CALIFORNIA'S STEM CELL AGENCY

CONSIDERATION OF AMENDMENTS TO CIRM MEDICAL AND ETHICAL STANDARDS

To: Members, Governing Board
From: Geoffrey Lomax, Senior Officer
Date: July 14, 2015
Re: Amendments to the CIRM Medical and Ethical Standards

Executive Summary

CIRM's Medical and Ethical Standards regulations – MES regulations – establish policies for oversight of CIRM awards. The MES regulations are generally modeled on the National Academies' Guidelines for Human Embryonic Stem Cell Research, with differences that reflect CIRM's distinct role and mission.

The MES regulations were adopted by the ICOC in August 2006. The MES regulations have been amended periodically to reflect experience gained from implementation and changes in the science of stem cell research.

In April of this year, the Scientific and Medical Accountability Standards Working Group convened to consider new amendments to the MES regulations. One of the primary goals of these amendments is to align the MES regulations with CIRM 2.0 and associated revisions to the Grants Administration Policy already approved by the ICOC. Thus, the proposed amendments (see attachment) are designed to provide agency-wide alignment of operations, procedures and policies.

Amendments for ICOC Consideration:

A series of amendments (see attachment) were considered at a public meeting of the CIRM Scientific and Medical Accountability Standards Working Group in April 2015. The proposed amendments are grouped into three categories.

(1) Amendments intended to align MES Regulations with CIRM 2.0 & GAP revisions

These amendments primarily involve incorporating terms such as "grantee" that are in the revised GAP. In addition, the term "human subjects research" is defined to align the MES regulations with Federal policies for protection of research subjects.

(2) Amendments intended to make the regulations clearer and easier to implement

These amendments primarily involve section 100050 Compliance and 100085 Fetal Tissue. Section 100050 contains provisions identical to those in CIRM's Grants Administration Policy. Rather that re-state the requirements here, CIRM proposes referring to the applicable section of the GAP. Section 100085 reiterates Federal policy regarding use of fetal tissue in research. CIRM proposes referencing the applicable Federal policy requirement.

(3) Amendments to regulatory review and oversight

Two policy changes relating to animal studies are proposed. The first change to section 100030 would allow the breeding of animals where covered stem cell lines have been introduced provided human genetic material does not contributed to the germ line. This policy is consistent with the 2010 National Academies' Guidelines for Human Embryonic Stem Cell Research and is designed to allow multi-generational safety studies of stem cell therapies in animal models.

The second change proposes to exempt pre-clinical animal studies, where human neural progenitor cells are transplanted to the brains of mature animals, from review by a stem cell research oversight committee provided the study is being performed pursuant to an FDA IND or IDE. The rationale for this change is twofold. First, institutional animal care and use committees (IACUCs) provide oversight for animal studies. Second, a major goal of the CIRM 2.0's Late Stage Preclinical Projects is to speed the introduction of therapies into the clinic. Organizations applying under CIRM 2.0 may not have access to a stem cell research oversight committee thus creating a potential barrier to entry.

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

The CIRM Medical and Ethical Standards Regulations

Notes to the reader:

- This document contains a reformatted version of the CIRM Medical and Ethical Standards regulations. The official version of these regulations may be found at http://www.oal.ca.gov/.
- Additional regulations may be applicable to CIRM funded research. See: http://www.cirm.ca.gov/cirm-operations/Regulations

§ 100010. Scope of Chapter 2 – Stem Cell Research.

The standards set forth in this chapter apply to ~~all institutions~~ awardees, as defined by Title 17, California Code of Regulations, section 100020, subdivision (XX), performing research, as defined in Title 17, California Code of Regulations, section 100020, subdivision (d), funded by the California Institute for Regenerative Medicine (CIRM) as authorized by Article XXXV of the California Constitution.

§ 100020. Definitions.

As used in this chapter:

(a) "Acceptably derived" means derived in accordance with the requirements of Code of California Regulations, Title 17, sections 100080 and 100090.

(b) "CIRM" means the California Institute for Regenerative Medicine.

