**Section 995.90 Research Requirements and Limitations**

All grantees shall comply with the following requirements in the course of performing stem cell research funded by a grant under this Part:

a) All research shall be undertaken according to the National Academies of Science Guidelines for Human Embryonic Stem Cell Research. The research shall be approved by the ESCRO committee and submitted with the application. Any changes from the National Academies of Science Guidelines for Human Embryonic Stem Cell Research shall be submitted to the Department prior to implementation to assure compliance with this Part and the grant agreement. Any use of human embryonic stem cells shall be consistent with the National Academies of Science Guidelines for Human Embryonic Stem Cell Research.

b) All research shall at all times comply with all applicable federal laws, including, but not limited to, the Occupational Health and Safety Act and HIPAA, and the following federal regulations: Institutional Animal Care and Use Committee (IACUC) and Attending Veterinarian and Adequate Veterinarian Care. Grantees shall comply with the U.S. Department of Health and Human Services regulations titled Protection of Human Subjects and the U.S. Department of Agriculture regulations titled Attending Veterinarian and Adequate Veterinarian Care and Institutional Animal Care and Use committee (IACUC) (see Section 995.15).

c) Grantees shall be responsible for supervising their investigators to ensure that they conduct themselves in accordance with the grant agreement and professional standards.

d) The project period shall be up to 24 months.

e) Grantees shall obtain the informed consent of all research donors, patients and participants, including a new consent from individuals who had indicated their intent to donate to research any blastocysts that remain after clinical care at the time of the original harvesting. Donors shall be informed that they retain the right to withdraw consent until the blastocysts are actually used in cell line derivation. A research project's informed consent procedures shall satisfy each of the following requirements:

1) In seeking informed consent, the following information shall be provided to each research donor, patient or participant:

A) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

B) A description of any reasonably foreseeable risks or discomforts to the donor;

C) A description of any benefits to the donor or to others that may reasonably be expected from the research;

D) A disclosure of appropriate alternative options pertaining to use of the embryos;

E) A statement describing the extent, if any, to which confidentiality of records identifying the donor will be maintained;

F) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

G) An explanation of whom to contact for answers to pertinent questions about the research and research donors' rights, and whom to contact in the event of a research-related injury to the donor; and

H) A statement that participation or donation is voluntary; that refusal to participate and/or donate will involve no penalty or loss of benefits to which the donor is otherwise entitled; and that the donor may discontinue participation at any time without penalty or loss of benefits to which the donor is otherwise entitled.

2) When appropriate, the following additional elements of information shall also be provided to each research donor:

A) Anticipated circumstances under which the donor's participation in the research may be terminated without the donor's consent;

B) The consequences of the donor's decision to withdraw from the research, and procedures for the donor's orderly termination of participation; or

C) Significant new findings developed during the course of the research that may relate to the donor's willingness to continue participation.

3) The grantee shall develop the precise form of the informed consent specifically for the particular study protocol or procedure for which the consent is being sought, and the informed consent form shall be approved by the grantee's ESCRO committee.

4) The language in the informed consent shall be clear and understandable.

5) When donor gametes have been used in the in vitro fertilization process, resulting blastocysts shall not be used for research without consent of all gamete donors.

6) The informed consent shall otherwise conform to the requirements for research funded by the National Institutes of Health and be consistent with the Guidelines for Human Embryonic Stem Cell Research published by the National Academies of Science (see Section 995.15).

f) Financial Incentives Prohibited

No cash or in-kind payments shall be provided for the solicitation or donation of blastocysts, gametes or somatic cells for research purposes or of somatic cells for use in nuclear transfers.

g) Standards of Clinical Care

1) Consenting or refusing to donate gametes or blastocysts for research shall not affect or alter in any way the quality of care provided to prospective donors. Clinical staff shall provide care to patients without prejudice regarding their decisions about disposition of their embryos.

2) Researchers shall not ask members of the infertility treatment team to generate more oocytes than necessary for the optimal chance of reproductive success. An infertility clinic or other third party responsible for obtaining consent or collecting materials is not to pay for or be paid for the material obtained (except for specifically defined cost-based reimbursements and payments for professional services).

h) Privacy and Confidentiality

1) Grantees shall at all times ensure that donors' personal health information is protected and kept confidential. Investigators and institutions shall comply with applicable laws, including, but not limited to, HIPAA.

2) Grantees shall ensure that authorizations are received from donors, as required by HIPAA, for the confidential transmission of personal health information to repositories or to investigators who are using embryonic stem cell lines derived from donated materials.

3) When the FDA requires that the identity of the donor source be preserved, investigators and institutions shall ensure that the confidentiality of the donor is protected; that the donor understands that the donor's identity will be maintained; and that, where applicable, human subject protections as defined in HIPAA are followed.

i) Derivation of Stem Cell Lines

1) Requests from the investigators to the ESCRO committee for permission to attempt derivation of new embryonic stem cell lines from donated embryos or blastocysts or from any other source or by another procedure not previously approved by the IRB shall include the IRB's written approval of the procurement process.

