CALIFORNIA CODE OF REGULATIONS
TITLE 17, DIVISION 4
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

CHAPTER 1. HUMAN STEM CELL RESEARCH

Section 100000 Scope of Chapter & Intent

Under the authority of the California Health and Safety Code Section 125290.35 the Independent Citizens Oversight Committee (ICOC) establishes medical and scientific accountability standards for the conduct of stem cell research as authorized by Article 35 of the California Constitution. It is the intent of the ICOC in the enacting this chapter to assure that research is conducted safely, in accordance with the highest ethically standards, and in compliance with state and national policies that protect patient safety, patient rights and patient privacy.

The standards set forth in this chapter apply to all *institutions* (as defined by CFR 46.102) performing *research* (as defined in 45 CFR Part 46.102) funded by the California Institute of Medicine (CIRM) (as authorized by Article 35 of the California Constitution).

The policy is intended to govern the review and oversight of research involving the derivation and use of human stem cells (as defined in California Health and Safety Code Section 125292.10.?), germ cells and cell-based products. It is the intent of the ICOC, in the enacting this chapter, to require each funded institution to be responsible for providing **assurance satisfactory to CIRM** that research complies with the requirements set forth in this policy.

Section 100001 Definitions

As used in this policy the following terms have the following meaning:

(a) *ESCRO:* means embryonic stem cell research oversight committee established in accord with Section 100004 for the purpose expressed in this policy.

(b) *Ethically derived:* Stem cells derived in accordance with the requirements of section 100006.

(c) *Funded research:* research as defined by CFR 46.102 supported [in whole or part?] by funds authorized by article XXXV of the California Constitution.

(d) *Institution:* as defined by CFR 46.102.

(e) *Research:* as defined by CFR 46.102.

(f) *Somatic Cell Nuclear Transfer (SCNT):* The transfer of a cell nucleus from a somatic cell into an egg from which the nucleus has been removed.

(g) *Stem Cells:* Refers to undifferentiated (i.e., nonspecialized) cells that have the capacity to self-renew (i.e., one or both progeny retain the undifferentiated state) and, to differentiate into mature cells with specialized functions.

Section 100002 Activities Not Eligible for CIRM Funding

(a) Reproductive uses of SCNT prohibited by article XXXV section 3 of the California Constitution

(b) The culture in vitro of any intact human embryo, regardless of derivation method, after the appearance of the primitive streak or after 12 days whichever is earlier. The 12 day prohibition does not count any time during which the blastocysts and/or cells have been stored frozen.

(c) The introduction of human stem cells into nonhuman primate blastocysts and the introduction of any embryonic stem cells into human blastocysts

(d) Research leading to or resulting in the breeding of any animal into which human stem cells have been introduced.

Section 100003 Institutional Assurances of Compliance

All funded research institutions and their investigators shall be responsible for providing written **assurance satisfactory to CIRM** that funded research complies with the requirements set forth in this policy.

Each institution shall at a minimum:

(a) Designate an institutional official responsible for oversight and documentation of compliance for CIRM-funded research.

(b) Designate one or more ESCRO established in accordance with the requirements of section 100004 of this policy.

(c) Designate one or more IRB established in accordance with 45 CFR Part 46 to ensure compliance with section 100005 of this policy.

(d) Ensure that clinical personnel who have a conscientious objection to stem cell research not be required to participate in providing donor information or securing donor consent for research use of gametes or blastocysts. That privilege shall not extend to the care of a donor or recipient.

(e) Failure to comply with requirements set forth in this policy constitutes ground for non-continuation of existing, or disqualification for future, CIRM funding.

Section 100004 ESCRO Requirements

The ESCRO shall provide scientific and ethical review of CIRM-funded research consistent with the requirements of Section 100005, and other applicable CIRM-regulations and policies. The ESCRO shall facilitate the education of investigators involved in stem cell research. An institution, a group of institutions, the CIRM or other State Agency may convene an ESCRO. An

ESCRO may provide oversight for two or more funded research institutions, provided the ESCRO has oversight authority consistent with the requirements of this policy.

