*2/6/2006 – Proposed CIRM MES Regulations: Recommended by the Scientific and Medical Accountability Standards Working Group*

As part of its commitment to public participation in the development of scientific, medical and ethical standards; the Scientific and Medical Accountability Standards Working Group of the California Institute of Regenerative Medicine is providing Draft CIRM Regulations to all interested parties. Additional supporting document may be found at: http://www.cirm.ca.gov/working_group/standards.asp. The Scientific and Medical Accountability Standards Working Group is committed to an open, inclusive and deliberative process. This working group invites participation at all of its open meetings. CIRM and its working groups' commitment to public participation goes beyond that required by California law. Pursuant to the California Administrative Procedure Act, additional public participation will be invited once the rulemaking record is open.

# DRAFT RECOMMENDED REVISIONS TO CALIFORNIA CODE OF REGULATIONS TITLE 17, DIVISION 4 CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

## CHAPTER 1. STEM CELL RESEARCH

### Section 100000 Scope of Chapter & Intent

Under the authority of the California Health and Safety Code Section 125290.35 [cite date] the Independent Citizen's 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 CIRM-funded research is conducted safely, in accordance with the highest ethical 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) [cite date] performing *research* (as defined in 45 CFR Part 46.102) [cite date] funded by the California Institute of Medicine (CIRM) as authorized by Article 35 of the California Constitution [cite date].

The policy is intended to govern the oversight of CIRM-funded research. 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 chapter:

"Covered stem cell line" means a culture-derived, human stem cell population that is capable of: 1) sustained propagation in culture; 2) differentiation along multiple cell lineages; and 3) self-renewing to produce daughter cells with equivalent developmental potential. This definition includes both embryonic and non-embryonic human stem cell lines regardless of the tissue of origin.

(a) "Acceptably derived" means derived in accordance with the requirements of section 100007 and 100008.

(b) "Permissible expenses" means necessary and reasonable costs directly incurred as a result of donation or participation in research activities. Permissible expenses may include but are not limited to costs associated with travel, housing, child care, medical care, health insurance and actual lost wages.

(c) "Research" means activities defined as research by 45 CFR 46.102 [cite date].

(d) "Funded research" means research supported in whole or part by funds authorized by article XXXV of the California Constitution. For the purpose of this chapter, training activities supported by such funds shall be considered funded research.

(e) "Human subjects" means individuals defined as research subjects by 45 CFR 46.102 [cite date].

(f) "Institution" means entities defined as institutions in by 45 CFR 46.102 [cite date].

(g) "Stem Cell Research Oversight Committee (SCRO committee)" means a committee established in accordance with Section 100005.

(h) "Somatic Cell Nuclear Transfer (SCNT)" means the transfer of a cell nucleus from a somatic cell into an oocyte from which the nucleus has been removed.

**Section 100002 Activities Not Eligible for CIRM Funding**

The following activities are not eligible for CIRM funding:

(a) Human reproductive cloning (as defined in H&S Code 125292.10(k)) [cite date] or reproductive uses of SCNT prohibited by article XXXV section 3 of the California Constitution [cite date].

(b) The culture in vitro of (i) any intact human embryo or (ii) any product of SCNT, parthogenesis or androgenesis, 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 embryos and/or cells have been stored frozen.

(c) The introduction of stem cells from a covered stem cell line into nonhuman primate embryos.

(d) The introduction of stem cells from a covered stem cell line into human embryos.

(e) The introduction of any stem cells, whether human or nonhuman, into human embryos.

(f) Breeding any animal into which stem cells from a covered stem cell line have been introduced.

**Section 100003 Institutional Assurances of Compliance**

All research institutions shall be responsible for providing written assurance satisfactory to CIRM that CIRM-funded research complies with the requirements set forth in this chapter.

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 SCRO committee(s) established in accordance with the requirements of section 100005.

(c) Designate one or more IRB(s) established in accordance with 45 CFR 46.XXX [cite date].

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

**Section 100004 Compliance**

Grantees must report promptly to CIRM any failure to comply with the terms and conditions of an award. If a grantee fails to comply with the terms and conditions of an award, CIRM may take one or more actions, depending on the severity and duration of the non-compliance. Depending on the nature of the deficiency, CIRM actions may include, but are not limited to the following:

(a) Temporary withholding of payment;

(b) Placing special conditions on awards;

(c) Conversion to a reimbursement payment method;

(d) Precluding the grantee (PI or grantee organization as appropriate) from obtaining future awards for a specified period;

(e) Debarment from receipt of further CIRM funds;

(f) Recovery of previously awarded funds;

(g) Civil action, including referring the matter to the Office of the Attorney General of California for investigation and enforcement;

(h) Other available legal remedies.