2) The investigator shall present the scientific rationale for the need to generate new embryonic stem cell lines, by whatever means, to the ESCRO committee, and the investigators shall justify the basis for the numbers of embryos and blastocysts needed.

3) Blastocysts made using nuclear transfer (whether produced with human or nonhuman oocytes) and parthenogenetic or androgenetic human embryos shall not be transferred to a human or nonhuman uterus and shall not be cultured as intact embryos in vitro.

4) Cells shall not be extracted from blastocysts more than 12 days after cell division begins, not counting any time during which the blastocysts or cells have been stored frozen.

5) Investigators shall document how they will characterize, validate, store and distribute the new embryonic stem cell lines and how they will maintain the confidentiality of any coded or identifiable information associated with the lines.

j) Storage and Distribution of Stem Cell Lines

1) Cell lines derived or modified in any way with IRMI grant funds shall be deposited in a bank in a timely manner as defined in the grant agreement. Grantees shall allow stem cell lines to be shared with other investigators.

2) Grantees that are banking or plan to bank embryonic stem cell lines shall establish uniform guidelines to ensure that records are maintained about all aspects of cell culture, and shall establish uniform tracking systems and common guidelines for distribution of cells.

3) Grantees engaged in obtaining and storing embryonic cell lines shall:

A) Create a committee for policy and oversight purposes and create clear and standardized protocols for banking and withdrawals.

B) Establish documentation requirements for investigators and sites that deposit cell lines, including:

i) Providing a copy of the donor consent form;

ii) Providing proof of written approval of the procurement process by the depositor's IRB and the grantee's IRB;

iii) Providing available medical information on the donors, including results of infectious disease screening;

iv) Providing available clinical, observational or diagnostic information about the donors;

v) Providing critical information about culture conditions (such as media, cell passage and safety information); and

vi) Providing available cell lines characterization (such as karyotype and genetic markers).

C) Establish a secure system for protecting the privacy of donors when materials retain information that could lead to the identification of the patient, including, but not limited to:

i) A schema for maintaining confidentiality, such as a coding system;

ii) A system for a secure audit trail from primary cell lines to those submitted to the repository, which identifies all individuals who have accessed the information; and

iii) A policy governing whether and how to deliver clinically significant information to donors.

D) Establish the following standard practices:

i) A process for assignment of a unique identifier to each sample;

ii) A process for characterizing cell lines;

iii) A process for expanding, maintaining and storing cell lines;

iv) A system for quality assurance and control;

v) A website that contains specific descriptions and data related to the cell lines available;

vi) A procedure for reviewing applications for cell lines;

vii) A process for tracking disbursed cell lines and recording their status when shipped, including number of times the stem cell line has been subcultured or transferred;

viii) A system for auditing compliance;

ix) A schedule of charges;

x) A statement of intellectual property policies;

xi) A process to create a material transfer agreement or user agreement;

xii) A liability statement; and

xiii) A system for disposal of material.

E) Establish clear criteria for distribution of cell lines, including, but not limited to, written approval of the research by the ESCRO committee or equivalent body at the recipient institution.

k) Research Use of Stem Cell Lines

1) Once stem cell lines have been derived, investigators and grantees shall monitor their use in research.

2) Grantees shall require documentation of the source of all stem cell lines, including whether the cells were imported into the institution or generated locally. The investigator's notice to the institution shall include evidence of written IRB approval of the procurement process, and adherence to Guidelines for Human Embryonic Stem Cell Research. In the case of lines imported from another institution, documentation that these criteria were met at the times of derivation will suffice.

3) Each grantee shall maintain a registry of its investigators who are conducting stem cell research.

4) The investigators shall submit all protocols involving the combination of embryonic stem cells with nonhuman embryos, fetuses or adult animals to the ESCRO committee for consideration of the consequences of the human contributions to the resulting chimeras.

5) The ESCRO committee shall review experiments in which embryonic stem cells, their derivatives or other pluripotent cells are introduced into nonhuman fetuses and allowed to develop into adult chimeras, including consideration of any major functional contributions to the brain.

6) The IRB shall review use of existing stem cells when the research involves introduction of the stem cells or their derivatives into patients or the possibility that the identity of the donors of the blastocysts, gametes or somatic cells is readily ascertainable or might become known to the investigator. Documentation of the IRB's review shall be included with the grant application (see Section 995.100(c)(17)).

l) Research involving nonhuman mammals

1) Standards for the review of research involving nonhuman mammals shall be based on the requirements of the Animal Welfare Act and the Public Health Service Policy on Humane Care and Use of Laboratory Animals (see Section 995.15). All research involving nonhuman animals shall be approved by the institution's IACUC.

2) Introduction of embryonic stem cells into nonhuman mammalian blastocysts shall be considered by investigators and approved by the ESCRO committee only under circumstances in which no other experiment can provide the information needed.

3) Animal embryonic stem cells shall not be transplanted into a human blastocyst.

4) Human embryonic stem cells shall not be transplanted into nonhuman primates.