Summary and Response to Public Comment for the Proposed Revisions to CIRM MES Regulations §100080, 100100

#	Section	Summary of Public Comment(s)	Response to Public Comment	Ref.
	100080	**Acceptable Research Materials**		
1	(a)(2)(C)	As stem cell research becomes a more global enterprise, there are increased challenges to ensure that stem cell lines used in CIRM-funded research are ethically derived. We believe that the provisions in §100080 should be strengthened. In articular we are concerned with section (a)(2)(C) and the term "IRB-equivalent." We understand that this term is modeled after the National Academies guidelines, however, we recommend that there be additional provisions to clarify the meaning of the term. In addition, we recommend incorporation of the NAS recommendation that holds the SCRO accountable for ascertaining that the foreign institution affords sufficient protections. We recommend that (a)(2)(C) be revised as follows: Donation of human gametes, embryos, somatic cells or tissue was overseen by an IRB, or in the case of foreign sources, by an IRB equivalent. The SCRO shall be required to ascertain that any such IRB-equivalent affords protections no less than those afforded under the authorized authorities enumerated in section (a)(1).	The comment is not an accurate reflection of the NAS repot, page 108: In international collaboration SCRO *may determine that the procedures prescribed by the foreign institutions afford protections equivalent with these guidelines and may approve the substitution of some or all foreign protections for its own.* SCRO committees do look at the review procedures in the other countries to assure adequate oversight. The NAS guidelines leave discretion to the individual SCRO to determine what is equivalent; such discretion is allowed for international research under the Common Rule or Helsinki Accord. Further, the proposed language constitutes a burdensome standard that results in unclear and unnecessarily complex standard for compliance. The comment suggests that CIRM regulations cite five different national and international standards organizations. Effective persons would then be required to determine that a third-party is in substantial compliance with all the standards. Such determinations would need to be ongoing since each organization routinely modifies its standards. CIRM believes the language would violate Government Code Sec. 11349(c) because directly effected persons would be face continuous conditions of uncertainty regarding compliance because compliance may: 1. Have multiple meaning depending on the benchmark standard. 2. The national and international standards contain numerous undefined terms. 3. There are no valid (legally-binding) citations for some of the standards recommended.	WC_042

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2	(a)(3)(B)(3)	We would like to raise serious privacy concerns about any policies that allow the release of key identifying information, even after the donor's death. The families of donors could suffer adverse consequences from the identification of genetic information. Therefore we recommend that the phrase "until the donor is deceased" be deleted from sections (ii), (iii), and (iv).	The noticed language is identical to Federal guidelines and was included for reasons of consistency with existing practice governing biomedical research. The comment identifies a potential harm that may result from incorporating the existing Federal standard. The consistency standard must be balanced against CIRM statutory obligation to assure patient privacy, H&S Code 125290.35. In addition, the Federal Genetic Information Nondiscrimination Act of 2007 advances Federal privacy protection policy. In the interest of ensuring patient privacy the recommendation has been incorporated.	WC 042
3	100080(b)(1)	We are concerned about the open-ended extension beyond the current 12 day limit on using covered stem cell lines derived from embryos, SCNT, etc. There is an international consensus on limiting the use of such materials beyond 14 days. The National Academies guidelines state: (c) Research that should not be permitted at this time: Research involving *in vitro* culture of any intact human embryo, regardless of derivation method, for longer than 14 days or until formation of the primitive streak begins, whichever occurs first. The International Society for Stem Cell Research concurs: 12.1e) Embryos made via nuclear transfer, parthenogenesis, androgenesis, or other *in vitro* mean of embryo production shall not be transferred to a human or non-human uterus or cultured *in vitro* intact as embryos for longer than 14 days or until formation of the primitive streak, whichever occurs first. We believe that CIRM should adopt these clear boundaries. In addition, we recommend that the Medical and Ethical Standards Working Group develop clear criteria under which the ICOC could approve an extension from 12 to 14 days. We recommend that §100080(b)(1) be revised as follows: 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 [citation omitted], however under no	The assertion that the proposed language constitutes an "open-ended extension" is incorrect. The amendment creates a mechanism where research materials could be utilized after a 12 day limited provided such use is approved by the ICOC. The amendment is designed to provide a mechanism for effected persons to utilize materials that comply with national and international consensus standards. The comment suggests there is value in restating the international consensus standard in regulation. This recommendation has been incorporated in a manner consistent with H&S Code 125290.15.	WC 042