**Section 100005 SCRO Committee Membership and Function**

(a) An SCRO committee shall be comprised of persons with expertise including but not limited to developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical issues in stem cell research. An SCRO committee shall include at least one representative of the public who is not employed by, appointed to, or remunerated by the relevant research institution. In addition, an SCRO committee shall include at least one patient advocate. No SCRO committee member may have a financial conflict of interest in the research under review.

(b) The designated SCRO committee shall provide scientific and ethical review of CIRM-funded research consistent with the requirements of Section 100006 and other applicable CIRM requirements.

(c) The SCRO committee shall facilitate education of investigators with applicable requirements of this chapter.

(d) An SCRO committee may provide oversight for two or more funded research institutions, provided the SCRO committee has oversight authority consistent with the requirements of this chapter.

(e) An SCRO committee may be convened by an institution, a group of institutions, the CIRM or other state agency.

**Section 100006 SCROC Review & Notification**

(a) CIRM-funded research involving ***derivation of covered stem cell lines or use of human oocytes or embryos*** in stem cell research may not commence without SCRO committee review and approval in writing. The designated SCRO committee may require that modification be made to proposed research or documentation of compliance with the requirements of 100006(a)(3) as a condition of granting its approval. At a minimum, the SCRO committee shall require the investigator to:

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

(2) Demonstrate experience, expertise or training in derivation or culture of human or nonhuman stem cell lines .

(3) Provide documentation of compliance with any required review of the proposed research by an IRB, IACUC, IBC, or other mandated review.

(4) Document how stem cell lines will be characterized, validated, stored, and distributed to ensure that the confidentiality of the donor(s) is protected.

(b) CIRM-funded research ***introducing covered stem cell lines into human or non-human animals*** at any state of embryonic, fetal, or postnatal development may not commence without SCRO committee review and approval in writing. The designated SCRO committee may require that modification be made to proposed research or documentation of compliance with the requirements of 100006(b)(3) as a condition of granting its approval. At a minimum, the SCRO Committee shall require the investigator to:

(1) Provide assurance that all covered stem cell lines have been acceptably derived.

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

(3) Provide documentation of compliance with any required review of the proposed research by an IRB, IACUC, IBC, or other mandated review.

(c) CIRM-funded ***purely in vitro research*** utilizing covered stem cell lines may not commence without written notification to the designated SCRO Committee. At a minimum, the notification shall:

(1) Provide assurance that all covered stem cell lines have been ethically derived.

(2) Provide documentation of compliance with any required review of the proposed research by an IRB, IACUC, IBC, or other mandated review.

**Section 100007 Acceptable Research Materials**

All covered stem cell lines used in CIRM-funded research must be acceptably derived. To be acceptably derived, the stem cell line must either:

(a) Have been approved by the National Institutes of Health, or

(b) Been deposited in the United Kingdom Stem Cell Bank, or

(c) Been derived by, or approved for use by, a licensee of the United Kingdom Human Fertilisation and Embryology Authority, or

(d) Been 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) Have been derived under the following conditions:

(1) Donors of gametes, embryos, somatic cells or human tissue gave voluntary and informed consent.

(2) Donors of gametes, embryos, somatic cells or human tissue did not receive valuable consideration. This provision does not prohibit reimbursement for permissible expenses as determined by an IRB;

(3) Donation of gametes, embryos, somatic cells or human tissue was overseen by an IRB (or, in the case of foreign sources, an IRB-equivalent);

(4) Individuals who consented to donate stored gametes, embryos, somatic cells or human tissue were not be reimbursed for the cost of storage prior to the decision to donate.

**Section 100008 Additional Requirements for CIRM-Funded Derivation**

Where CIRM funds are to be used to derive new human stem cell lines, in addition to the requirements of Section 100007(e), the SCRO must confirm that the following additional requirements have been met:

(a) Donors of gametes, embryos, somatic cells or human tissue have given voluntary and informed consent in accordance with section 100009.

(b) When procurement of oocytes are required for derivation, the following conditions have been met:

(1) For women providing oocytes for research and clinical infertility treatment (either for herself or another women), research shall not compromise the optimal reproductive success of the woman in infertility treatment.

(2) The funded institution has assumed the cost of any medical care required as a direct and proximate result of oocyte donation for research.

(3) The physician attending to any donor and the principal investigator shall not be the same person unless exceptional circumstances exist and an IRB has approved an exemption from this requirement.

(c) The researcher or institution maintains a record of every gamete, somatic cell, embryo donation or product of SCNT that has been donated, created or used. This record should be sufficient to determine the provenance and disposition of such materials.

**Section 100009 Informed Consent Requirements**

All CIRM-funded human subjects research shall be performed in accordance with 45 CFR 46 Subpart A [cite date] (Protection of Human Subjects) and California Health and Safety Code Section 24173 [cite date]. In accordance with existing law, California Health and Safety Code Section 24173 does not apply to a person who is conducting research as an investigator within an institution that holds an assurance with the United States Department of Health and Human Services pursuant to 45 CFR Part 46 [cite date] and who obtains informed consent in the method and manner required by those regulations.