(c) "Covered stem cell line" means a culture-derived, human pluripotent stem cell population that is capable of: (1) sustained propagation in culture; and (2) self-renewal 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. "Pluripotent" means capable of differentiation into mesoderm, ectoderm, and endoderm.

(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 subject" means a living individual about whom an investigator (whether professional or student) conducting research obtains:

(1) Data through intervention or interaction with the individual, or

(2) Identifiable private information.

(ee) "Human subjects research" is research defined by Title 45 Code of Federal Regulations, Part 46 (Protection of Human Subjects), revised June 23, 2005.

(f) ~~"Institution" means any public or private entity or agency (including federal, state, local or other agencies).~~

"Awardee" An Organization that is the Recipient of an Award and that is legally responsible and accountable for the use of the funds provided and for the performance of the CIRM funded Project or Activity. The Awardee is the entire legal entity even if a particular component is designated in the NGA. Campuses of the University of California shall be considered as separate and individual Awardees.

(g) "Institutional Review Board" ("IRB") is an entity established in accordance with Title 45, Code of Federal Regulations, section 46.107, revised June 23, 2005.

(h) "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.

(i) "Research" means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of these regulations, whether or not they are conducted or supported under a program which is considered research for other purposes.

(j) "Somatic Cell Nuclear Transfer" ("SCNT") means the transfer of a somatic cell nucleus into an oocyte.

(k) "Stem Cell Research Oversight Committee" ("SCRO" committee) means a committee established in accordance with Code of California Regulations, Title 17, section 100060.

§ 100030. Activities Not Eligible for CIRM Funding.

The following activities are not eligible for CIRM funding:

(a) Human reproductive cloning, as defined in California Health and Safety Code Section 125292.10. subdivision (k), or reproductive uses of SCNT prohibited by article XXXV, section 3, of the California Constitution.

(b) The culture in vitro of (i) any intact human embryo or (ii) any product of SCNT, parthenogenesis 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 any stem cells, whether human or nonhuman, into human embryos.

(e) Breeding any animal into which covered stem cells ~~from a covered stem cell line~~ have been introduced such that they could contribute to the germ line.

(f) The transfer to a uterus of a genetically modified human embryo.

§ 100040. Institutional Assurance of Compliance.

(a) All ~~research institutions~~ awardees 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~~

(1) All awardees shall ensure that the chancellor, chief executive officer or person with plenary authority designates an institutional official responsible for oversight of and documentation of compliance ~~for CIRM-funded research~~;

(b) All awardees conducting human subjects research or research requiring SCRO committee review and approval under Code of California Regulations, title 17, section 100070 shall.

(1) Designate one or more IRB(s);

(2) Designate one or more SCRO committee(s) established in accordance with the requirements of Code of California Regulations, title 17, section 100060.

(c) All awardees shall ensure that clinical personnel conducting human subjects research, 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.

§ 100050. Compliance.

[Cite: Failure Compliance and Award Termination from Grants Administration Policy; regulation below is duplicative if this section of the GAP]

~~Grantees must report promptly to CIRM any failure to comply with the terms and conditions of an award. Depending on the severity and duration of the non-compliance, 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 (principal investigator (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 the State of California for investigation and enforcement;~~
~~(h) Other available legal remedies.~~

§ 100060. SCRO Committee Membership and Function.

(a) A SCRO committee shall be comprised of persons with expertise in, including but not

limited to, developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical issues in stem cell research. A SCRO committee shall include at least one non-scientist member of the public who is not employed by, or part of the immediate family of a person who is affiliated with the institution. In addition, a SCRO committee shall include at least one patient advocate.

(b) Any member of a SCRO committee may be reimbursed for reasonable out-of-pocket expenses for attending the meeting, not including lost wages. No SCRO committee may have a member participate in the SCRO committee's initial or continuing review of any project in which the member has a conflicting interest, except to provide information to the SCRO committee.

(c) The designated SCRO committee shall provide scientific and ethical review of CIRM-funded research consistent with the requirements of Section 100070 and other applicable CIRM requirements.

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

(e) A 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.

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

§ 100070. SCRO Committee Review and Notification.

