



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/>.
- This version reflects revisions to the regulations effective June 29, 2008.
- Additional regulations may be applicable to CIRM funded research. See: <http://www.cirm.ca.gov/reg/default.asp>

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

The standards set forth in this chapter apply to all institutions, as defined by Title 17, California Code of Regulations, section 100020, subdivision (f), 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.
- (f) "Institution" means any public or private entity or agency (including federal, state, local or other agencies).
- (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 stem cells from a covered stem cell line have been introduced.
- (f) The transfer to a uterus of a genetically modified human embryo.

§ 100040. Institutional Assurance of Compliance.

- (a) 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.
- (b) Each institution shall:
 - (1) 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;
 - (2) Designate one or more SCRO committee(s) established in accordance with the requirements of Code of California Regulations, title 17, section 100060;
 - (3) Designate one or more IRB(s);
 - (4) 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.

§ 100050. Compliance.

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 appointed to, or remunerated by the relevant research institution and who is not 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 may not commence without SCRO committee review and approval in writing. For such SCRO committee review and approval, 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 use oocytes including a justification for the number needed. 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 use of human 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 use 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 research with the aim to derive or create a covered stem cell line 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 (c)(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 rationale for the need to derive a covered stem cell line.
- (2) If SCNT is proposed as a route to generating human stem cell lines, a justification for SCNT shall be provided.
- (3) Demonstrate experience, expertise or training in derivation or culture of human or nonhuman stem cell lines.
- (4) Provide documentation of compliance with any required review of the proposed research by an IRB, Institutional Bioethics Committee (IBC), or other mandated review.
- (5) 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 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 acceptably derived.
 - (2) Provide documentation of compliance with any required review of the proposed research by an IRB, IACUC, IBC, or other mandated review.
- (e) CIRM-funded research introducing covered stem cell lines into non-human animals or introducing 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. 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 stem 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 rationale for 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 stem cell line must meet one of the following three criteria:
- (1) The 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 in accordance with California Code of Regulations, title 17, section 100090.
- (2) The stem cell line is derived from human gametes, embryos, somatic cells, or tissue 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, embryos, somatic cells or tissue did not receive valuable consideration. This provision does not prohibit reimbursement for permissible expenses as defined in California Code of Regulations, title 17, section 100020, subdivision (h), as determined by an IRB; 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 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.

§ 100085. Use of Fetal Tissue.

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. Additional Requirements for CIRM-Funded Derivation.

- (a) Where CIRM funds are to be used for research intended to derive a covered stem cell line from human gametes, embryos, somatic cells or tissue, the SCRO committee must determine the requirements of Code of California Regulations, title 17, section 100080, subdivision (a)(2), have been met. For CIRM-funded derivation occurring after November 22, 2006, the SCRO committee must also confirm that donors provided voluntary and informed consent in accordance with Code of California Regulations, title 17, section 100100, subdivision (b).
- (b) California Code of Regulations title 17, section 100090(a), does not apply to CIRM funded research intended to derive a covered stem cell line from somatic cells when the SCRO committee has determined the requirements of California Code of Regulations title 17, section 100080, subdivisions (a)(3)(A) and (a)(3)(B), have been met.
- (c) The modification of an acceptably derived stem cell line shall not be considered a CIRM-funded derivation.

§ 100095. Additional Requirements for CIRM-Funded 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.

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