(a) CIRM-funds may not be used for research that violates the documented preferences of donors with regard to the use of their donated materials. To ensure donors are fully informed of the potential uses of donated materials, researchers shall disclose, in addition to the general requirements for informed consent, all of the following, unless a specific item has been determined by the SCRO or IRB to be inapplicable to the current of potential future uses:

(1) Derived cells or cell products may be kept for many years.

(2) Whether the identity(ies) of the donor(s) will be ascertainable to those who work with the resulting cells or cell products. If the identities of the donor(s) are retained (even coded), CIRM-funded researchers must discuss any plans for recontact of donors of materials used to derive cell lines and obtain consent for recontact. This requirement includes both recontacting donors to provide information about research findings and recontacting donors to ask for additional health information. Donors may be recontacted in the future only if they consent to recontact at the time of donation.

(3) Researchers may use cell lines for future studies, some of which may not be predictable at this time.

(4) Derived cells or cell products may be used in research involving genetic manipulation.

(5) Derived cells or cell products may be transplanted into humans or animals.

(6) Derived cells or cell products are not intended to provide direct medical benefit to the donor(s), except in the case of autologous donation.

(7) The donation is being made without restriction regarding who may be the recipient of transplanted cells, except in the case of autologous donations.

(8) That neither consenting nor refusing to donate materials for research will affect the quality of any future care provided to potential donors.

(9) That the results of research may be patentable or have commercial potential, and that the donor will not receive patent rights and will not receive financial or any other benefits from future commercial development.

(b) Researchers shall offer donors an opportunity to document their preferences regarding future uses of their donated materials. Researchers may choose to use materials only from donors who agree to all future uses.

(c) For CIRM-funded research involving the donation of oocytes, the following additional requirements apply:

(1) The description of foreseeable risk shall include but not be limited to information regarding the risks of ovarian hyperstimulation syndrome, bleeding, infection, anesthesia and pregnancy.

(2) Steps shall be taken to enhance the informed consent process. Measures to do so shall include, but are not limited to, an adequate period of time, as determined by an IRB, to deliberate about the decision to donate. In the case of such periods of deliberation, researchers may not solicit potential donors until they have initiated recontact with the researchers.

(3) The researcher shall ascertain that the donor has understood the essential aspects of the research. Researchers may meet this requirement by following a process that is approved by the designated Institutional Review Board or SCRO committee. Understanding the essential aspects of the research includes understanding at least that:

A. Their eggs will not be used for reproductive purposes.
B. There are medical risks in oocyte donation, including the risks of ovarian hyperstimulation syndrome, bleeding, infection, anesthesia, and pregnancy.
C. The research will not benefit them or any other individuals directly at this time.
D. Whether stem cell lines will be derived from their oocytes through fertilization, SCNT, parthenogenesis, or some other method.
E. Stem cell lines developed from their oocytes will be grown in the lab and shared with other researchers for studies in the future.
F. If stem cells are to be transplanted into patients, researchers might recontact the donor to get additional health information.
G. Donors receive no payment beyond reimbursement for permissible expenses.
H. Stem cell lines derived as a result of their oocyte donation may be patented or commercialized, but donors will not share in patent rights or in any revenue from

the patents.

(d) For CIRM-funded research involving the donation of embryos for stem cell research, the informed consent process, should, include a statement that embryos will be destroyed in the process of deriving embryonic stem cells.

(e) For CIRM-funded research involving the donation of the umbilical cord, cord blood or the placenta, consent shall be obtained from each known legal parent, guardian or progenitor. Informed consent should include a statement as to whether the donated cells may be available for autologous treatment in the future.

(f) For CIRM-funded research involving the donation of somatic cells for SCNT, informed consent shall include a statement as to whether the donated calls may be available for autologous treatment in the future.

**Section 100010 Fairness and Diversity in Research**

CIRMgrantees shall comply with the California Health Research Fairness Act (Health and Safety Code, Sections 439.900-439.906) [cite date] and Inclusions of Women and Minorities in Clinical Research Act (Health and Safety Code, Sections 100237-100239) [cite date].

**Section 100011 Record Keeping**

Each grantee's institution shall maintain records of all CIRM-funded research activities. At a minimum, the institution shall maintain a research registry that includes, but is not limited to, documentation of:

(1) CIRM-funded stem cell research conducted by the institution;
(2) Any required review or notification requirement as described in Section 100006,
(3) The methods utilized to characterize and screen the materials for safety;
(4) The conditions under which the materials have been maintained and stored.
(5) Any additional requirements set forth in CIRM grants policy [cite regulations].

**Section 100012 Materials Sharing**

Stem cell lines and biomedical materials developed with CIRM funding at academic, commercial research and development organizations shall be broadly disseminated. CIRM-funded research institutions shall comply with the CIRM-IP policy intended to ensure data and materials sharing.