(a) ~~CIRM-funded~~ Research involving the procurement or use of human oocytes or the creation of human gametes may not commence without SCRO committee review and approval in writing. If ~~CIRM-funded~~ research involves the procurement of human oocytes from a living donor, a member of the committee with expertise in assisted reproduction shall be present. The designated SCRO committee may require that modification be made to proposed research or documentation of compliance with the requirements of subdivision (a)(3) of this regulation as a condition of granting its approval. At a minimum, the SCRO committee shall require the investigator to:

(1) Provide an acceptable scientific rationale for the need to procure or use human oocytes or create human gametes. In the case of human oocyte procurement a justification for the number needed shall be provided. If SCNT is proposed a 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, Institutional Animal Care and Use Committee (IACUC), Institutional Bioethics Committee (IBC), or other mandated review.

(b) ~~CIRM-funded~~ Research involving procurement, creation or use of human blastocysts or embryos 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 subdivision (b)(3) of this regulation as a condition of granting its approval. At a minimum, the SCRO committee shall require the investigator to:

(1) Provide an acceptable scientific rationale for the need to create or use blastocysts or embryos including a justification for the number needed.

(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, Institutional Animal Care and Use Committee (IACUC), Institutional Bioethics Committee (IBC), or other mandated review.

(c) ~~CIRM-funded~~ Human subjects research, ~~as defined by Title 45 Code of Federal Regulations, Part 46 (Protection of Human Subjects), revised June 23, 2005, and California Health and Safety Code section 24173~~ with the aim to create, from sources other than human gametes, blastocysts or embryos, ~~or use~~ a covered stem cell line may not commence without written notification of the SCRO committee. A

statement from the designated institutional official (section 100040(b)(1)) may be provided in lieu of SCRO committee notification. The institutional official shall submit documentation of any required review of the proposed research by an IRB, IACUC, IBC, or other mandated review. Research may include animal assays to evaluate pluripotency; however, subsequent introduction of derived covered stem cell lines in non-human animals shall be reviewed in accordance with section (e). The designated SCRO committee may require the investigator to:

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

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

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

(d) ~~CIRM-funded~~ Purely in vitro research with the aim to create or use a covered stem cell line from non-identifiable cells may not commence with out written notification of the SCRO committee. A statement from the designated institutional official (section 100040(b)(1)) may be provided in lieu of SCRO committee notification if human somatic cells conform to the requirements of Section 100080(a)(3); or the covered stem cell line(s) are recognized by an authorized authority. At a minimum the statement shall certify the:

(1) Human somatic cells conform to the requirements of Section 100080(a)(3); or

(2) The covered stem cell lines are recognized by an authorized authority.

In addition, the institutional official shall submit documentation of any required review of the proposed research by an IRB, IACUC, IBC, or other mandated review. Research may include animal assays to evaluate pluripotency; however, subsequent introduction of derived covered stem cell lines in non-human animals shall be reviewed in accordance with section (e).

(e) The introduction of covered stem cells into nonhuman mammalian blastocysts or fetuses or introducing human neural-progenitor cells into the brain of non-human animals at any state of embryonic, fetal, or postnatal development may not commence without SCRO committee review and approval in writing. Studies involving postnatal animals performed pursuant to a FDA Investigational New Drug (IND) or Device application are exempt from SCRO committee review and approval. The designated SCRO committee may require that modification be made to proposed research or documentation of compliance with the requirements of subdivision (e)(3) of this regulation as a condition of granting its approval. The SCRO committee may establish guidelines and procedures for expedited review of animal research so that review by the entire SCRO committee is not required. At a minimum, the SCRO committee shall require the investigator to:

(1) Provide an acceptable scientific rationale for introducing stem cells into non-human animals.

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

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

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

(f) CIRM-funded research introducing cells from covered stem cell lines into a live born human 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 subdivision (f)(4) of this regulation as a condition of granting its approval. At a minimum, the SCRO committee shall require the investigator to:

(1) Provide an acceptable scientific for rationale introducing stem cells into humans.

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

(3) Evaluate the probable pattern and effects of differentiation and integration of the human cells into the human tissues.
(4) Provide documentation of compliance with any required review of the proposed research by an IRB, IACUC, IBC, or other mandated review.

