

**APPROVED MEETING MINUTES**

**California Department of Health Services, Human Stem Cell Research Advisory Committee  
December 5, 2006  
Teleconference  
2:00 PM – 3:00 PM PST**

**Attendance:**

**California Department of Health Services (CDHS), Human Stem Cell Research (HSCR)  
Advisory Committee Members**

Elizabeth Helen Blackburn, PhD  
Samuel Cheshier, MD, PhD  
Henry Greely, JD  
Bernard Lo, MD  
Bertram Lubin, MD  
David Magnus, PhD  
Otoniel Martinez-Maza, PhD  
Margaret McLean, PhD  
Radhika Rao, JD

**CDHS**

Shabbir Ahmad, Manager, Human Stem Cell Research Unit, CDHS  
Cindy Chambers, Human Stem Cell Research Unit, CDHS  
Amber Christiansen, Human Stem Cell Research Unit, CDHS  
Heidi Mergenthaler, Human Stem Cell Research Unit, CDHS  
Patricia Rodriguez, CDHS Legal Counsel  
Jackie Wilson, CDHS Staff

**Members of the Public**

Susan Fogel, Pro-Choice Alliance for Responsible Research  
Nicole Vazquez, Senate Health Committee  
Emily Galpern, Center for Genetics and Society

**Opening Remarks**

Professor Greely noted the decision to hold a teleconference instead of an in-person meeting was based on having received only one set of public comments. Despite three more sets being submitted after the decisions was made, he hoped the Committee would still be able to respond to the public comments in the time allotted since many of them did not seem controversial. He explained the rules of a teleconference are different than a meeting in that members of the public are in "hear only mode" until the phone line is opened to the public for comments.

**Approval of Minutes**

The September 20, 2006 CDHS HSCR Advisory Committee meeting minutes were approved. They can be viewed at: [http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-Sept20\\_Minutes-08-2007.pdf](http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-Sept20_Minutes-08-2007.pdf).

**Agenda Item #1: Report from the Department**

Dr. Shabbir Ahmad briefly summarized Senate Bills (SB) 322 and 1260. He noted SB 1260 did not include provisions for the continuation of the HSCR Advisory Committee beyond December 31, 2006. But given the ethical issues and ever-changing field of stem cell research, CDHS decided to extend the tenure of the Committee for two years to provide advice and recommendations to the Human Stem Cell Research Unit.

Dr. Ahmad indicated that once the final recommended guidelines are submitted by the Committee through Professor Greely, they will be internally reviewed by the administration and legal counsel of CDHS. After final approval, the guidelines will be posted to the Human Stem Cell Research Unit Web site.

Professor Greely thanked the Department for continuing the tenure of the Committee. He then read a letter he received from President Robert Dynes of the University of California, Office of the President to the Secretary of the California Health and Human Services Agency, which thanked CDHS and the Committee for their contributions to developing the guidelines and addressing the multi-faceted issues of human stem cell research. The letter also urged the Agency to consider establishing the Committee as a standing advisory group to CDHS.

## **Agenda Item #2: Discussion of Draft Recommendations in Light of Public Comments and CIRM Regulation Changes**

In an effort to efficiently discuss each public comment, Professor Greely suggested the Committee decide on whether to accept, reject, or modify the public recommendations and to assign committee members to draft any language changes after the teleconference. These revisions would then be reviewed by the entire Committee before the final guidelines were sent to Dr. Ahmad.

Professor Greely indicated the public comments had been submitted by the Pro-Choice Alliance for Responsible Research, the Center for Genetics and Society, State Senator Deborah Ortiz, and the University of California, Office of the President (UCOP). The first three were more similar in content, while the UCOP comments raised some additional issues. The public comments can be viewed at: <http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-PublicCommentsMatrix-08-2007.pdf>.

Aside from the public comments, Professor Greely pointed out that some changes to the guidelines would need to be made based on the passage of SB 1260, which occurred after the September 20<sup>th</sup> Committee meeting. Other changes would be based on wording changes to the California Institute for Regenerative Medicine (CIRM) regulations since the previous meeting. The draft guidelines can be viewed at:

<http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-HSCRGuidelines-08-2007.pdf>.

CIRM regulations (current at the time of the meeting) can be viewed at:

<http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-CIRMReport-09-2007.pdf>.