(a) Membership: An ESCRO shall be comprised of persons with expertise in developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical and legal issues in stem cell research and at least one person not otherwise affiliated with the research institution.

(b) Function and operation: The designated ESCRO shall provide expertise to support the scientific and ethical review of CIRM-funded research consistent with the requirements of Section 100005, and other applicable CIRM requirements. The ESCRO shall facilitate education of investigators with applicable requirements of this policy.

Section 100005 ESCRO Review & Notification

(a) The designated ESCRO shall **review and have authority to approve**, require modification in, or disapprove in writing all funded research attempting to **derive** human stem cells. At a minimum, the ESCRO shall require the investigator to:

(1) Provide a clearly presented scientific rationale for the need to derive new cell lines. When such research involves the use of embryos and blastocysts a justification for the number needed for derivation shall be provided. If SCNT involving either human or nonhuman oocytes is proposed as a route to generating stem cells justification for SCNT shall be provided.

(2) Demonstrate appropriate expertise or training in derivation or culture of human or nonhuman stem cells before approval is given.

(3) Provide **documentation of compliance** with any required review of the proposed research by an IRB, IACUC, ICB, or other mandated review **prior to commencing research** (recruitment of human subjects) including the requirements of section 100007 of this policy.

(4) Document how stem cells will be characterized, validated, stored, and distributed in accordance with Section 100008 of this policy.

(b) The designated ESCRO shall **review and have authority to approve**, require modification in, or disapprove in writing all funded research attempting to **introduce** human stem cells into nonhuman animals at any state of embryonic, fetal, or postnatal development. At a minimum, the ESCRO shall require the investigator to:

(1) Provide evidence that all human stem cells have been ethically derived

(2) Evaluate the probable pattern and effects of differentiation and integration of the human cells into the nonhuman animal tissues.

(3) Provide **documentation of compliance** with any required review of the proposed research by an IRB, IACUC, ICB, or other mandated review **prior to commencing research**.

(c) The investigator shall **provide written notification** to the designated ESCRO for all purely in vitro funded research utilizing stem cells. At a minimum, the notification shall:

(1) Provide evidence that all human stem cells have been ethically derived

(2) Provide **documentation of compliance** with any required review of the proposed research by an IRB, IACUC, ICB, or other mandated review prior to commencing research.

Section 100006 Ethically Derived Materials

(a) For human stem cells derived **with CIRM funding after** the effective date of this policy to be considered ethically derived, the ESCRO must determine all of the following requirements are satisfied.

(1) Informed consent has been has been obtained in accordance with section 100007.

(2) No payments, cash or in-kind, have been provided for donating oocytes, gametes, blastocysts, or eggs. Individuals may be reimbursed for expenses incurred as a result of a clinical procedure, as determined by an IRB. Individuals who consent to donate stored gamets, blastocysts or eggs may not be reimbursed for the cost of storage prior to the decision to donate.

(3) The physician attending to any donor involved in infertility treatment and the funded researcher shall not be same person unless an IRB has approved an exemption from this requirement.

(4) Assurances are provide that human subjects involved in infertility treatment are not requested to generate more oocytes than necessary for the optimal chance of reproductive success and any infertility clinic or third party responsible for obtaining consent or collecting materials conforms with section (2).

(b) For human stem cells derived **without CIRM funding after** the effective date of this policy to be considered ethically derived, the ESCRO must determine all of the following requirements are satisfied.

(1) All human stem cells used in CIRM-funded research were derived under the oversight of an IRB (or, in the case of foreign sources, an IRB-equivalent) and without payment beyond reimbursement of out-of-pocket costs to the egg, sperm, somatic cell and/or embryo donors.
(2) At a minimum comply with Section ?.

