation is made without any restriction or direction regarding the individual ( s ) who may be the recipient ( s ) of transplantation of the cells derived from the embryo;
- ( iii ) A statement as to whether or not information that could identify the donors of the embryos, directly or through identifiers linked to the donors, will be removed prior to the derivation or the use of human pluripotent stem cells;
- ( iv ) A statement that derived cells and/or cell lines may be kept for many years;
- ( v ) Disclosure of the possibility that the results of research on the human pluripotent stem cells may have commercial potential, and a statement that the donor will not receive financial or any other benefits from any such future commercial development;
- ( vi ) A statement that the research is not intended to provide direct medical benefit to the donor; and

- ( vii ) A statement that embryos donated will not be transferred to a woman's uterus and will not survive the human pluripotent stem cell derivation process.
- f. Derivation protocols should have been approved by an IRB established in accord with 45 CFR §46.107 and §46.108 or FDA regulations at 21 CFR §56.107 and §56.108.

## B. Utilization of Human Pluripotent Stem Cells Derived From Human Fetal Tissue

### 1. Submission to NIH

Intramural or extramural investigators who are intending to use existing funds, are requesting an administrative supplement, or are applying for new NIH funding for research using human pluripotent stem cells derived from fetal tissue must submit to NIH the following:

- a. An assurance signed by the responsible institutional official that the pluripotent stem cells were derived from human fetal tissue in accordance with the conditions set forth in Section II.B.2 of these Guidelines and that the institution will maintain documentation in support of the assurance;
- b. A sample informed consent document ( with patient identifier information removed ) and a description of the informed consent process that meet the criteria for informed consent set forth in Section II.B.2.b of these Guidelines;
- c. An abstract of the scientific protocol used to derive human pluripotent stem cells from fetal tissue;
- d. Documentation of IRB approval of the derivation protocol;
- e. An assurance that the stem cells to be used in the research were or will be obtained through a donation or through a payment that does not exceed the reasonable costs associated with the transportation, processing, preservation, quality control and storage of the stem cells;
- f. The title of the research proposal or specific subproject that proposes the use of human pluripotent stem cells;
- g. An assurance that the proposed research using human pluripotent stem cells is not a class of research that is ineligible for NIH funding as set forth in Section III of these Guidelines; and
- h. The Principal Investigator's written consent to the disclosure of all material submitted under Paragraph B.1 of this Section, as necessary to carry out the public review and other oversight procedures set forth in Section IV of these Guidelines.

### 2. Conditions for the Utilization of Human Pluripotent Stem Cells Derived From Fetal Tissue

- a. Unlike pluripotent stem cells derived from human embryos, DHHS funds may be used to support research to derive pluripotent stem cells from fetal tissue, as well as for research utilizing such cells. Such research is governed by Federal statutory restrictions regarding fetal tissue research at 42 U.S.C. §289g-2 ( a ) and the Federal regulations at 45 CFR §46.210. In addition, because cells derived from fetal tissue at the early stages of investigation may, at a later date, be used in human fetal tissue transplantation research, it is the policy of NIH to require that all NIH-funded research involving the derivation or utilization of pluripotent stem cells from human fetal tissue also comply with the fetal tissue transplantation research statute at 42 U.S.C. §289g-1 and with 42 U.S.C. §289g-2 ( b ) .

#### b. Informed Consent

As a policy matter, NIH-funded research deriving or utilizing human pluripotent stem cells from fetal tissue should comply with the informed consent law applicable to fetal tissue transplantation research ( 42 U.S.C. §289g-1 ) and the following conditions.

The informed consent process should have included discussion of the following information with potential donors, pertinent to making the decision whether to donate fetal tissue for research purposes.

Informed consent should have included:

- ( i ) A statement that fetal tissue will be used to derive human pluripotent stem cells for research that may include human transplantation research;
- ( ii ) A statement that the donation is made without any restriction or direction

regarding the individual (s) who may be the recipient (s) of transplantation of the cells derived from the fetal tissue;

- (iii) A statement as to whether or not information that could identify the donors of the fetal tissue, directly or through identifiers linked to the donors, will be removed prior to the derivation or the use of human pluripotent stem cells;
  - (iv) A statement that derived cells and/or cell lines may be kept for many years;
  - (v) Disclosure of the possibility that the results of research on the human pluripotent stem cells may have commercial potential, and a statement that the donor will not receive financial or any other benefits from any such future commercial development; and
  - (vi) A statement that the research is not intended to provide direct medical benefit to the donor.
- c. Derivation protocols should have been approved by an IRB established in accord with 45 CFR §46.107 and §46.108 or FDA regulations at 21 CFR §56.107 and §56.108

### **III. Areas of Research Involving Human Pluripotent Stem Cells that are Ineligible for NIH Funding**

Areas of research ineligible for NIH funding include:

- A. The derivation of pluripotent stem cells from human embryos;
- B. Research in which human pluripotent stem cells are utilized to create or contribute to a human embryo;
- C. Research utilizing pluripotent stem cells that were derived from human embryos created for research purposes, rather than for fertility treatment;
- D. Research in which human pluripotent stem cells are derived using somatic cell nuclear transfer, i.e., the transfer of a human somatic cell nucleus into a human or animal egg;
- E. Research utilizing human pluripotent stem cells that were derived using somatic cell nuclear transfer, i.e., the transfer of a human somatic cell nucleus into a human or animal egg;
- F. Research in which human pluripotent stem cells are combined with an animal embryo; and
- G. Research in which human pluripotent stem cells are used in combination with somatic cell nuclear transfer for the purposes of reproductive cloning of a human.

### **IV. Oversight**

- A. The NIH Human Pluripotent Stem Cell Review Group (HPSCRG) will review documentation of compliance with the Guidelines for funding requests that propose the use of human pluripotent stem cells. This working group will hold public meetings when a funding request proposes the use of a line of human pluripotent stem cells that has not been previously reviewed and approved by the HPSCRG.
- B. In the case of new or competing continuation (renewal) or competing supplement applications, all documentation of compliance with the Guidelines will be reviewed by HPSCRG and all applications will be reviewed for scientific merit by a Scientific Review Group. In the case of requests to use existing funds or applications for an administrative supplement or in the case of intramural proposals, Institute or Center staff should forward material to the HPSCRG for review and determination of compliance with the Guidelines prior to allowing the research to proceed.
- C. The NIH will compile a yearly report that will include the number of applications and proposals reviewed and the titles of all awarded applications, supplements or administrative approvals for the use of existing funds, and intramural projects.
- D. Members of the HPSCRG will also serve as a resource for recommendations to the NIH with regard to any revisions to the NIH Guidelines for Research Using Human Pluripotent Stem Cells and any need for human pluripotent stem cell policy conferences.