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		circumstances shall the ICOC approve such usage after 14 days in culture or until formation of the primitive streak, whichever occurs first. The 12-14 day limit does not include any time during which the cells have been frozen.		
4	(b)(3)	We appreciate that the prohibition against valuable consideration being paid to the donor of materials has been addressed elsewhere in the regulations, there is an additional concern that the deletion of this section could allow for-profit or other brokering of human tissues. Allowing the purchase or sale of these materials could, for example, provide a financial incentive for an egg broker to facilitate the over-stimulation of egg donors, with the attendant increased health risks, in order to create more eggs for profit. We recommend that the first sentence of the deleted section (3) be retained in the regulations. (3) A person may not knowingly, for valuable consideration, purchase or sell gametes, embryos, somatic cells, or human tissue for research purposes.	The proposed amendment is designed to resolve an existing inconsistency with the enabling legislation embodied in H&S Code 125290.35, subdivision (b)(5). Inclusion of the language proposed by the commenter would perpetuate this inconsistency with regard to cells and tissue. The original regulatory language with regard to gametes and embryos has been retained in Section (b)(2). Retaining this language addresses the commenter's concern with regard to gamete donation while resolving an inconsistency in the previous standard.	WC 042
	100100	**Definitions**		
5	(b)(2)	should read: A donor must be given the opportunity to impose restrictions on future uses of donated materials.	The commenter is correct; this language was inadvertently struck out in the original posting.	WC 042
6	(b)(3)(D)(vi)	add: only if the donor has consented to recontact under (b)(1)(B)	The comment pertains to a section of the regulation requiring effected persons to confirm that a research donor has understood the essential aspects of the consent process. The proposed language is intended to "point" the effected persons to the underlying regulatory requirement. While well intended, the addition is not necessary substantively (e.g. effected persons must comply with (b)(1)(B)).	WC 042
7	100020 (b)(4)	should read: For CIRM-funded research	The OAL handbook for rulemaking under the California APA recommends use of only necessary words. Section 100010 clearly defines the exclusive scope of these regulations to be CIRM-funded research. We recognize the well intend effort to remind effected persons of the scope of the regulations; however, the language is not necessary.	WC 042
8	100020 (b)(5)	should read: For CIRM-funded research		
9	100020 (b)(6)	should read: For CIRM-funded research		

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	100120			
	Note: Section 100120 was noticed on November 20, 2007 for a fifteen day comment period. CIRM received no comments before the December 5, 2007 deadline for public comments. The comments below were received on The PCARR Comments on CIRM Medical and Ethical Standards regulations were received on December 13, 2007, eight days after the close of the comment period for section 100120. While CIRM is not obligated to respond to comments received after the close of the 15 comment period pursuant to Government Code 11346.8, a response is provided below.			
10	**General**	Comments were submitted earlier.	These comments were originally addressed in regulatory filing 06-0825-025.	WC 042
11		CIRM is waiting on CDPH development of regulatory requirements.	The commenter is correct in asserting that CIRM is tracking the development of reporting requirements by the California Department of Public Health. On August 7, 2007 CIRM provided a detailed response to the commenter's May 7, 2007 correspondence describing the rationale for this position. In addition, the substance of the May 7 letter was discussed by a CIRM advisory group on May 10, 2007 which is reflected in the public record. CIRM's August 7 response was also included in the administrative record. CIRM sent a second letter reiterating its position on January 14, 2008. To reiterate here, California state legislation contains substantially similar requirements as those proposed by the commenter. The CDPH is the lead agency for implementation of SB 1260 (Ortiz, 2006) (H&S Code 125330-125355). Pursuant to this mandate the department has performed the following: • Convened an expert committee comprised of 13 national and international specialists. The Human Stem Cell Research (HSCR) Advisory Committee advises the Department in the development of statewide guidelines for human stem cell research and the update of these	WC 042

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			guidelines. • Developed draft reporting forms towards implementation of the SB 1260 reporting requirements. • Compiled public comments and facilitated public meetings to support ongoing development of the reporting regulations. SB 1260 declared: *The intent of the Legislature is to avoid inconsistencies for stem cell research oversight committees established pursuant to this article with other existing standards for research conducted in California.* Given the Legislature's desire for consistency in stem cell regulation and oversight and the inherent complexity in developing a reporting system, CIRM believes it is appropriate to let CDPH complete the development and implementation of its reporting requirements prior to considering new record-keeping regulations for CIRM funded research.	
		12-20 are Record-keeping requirements previously submitted.		
12	(e)	summaries of proposed research activities that went before the SCRO and the IRB, and whether they were approved.	This information is routinely provided by CIRM and additional regulatory requirements are not necessary. CIRM publishes an annual report titled *Awards and Applications Approved for Funding*. This report provides summaries of research activities. Under the CIRM Grants Administration Policy for Academic and Non-Profit Institutions awards are only approved for funding when required SCRO and IRB reviews have been performed and certified by the applicant institution.	WC_042
13	(f)	policies and procedures adopted by the SCRO.	The CIRM regulations mirror existing state and Federal regulations governing the conduct of biomedical research. H&S Code 125290.35 states: *The ICOC shall establish standards for the review of research involving human subjects which initially shall be generally based*	WC_042