(g) In cases where SCRO committee approval is required, a SCRO committee shall notify investigators in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure SCRO committee approval of the research activity. If the SCRO committee decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(h) SCRO committee approvals shall be reviewed no less frequently than once per year. The renewal review shall confirm compliance with all applicable rules and regulations. The SCRO committee may establish guidelines and procedures for expedited review of renewals so that review by the entire SCRO committee is not required.

§ 100080. Acceptable Research Materials.

All covered stem cell lines used in CIRM-funded research must be "acceptably derived."

(a) To be "acceptably derived," the covered stem cell line must meet one of the following three criteria:
(1) The covered stem cell line is recognized by an authorized authority. To be recognized by an authorized authority the stem cell line must:
(A) Be approved by the National Institutes of Health; or
(B) Be deposited in the United Kingdom Stem Cell Bank; or
(C) Be derived by, or approved for use by, a licensee of the United Kingdom Human Fertilization and Embryology Authority; or
(D) Be 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) Be derived in accordance with the Japanese Guidelines for Derivation and Utilization of Human Embryonic Stem Cells; or
(F) Be derived under license of the Australian National Health and Medical Research Council; or
(G) Be derived in accordance with California Code of Regulations, title 17, section 100090.
(2) The covered stem cell line is derived under the following conditions:
(A) Donors of human gametes, embryos, somatic cells or tissue gave voluntary and informed consent; and
(B) Donors of human gametes or embryos did not receive valuable consideration. For embryos originally created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose "valuable consideration" does not include payments to original gamete donors in excess of "permissible expenses." Original gamete donors may receive reimbursement for permissible expenses as defined in California Code of Regulations, title 17, section 100020, subdivision (h), and
(C) Donation of human gametes, embryos, somatic cells or tissue was overseen by an IRB (or, in the case of foreign sources, an IRB-equivalent); and
(D) Individuals who consented to donate stored human gametes, embryos, somatic cells or tissue were not reimbursed for the cost of storage prior to donation.
(3) The covered stem cell line is derived from non-identifiable human somatic cells under the following conditions:
(A) The derivation did not result from the transfer of a somatic cell nucleus into a human oocyte (SCNT) or the creation or use of a human embryo; and
(B) The somatic cells have no associated codes or links maintained by anyone that would identify to the investigator(s) the donor of the specimens, or, if such

codes or links exist, that the identity of the donor is not readily ascertainable because, for example:

(i) The key to decipher the code or link is destroyed before the research begins;

(ii) An agreement prohibits release of the key to the investigators under any circumstances;

(iii) IRB-approved written policies and operating procedures for a repository or data management center prohibit releasing the key under any circumstances; or

(iv) The release of the key to the investigators is forbidden by law.

(b) In addition to the requirements of subdivision (a) of this chapter, the following requirements apply to the derivation and use of all covered stem cell lines.

(1) Any covered stem cell line derived from any intact human embryo, any product of SCNT, parthenogenesis or androgenesis after 12 days in culture may not be used unless prior approval is obtained from the Independent Citizens Oversight Committee, constituted under Health & Safety Code, section 125290.15. Use of any covered stem cell line derived from any intact human embryo, any product of SCNT, parthenogenesis or androgenesis after 14 days or after the appearance of the primitive streak is prohibited. The 12-14 day limit does not include any time during which the cells have been frozen.

(2) Any payments for the purchase of covered stem cell lines, somatic cells, or human tissue to persons other than the original donors shall be limited to those costs identified in Health & Safety Code, section 125290.35, subdivision (b)(5). Any payment for gametes and embryos, to persons other than the original donors, shall be limited to necessary and reasonable costs directly incurred as a result of providing materials for research, which include but are not limited to expenditures associated with processing, quality control, storage, or transportation.

§ 100081. Petition for Lines Derived Prior to November 22, 2006.