[This section still needs development and discussion; unclear what our standards are for Non-CIRM lines]

(c) For human stem cells derived before the effective date of this policy to be considered ethically derived, the ESCRO must determine all of the following requirements are satisfied:

(1) The human cell lines have been approved by the National Institutes of Health, deposited in the United Kingdom Stem Cell Bank, or derived by, or approved for use by, a licensee of the Human Fertilisation and Embryology Authority or

(2) The human cell lines have been derived under equivalent standards to the United Kingdom Stem Cell Bank or such other benchmark organizations, as recommended by the Standards Working Group and approved by the Independent Citizens' Oversight Committee (as described in CA Health and Safety Code Section 125290.20). At a minimum comply with x-xxy sections 100006 & 100007 (this section and informed consent section)?

Section 100007 Informed Consent Requirements

(a) All funded research involving human subjects as defined in CFR 46.102 shall be performed in accordance with CFR 46 Protection of Human Subjects and California Health and Safety Code Section 24170-24179.5. In addition, to the general requirements for informed consent of the California Health and Safety Code Section 24173 the IRB shall require the following:

(1) For research involving the procurement or derivation of cells or cell derived materials:

(A) A statement as to whether the identities of the donors will be readily ascertainable to those who derive or work with the resulting stem cells.

(B) If the identities of the donors are retained (even if coded), a statement as to whether donors wish to be contacted in the future to receive information obtained through studies of stem cells.

(C) An assurance that participants in research projects will follow applicable and appropriate best practices for donation, procurement, culture, and storage of stem cells, in particular, the traceability of stem cells; provided, however, that traceable information shall be secured to ensure confidentiality.

(D) A statement that stem cells might be kept for many years.

(E) A statement that the stem cells may be used for research involving human transplantation.

(F) A statement that the stem cells s might be used in research involving genetic manipulation of the cells or the mixing of human and nonhuman cells in animal models.

(G) Disclosure of the possibility that the results of research may have commercial potential and a statement that the donor will not receive financial or any other benefits from any future commercial development;

(H) A statement that the research is not intended to provide direct medical benefit to the donor(s) except in the case of autologous donation.

(I) A statement that embryos will be destroyed in the process of deriving stem cells.

(J) A statement that neither consenting nor refusing to donate embryos for research will affect the quality of any future care provided to potential donors.

(2) In addition to the requirements of section (1), research involving the use of identifiable blastocysts, gametes or cells derived from fetal tissue, the umbilical cord or placenta consent shall be obtained from each donor or parent.

(b) The consent process shall ascertain whether donors have objections to any specific forms of research to ensure that their wishes are honored, and donors shall be offered the option of agreeing to some forms of research but not others.

Section 100008 Research Tracking, Materials Banking & Distribution

Stem cell lines derived through CIRM-funded research shall be tracked, banked and distributed in accordance with this section.

(a) Each institution shall track CIRM-funded research activities. At a minimum, the institution shall maintain a research registry that includes, but is not limited to, documentation of:
(1) stem cell research conducted by the intuition;
(2) stem cells lines derived or used by institutional investigators;
(3) any required review or notification requirement as described in Section 100005,
(4) the methods utilized to characterize and screen the materials for safety;
(5) the conditions under which the materials have been maintained and stored.
(6) any additional requirements set forth in CIRM grants policy (cite regulations).

(b) Cell lines derived thorough CIRM-funded research shall be made available to other investigators within 12 months of filing a full patent or upon the date of publication of an article regarding the research in a peer review journal, which ever is earlier. Cell lines shall be made available in a manner to enable ["functional replication" or/and "full enabling replication"] of such lines. A requirement of ESCRO review or notification, consistent with the requirements of Section 100006, may be required as a condition of release of cell lines to other investigators [counter signature]. Cell lines may be made available through:
(1) the institution or investigator responsible for the original derivation;
(2) an designated stem cell bank;
(3) a CIRM designated stem cell bank