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			on the Institutional Review Board standards promulgated by the National Institutes of Health and in effect on January 1, 2003, with modifications to adapt to the mission and objectives of the institute. Under NIH rules, existing state regulations and CIRM regulations oversight committees operate within a framework where they continually develop a range of operational procedures and policies. For CIRM-funded research, pursuant to their obligation under H&S code 100010 – 100120, SCRO committees must develop administrative and personnel policies, operational and governance polices and any number of procedures related to the operation of an intuitional review committee. None of the existing NIH rules or California regulation governing oversight of biomedical research require the level of reporting suggested by the commenter. Requiring open ended reporting of "policies and procedures" adopted by the SCRO would be unduly burdensome both to the effected persons and CIRM. The language as recommended constitutes an exceedingly burdensome standard which is very broad in scope. It is unclear how such a requirement would accomplish the goal of evaluating compliance with H&S code 100010 – 100120.	
14	(g)	an overview of any human stem cell research being done at the institution that is *not* following CIRM standards.	By definition all CIRM-funded research must comply with H&S code 100010 – 100120. CIRM does not have the authority to require reporting on non-CIRM funded research being performed at a grantee institution. See response #15, reporting requirements exist for the situation where a situation of non-compliance is identified pursuant to CIRM-funded research; thus, this requirement is duplicative with existing regulation. This compliance requirement is contained in the CIRM Grants Administration Policy p. 21-22 and the reporting requirement may be found on p. 34-36.	WC_042

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15	(h)	an overview of any failures to comply with these standards.	This requirement is duplicative with existing CIRM regulations. Reporting requirements pertaining to any failure of compliance is addressed in the CIRM Grants Administration Policy p. 34-36	WC 042
16	(i)	The demographics of the providers of oocytes or embryos used in the derivation of each cell line.	With regard to reporting of oocyte donation, CIRM believes it is appropriate to let CDPH complete the development and implementation of its reporting requirements pursuant to SB 1260 prior to considering new reporting regulations for CIRM funded research. There is no basis in existing policy for tracking the demographics of embryos donors. H&S Code 125290.35 includes an obligation to ensure patient privacy; the ICOC is committee to privacy protection. The ICOC believes CIRM should be extremely judicious in mandating the compilation of sensitive health information. In this case, the commenter is suggesting CIRM compile personal information.	WC 042
17	(j)	A summary of results, both positive and negative, of any CIRM-funded research or clinical trial	This requirement is duplicative with the requirements of the CIRM Grants Administration Policy p.34 *The programmatic report includes a summary of scientific progress; a listing of personnel who participated in the project and their level of effort; an updated listing of other support for the PI and other key personnel; a list of publications (including submitted or in press) resulting from the CIRM-supported project or activity; cumulative subject accrual and progress in conducting analyses for sex/gender and race/ethnicity differences in clinical trials; applicable public policy assurances (e.g., ESCRO, IRB, IACUC); an estimate of goods and services purchased from California suppliers; and a listing of inventions disclosed, patents filed, or licenses granted for the project period (see part 3, Other Reports).*	WC 042
18	(k)	Any significant adverse reactions in a clinical trial.	This requirement is already addressed in the CIRM Grants Administration Policy (see response #17).	WC 042
19	(l)	A disclosure of the personal, professional, and financial interests in biotechnology or biomedical companies of the	Consistent with our response #13, the proposed reporting requirement is beyond the scope of existing rules governing	

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		SCRO members.	biomedical research. Such disclosures are within the operation purview SCRO committee.	
20	(m)	Health outcomes of oocyte donors resulting from oocyte retrieval, including adverse health reactions resulting from ovarian stimulation.	With regard to reporting of oocyte donation, CIRM believes it is appropriate to let CDPH complete the development and implementation of its reporting requirements pursuant to SB 1260 prior to considering new reporting regulations for CIRM funded research. H&S Code 125290.35 includes an obligation to ensure patient privacy; the ICOC is committee to privacy protection. The ICOC believes CIRM should be extremely judicious in mandating the compilation of sensitive health information. It is reasonable to defer to the expertise of the CDPH prior to developing an independent reporting standard.	