November 29, 2005

Possible Options for Informed Consent Requirements in CIRM Regulations

Background:

The Standards Working will be considering informed consent requirements at its December meeting. As we have discussed previously, there are a range of options for this section. This document is intended to illustrate three possible approaches (1) existing language based on the NA Guidelines, (2) revised language based on existing CA regulations, and (3) minimal language incorporating existing Federal and State law by reference. Keep in mind that the Office of Administrative Law may favor one approach over another. We will likely approach the OAL on this issue once the SWG has come to some consensus.

Three possible options for informed consent are presented in this document. The intent is to orient you to possible approaches in advance of our November conference call and December meeting. Based on feedback from working group members, there has been interest in option 3, minimal language incorporating existing Federal and State law by reference, with a short list of additional requirements in key areas of concern. Some working group members are attempting to develop language to support additional requirements and will present them for review by the group. If we take the option 3 approach, then it is important to consider what additional requirements we would include in regulation.

[Option 1] **[Current Version Based on NA Guidelines]**

Section 100007 Informed Consent Requirements

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

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

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

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

(C) An assurance that participants in research projects will follow applicable and appropriate best practices for donation, procurement, culture, and storage of stem cells, in particular, the traceability of stem

cells; provided, however, that traceable information shall be secured to ensure confidentiality.

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

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

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

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

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

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

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

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

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

[Option 2] **[Draft Versions Based on Existing CA Regulations]**

Section 100007 Informed Consent Requirements

Except as otherwise provided in this chapter, no person shall participate in CIRM-funded research unless the consent of such person is obtained. Institutional Review Boards or ESCRO may not waive the requirement for obtaining informed consent. For the purpose of this chapter research includes, but is not limited to, activities intended to derive or use human embryonic stem cells, human embryonic germ cells, and human adult stem cells from any source, including somatic cell nuclear. When gametes have been used in the in vitro fertilization process, resulting blastocysts may not be used for CIRM-funded research without consent of all gamete donors.

(a) As used in this chapter, "informed consent" means the voluntary and freely given authorization given to participate in human subjects research after each of the following conditions have been satisfied:

[The following conditions are from H&S Code 24173]

(1) An explanation of the procedures to be followed in the research and any drug or device to be utilized.
(2) A description of any attendant discomfort and risks to the subject reasonably to be expected.
(3) An explanation of any benefits to the subject reasonably to be expected, or an explanation that no benefits to the subject are expected.
(4) A disclosure of any appropriate alternative procedures and their relative risks and benefits.
(5) An estimate of the expected recovery time of the subject after the procedure.
(6) An offer to answer any inquiries concerning the procedures involved.
(7) An instruction to the subject that he or she is free to withdraw prior consent at any time without prejudice to the subject.
(8) A statement that participation will not affect the quality of care provided to potential subjects.
(9) The name, institutional affiliation, if any, address, and telephone number of the person or persons primarily responsible for conducting the procedure.
(10) The name of the sponsor or funding source, if any, and or organization, if any, under whose general aegis the procedure is being conducted.
(11) The name, address, and phone number of the ESCRO responsible for oversight as described in section xx.
(12) The material financial stake or interest, if any, that the investigators or research has in the outcome of the CIRM-funded research. Disclosure that the result of study of donor material may have commercial potential and a statement that the donor will not receive direct financial or other benefits from any future commercial development.

(b) In the context of donation of gametes, *stem cells*, and somatic cells to derive cell lines, at a minimum the following shall be provided during the informed consent process:

[The following conditions are from H&S Code 125315]

(1) A statement as to whether embryos will be destroyed in the process of cell derivation.
(2) A statement that blastocysts or gametes will be used to derive cells for research that may include research on human transplantation.
(3) A statement that the donation is made without any restriction or direction regarding who may be the recipient of derived cells, except in the case of autologous donation.
(4) A statement as to whether the donor's identity will be readily ascertainable to those who derive or work with the resulting cell lines.
(5) Ascertainment as to whether the donors consent to being contacted to provide additional information to researchers.
(6) An assurance that best practices will be followed [existing CA laws?].
(7) A statement that cells or cell lines may be kept for many years.
(8) A statement that cells or cell lines might be used in research involving genetic manipulation of the cells or mixing of human and nonhuman cells in animal models.