For a covered stem cell line derived before November 22, 2006, the ICOC may find in public session that it is acceptably derived pursuant to the following procedure:

(a) A person or entity seeking ICOC approval for a covered stem cell line not otherwise acceptably derived under Title 17, California Code of Regulations, section 100080, shall submit a petition in a form as required by CIRM. That petition shall, at a minimum, provide the following information:

(1) The name or designation of the covered stem cell line;

(2) Information about the nature of the consents given by the donors of human gametes, embryos, somatic cells or tissue used to create the covered stem cell line, including copies of any such consents given;

(3) Information about whether the donors of human gametes, embryos, somatic cells or tissue used to create the covered stem cell line received valuable consideration in exchange for their donation, including copies of any documents reflecting such exchanges;

(4) Information about whether the donation of human gametes, embryos, somatic cells or tissue used to create the covered stem cell line was overseen by an IRB or equivalent, including copies of any documents reflecting such a review;

(5) Information about whether the donors of human gametes, embryos, somatic cells or tissue used to create the covered stem cell line were reimbursed for the cost of storage prior to donation, including copies of any documentation reflecting such reimbursements;

(6) Information regarding ”best practices” at the time of donation of human gametes, embryos, somatic cells or tissue, including any documents substantiating those practices for each type of donation;

(7) A statement describing the scientific and/or clinical necessity for granting the petition; and

(8) Information submitted in connection with the petition that is of a

confidential or proprietary nature as defined in H&S Code section 125290.30, subdivisions (e)(B) or (C), or that is protected from disclosure pursuant to other federal or state law shall not be subject to disclosure pursuant to those laws.

(b) Within 60 days of receipt of a complete petition, the President of CIRM will prepare a written recommendation to the ICOC, and provide a copy of that recommendation to the petitioner. The recommendation will describe the petition and the evidence without revealing confidential and proprietary information, will include an analysis of the petition, and a statement of reasons for granting or denying the petition.

(c) Within 30 days of receipt of the President's recommendation, the petitioner may submit a response to CIRM. Once that response is received, the petition will be placed on the agenda for the next regularly scheduled ICOC meeting.

(d) The President's recommendation and the petitioner's response shall be provided to the ICOC and the public (by posting on the CIRM website) at least ten days prior to the date of the meeting at which the ICOC will consider the petition.

(e) The ICOC must consider the merits of the petition in open session, and must vote to grant or deny the petition in open session. Members of the ICOC may request access to confidential and proprietary information in the petition during closed session before acting on the petition.

(f) The decision of the ICOC to grant or deny the petition is final and not subject to appeal.

§ 100085. Use of Fetal Tissue.

Reference Public Law 103-43; JUNE 10, 1993 sections (a)-(c[1][2]),

~~Fetal tissue shall be procured in accordance with 17 Cal. Code Regs. section 100080, subdivision (a)(2). In addition, research involving human fetal tissue will adhere to the following provisions:~~

~~(a) The woman who donates the fetal tissue must sign a statement declaring:~~

~~(1) That the donation is being made for research purposes, and~~

~~(2) The donation is made without any restriction regarding who may be the recipient(s) of materials derived from the tissue; and~~

~~(b) The attending physician must:~~

~~(1) Sign a statement that he or she has obtained the tissue in accordance with the donor's signed statement. In the case of tissue obtained pursuant to an induced abortion, the physician must sign a statement stating that he or she:~~

~~(A) Obtained the woman's consent for the abortion before requesting or obtaining consent for the tissue to be used for research;~~

~~(B) Did not alter the timing, method, or procedures used to terminate the pregnancy solely for the purpose of obtaining the tissue for research; and~~

~~(C) Performed the abortion in accordance with applicable law.~~

~~(2) Disclose to the donor any financial interest that the attending physician has in the research to be conducted with the tissue.~~

~~(3) Disclose any known medical risks to the donor or risks to her privacy that might be associated with the donation of the tissue and that are in addition to risks of such type that are associated with the woman's medical care.~~

~~(c) The principal investigator of the research project must sign a statement certifying that he or she:~~

~~(1) Is aware that the tissue is human fetal tissue obtained in a spontaneous or induced abortion or pursuant to a stillbirth;~~

~~(2) Is aware that the tissue was donated for research purposes;~~

~~(3) Had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy; and~~

~~(4) Is not the donor's attending physician.~~

§ 100090. Special Considerations for CIRM-Funded Procurement, Derivation and Transplantation

(a) Where CIRM funds are to be used for research intended to derive a covered stem cell line, the SCRO committee must determine or the designated institutional official must certify the applicable

requirements of Code of California Regulations, title 17, section 100080, subdivision (a)(2) or (a)(3) and title 17, section 100080, subdivision (b) have been met, subject to the following:

(1) For embryos created before November 22, 2006 consent exclusively from oocyte donors is sufficient provided the sperm donor cannot be identified and the donation was made in accordance with the legal requirements in force at the place and time of donation.