(c) The subject shall be provided with a signed and dated copy of the written consent form.

[Option 3] **[The Reference Existing Law Approach]**

Section 100007 Informed Consent Requirements

(a) All funded research involving human subjects, as defined in CFR 46.102, shall be performed in accordance with CFR 46.116 Protection of Human Subjects and California Health and Safety Code Section 24175. In addition, to the general requirements for informed consent the IRB shall require the following:

(1) List any additional general requirements or requirements related to a specific procedure.
(2) ?

CA Health and Safety Code Section 24175

24173. As used in this chapter, "informed consent" means the authorization given pursuant to Section 24175 to have a medical experiment performed after each of the following conditions have been satisfied:

(a) The subject or subject's conservator or guardian, or other representative, as specified in Section 24175, is provided with a copy of the experimental subject's bill of rights, prior to consenting to participate in any medical experiment, containing all the information required by Section 24172, and the copy is signed and dated by the subject or the subject's conservator or guardian, or other representative, as specified in Section 24175.

(b) A written consent form is signed and dated by the subject or the subject's conservator or guardian, or other representative, as specified in Section 24175.

(c) The subject or subject's conservator or guardian, or other representative, as specified in Section 24175, is informed both verbally and within the written consent form, in nontechnical terms and in a language in which the subject or the subject's conservator or guardian, or other representative, as specified in Section 24175, is fluent, of the following facts of the proposed medical experiment, which might influence the decision to undergo the experiment, including, but not limited to:

(1) An explanation of the procedures to be followed in the medical experiment and any drug or device to be utilized, including the purposes of the procedures, drugs, or devices. If a placebo is to be administered or dispensed to a portion of the subjects involved in a medical experiment, all subjects of the experiment shall be informed of that fact; however, they need not be informed as to whether they will actually be administered or dispensed a placebo.

(2) A description of any attendant discomfort and risks to the subject reasonably to be expected.

(3) An explanation of any benefits to the subject reasonably to be expected, if applicable.

(4) A disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.

(5) An estimate of the expected recovery time of the subject after the experiment.

(6) An offer to answer any inquiries concerning the experiment or the procedures involved.

(7) An instruction to the subject that he or she is free to withdraw his or her prior consent to the medical experiment and discontinue participation in the medical experiment at any time, without prejudice to the subject.

(8) The name, institutional affiliation, if any, and address of the person or persons actually performing and primarily responsible for the conduct of the experiment.

(9) The name of the sponsor or funding source, if any, or manufacturer if the experiment involves a drug or device, and the organization, if any, under whose general aegis the experiment is being conducted.

(10) The name, address, and phone number of an impartial third party, not associated with the experiment, to whom the subject may address complaints about the experiment.

(11) The material financial stake or interest, if any, that the investigator or research institution has in the outcome of the medical experiment. For purposes of this section, "material" means ten thousand dollars ($10,000) or more in securities or other assets valued at the date of disclosure, or in relevant cumulative salary or other income, regardless of when it is earned or expected to be earned.

(d) The written consent form is signed and dated by any person other than the subject or the conservator or guardian, or other representative of the subject, as specified in Section 24175, who can attest that the requirements for informed consent to the medical experiment have been satisfied.

(e) Consent is voluntary and freely given by the human subject or the conservator or guardian, or other representative, as specified by Section 24175, without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence.

45 CFR 46 below for reference

§46.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

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

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

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

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study.

(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

(1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and

(2) The research could not practicably be carried out without the waiver or alteration.

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.