(2) For gametes or embryos, procured from human subjects, after November 22, 2006, the SCRO committee must confirm that donors provided voluntary and informed consent in accordance with Code of California Regulations, title 17, section 100100, subdivision (b).

(3) For research involving the use of embryos originally created using in vitro fertilization for reproductive purposes, the physician performing oocyte retrieval or attending physician responsible for infertility treatment may not be the CIRM-funded Principal Investigator (as defined in title 17, California Code of Regulations, section 100500) unless the SCRO committee has approved an exemption from this requirement.

(4) For human somatic cells, procured from human subjects, after November 22, 2006, where the CIRM-funded research is designed to develop cells for transplantation into a live born human; the SCRO committee must confirm that donors provided voluntary and informed consent including the requirements of Code of California Regulations, title 17, section 100100, subdivision (b)(1)(E).

(b) CIRM funds may not be use to provide valuable consideration to donors of gametes, embryos, somatic cells or tissue. This provision does not prohibit reimbursement for permissible expenses as defined in California Code of Regulations, title 17, section 100020, subdivision (h).

(c) The modification of an acceptably derived stem cell line shall not be considered a CIRM-funded derivation.

§ 100095. Additional Requirements for Research Involving Oocytes.

When procurement of oocytes are required for CIRM-funded research, the SCRO committee must confirm the following conditions have been met:

(a) The clinic performing oocyte retrieval is a member of the Society for Assisted Reproductive Technology.

(b) The procurement and disposition for research purposes of oocytes initially provided for reproductive uses, either for use by the donor or another woman, shall not knowingly compromise the optimal reproductive success of the woman in infertility treatment. Pursuant to this requirement, the SCRO shall confirm the following:

(1) The infertility treatment protocol is established prior to requesting or obtaining consent for a donation for research purposes and that the prospect of donation for research does not alter the timing, method, or procedures selected for clinical care.

(2) The woman in infertility treatment makes the determination that she does not want or need the oocytes for her own reproductive success.

(3) The donation of oocytes for research is done without valuable consideration either directly or indirectly.

(4) If the procurement of oocytes involves a donor providing oocytes for another woman's reproductive use, then the donation to research must be expressly permitted by the original donor.

(5) If the procurement of oocytes involves use of materials donated for reproductive use by another woman and with valuable consideration in excess of reimbursement for permissible expenses for the oocyte donor, then oocytes may not be used for CIRM-funded research.

(c) The CIRM-funded institution shall develop procedures to ensure that an individual who donates oocytes for CIRM-funded research has access to medical care that is required as a direct and proximate result of that donation. Such care shall be provided at no cost to the donor. If a donor is medically insured, the donor shall not be required to claim any treatment costs through her own insurance policy.

(d) 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.

(e) The physician performing oocyte retrieval shall not have a financial interest in the outcome of the research.

§ 100100. Informed Consent Requirements.

(a) All CIRM-funded human subjects research shall be performed in accordance with Title 45 Code of Federal Regulations, Part 46 (Protection of Human Subjects), revised June 23, 2005, and California Health and Safety Code section 24173. 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 Title 45 Code of Federal Regulations Part 46, revised June 23, 2005, and who obtains informed consent in the method and manner required by those regulations.

(b) In addition to the requirements of Code of California Regulations, title 17, section 100080, subdivision (a)(2), the following provisions apply when CIRM funded research involves donation of human gametes, embryos, somatic cells or tissue for derivation of new covered stem cell lines:

(1) CIRM-funds may not be used for research that violates the documented preferences of donors with regard to the use of donated materials. The SCRO committee or IRB must confirm that donors have given voluntary and informed consent in accordance with this section. To ensure that donors are fully informed of the potential uses of donated materials in addition to the general requirements for obtaining informed consent identified in subdivision (a) of this regulation, researchers shall disclose all of the following, unless a specific item has been determined by the SCRO committee or IRB to be inapplicable:

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

(B) Whether or not the identity(ies) of the donor will be ascertainable by those who work with the resulting cells or cell products. If the identity of the donor is to remain associated with the cells or cell products, then the investigator must inform the donor of any plan for recontact whether for the purpose of providing information about research findings to donors, or for the purpose of requesting additional health information. After donation, an investigator may recontact a donor only if the donor consents at the time of donation.

(C) Cell lines may be used in future studies which are not now foreseeable.

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

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

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

(G) The donation is being made without restriction on the recipient of transplanted cells, except in the case where donation is intended for autologous transplantation.

(H) Neither consent nor refusal to donate materials for research will affect the quality of any care provided to a potential donor.

(I) Although the results of research including donated materials may be patentable or have commercial value, the donor will have no legal or financial interest in any commercial development resulting from the research.

(2) A donor must be given the opportunity to impose restrictions on future uses of donated materials. Researchers may choose to use materials only from donors who agree to all future uses without restriction.

(3) For CIRM-funded research involving the donation of oocytes, an IRB finding that potential risks of donation are reasonable even if there is no anticipated benefit to the donor shall

be documented and made available to the donor, SCRO and the CIRM. In addition, the following requirements apply:

(A) The description of foreseeable risk required in subdivision (a) of this regulation shall include but not be limited to information regarding the risks of ovarian hyperstimulation syndrome, bleeding, infection, anesthesia and pregnancy.

(B) Any relationship between the attending physician and the research or researcher(s) must be disclosed to an egg donor.

(C) Prospective donors shall be informed of their option to deliberate before deciding whether or not to give consent. If a deliberation period is chosen, the donor shall be informed of her right to determine the method of recontact. The donor must be informed that she has the option to initiate recontact. Investigators shall not initiate recontact unless the donor has consented, and this consent is documented in the research record.

(D) The researcher shall ascertain that the donor understands the essential aspects of the research involving donated materials, following a process approved by the designated IRB or SCRO committee. Understanding the essential aspects of the research includes understanding at least that:

(i) Eggs will not be used for reproductive purposes.

(ii) There are medical risks in oocyte donation, including the risks of ovarian hyperstimulation syndrome, bleeding, infection, anesthesia, and pregnancy.

(iii) The research is not intended to directly benefit the donor or any other individual.

(iv) Whether stem cell lines will be derived from her oocytes through fertilization, SCNT, parthenogenesis, or some other method.

(v) Stem cell lines developed from her oocytes will be grown in the lab and shared with other researchers for studies in the future.

(vi) If stem cells derived from her donation are to be transplanted into patients, researchers might recontact the donor to get additional health information.

(vii) Donors receive no payment beyond reimbursement for permissible expenses.

(viii) Stem cell lines derived as a result of her oocyte donation may be patented or commercialized, but donors will not share in patent rights or in any revenue or profit from the patents.

(4) For funded research involving the donation and destruction of human embryos for stem cell research, the informed consent process shall include a disclosure that embryos will be destroyed in the process of deriving embryonic stem cells.

(5) Research that uses human umbilical cord, cord blood or placenta, consent shall be obtained from the birth mother.

(6) For research involving the donation of somatic cells for SCNT, the informed consent process shall include disclosure as to whether the donated cells may be available for autologous treatment in the future.

§ 100110. Fairness and Diversity in Research.

CIRM grantees shall comply with the California Health Research Fairness Act, California Health and Safety Code, sections 439.900-439.906, and Inclusion of Women and Minorities in Clinical Research Act, Health and Safety Code, sections 100237-100239.

This document contains a reformatted version of the CIRM Medical and Ethical Standards regulations. The official version of these

regulations may be found at http://www.oal.ca.gov/. Additional regulations may be applicable to CIRM funded research.

See: http://www.cirm.ca.gov/cirm-operations/Regulations

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