Professor Greely then began addressing the CIRM regulation changes and public comments in relation to the guidelines as listed in a matrix provided by the HSCR Unit:

<http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-PublicCommentsMatrix-08-2007.pdf>.

*General & Preface comment 1:* The guidelines should be entirely consistent with SB 1260, rather than with conflicting or different policies that CIRM has adopted.

Discussion: Professor Greely agreed that SB 1260 controls the guidelines in a way that CIRM regulations cannot and accepted the comment that the guidelines should be consistent. He mentioned the Pro-Choice Alliance wanted the Preface to emphasize the consistency of the guidelines with SB 1260, in addition to CIRM regulations.

Decision: Professor Greely proposed the Preface be updated to reflect the current status of SB 1260, and where necessary, the body of the guidelines be changed to make clear the requirements of SB 1260. The Committee agreed.

*General comments 2 & 3:* Include additional data collection and reporting language.

Discussion: Dr. Magnus agreed this was a good idea but cautioned that if statutorily mandated data collection language was used in the guidelines, then the wording must indicate that these are actually requirements not guidelines. Professor Greely agreed that data collection issues should not be interpreted as voluntary. He pointed out that the guidelines could include data collection information on oocyte retrieval but it should be clear that some of this research also falls outside the scope of the guidelines.

Professor Rao questioned data reporting to the public on other research as well. She brought up the public comment regarding summaries of research activities and their approval status being disclosed. Dr. Magnus also added the public comment that clinical trial adverse reactions be disclosed. Given that some of these reporting comments were outside the mandates of SB 1260, Professor Rao asked if the guidelines should separate out the different data collection elements with “required” versus “suggested” language. Professor Greely noted that public reporting of adverse outcomes in clinical trials is typically considered proprietary information and not disclosed to the public, but there was some value in making this information available to the public. Professor Rao agreed, and Dr. Lubin further suggested the information could be sent to the Committee first before being available to the public.

Referring to the complete list of data collection public comments, Professor Greely thought the list involved substantial disclosure requirements that were unprecedented but not necessarily a bad idea. Dr. Magnus highlighted the comments about adverse event reporting to the public and disclosure of approval status of trials being reviewed by SCROs as possibly having some value but that companies would likely be opposed to such reporting primarily for financial reasons. Dr. Lo suggested more thought needed to be given to what type of information should be made publicly available. Serious adverse events or clinical trial termination might be appropriate public information but broader reporting of all positive and negative results outside the peer review process might be problematic. He suggested researchers be encouraged to publish all results in a peer-reviewed format and that clinical trials should be registered with the National Institutes of Health database so that the trials could be tracked. He also cautioned against superseding the role of Data Safety Monitoring Boards by directly informing the public of all adverse events.

Decision: Professor Greely suggested incorporating the data collection requirements of SB 1260 Section 125342, but that the remaining, more substantive data reporting issues required further Committee discussion that the teleconference timeframe did not allow. Dr. Blackburn further pointed out the ambiguity of the comments about providing an overview all human stem cell research. As the focus of SB 1260 and the guidelines is on pluripotent cells, she wondered if this was truly their intent. Professor Greely continued by suggesting the Committee revisit the remaining reporting issues at the next Committee meeting and amend the guidelines as necessary.

*General comment 4:* Clarify what wording (“must”, “should”, or “shall”) should be used for guidelines versus regulations.

Discussion: Professor Greely argued that following the guidelines which use the word “shall” would mean being in compliance with the guidelines, although the guidelines themselves don’t necessarily require compliance except where specified in SB 1260. He prefers using “shall” and noted CDHS legal counsel had supported this language. Dr. Lo agreed but

suggested adding a couple sentences explaining the use of this language and that the guidelines were not regulations. Dr. Magnus referred to the Preface which distinguishes between the guidelines that are voluntary and those that are mandatory. Dr. Lo suggested indicating this throughout the body of the guidelines, as well.

Decision: Professor Greely said this could be done but then the text may not flow well. He was open to adding to the Preface language that explains the non-binding nature of the guidelines.

*Specific comment 1:* Page 3, lines 10-12; clarify that not all research involving derivation or use of hESCs will require both IRB and SCRO approval and revise to “some research involving derivation or use...”

Discussion: Professor Greely thought this was an important point to include and suggested accepting the comment.

Decision: Accept change.

*Specific comment 2:* Page 4, lines 7-19; place a prohibition against “the transfer to a uterus of a genetically modified human embryo” into the guidelines.

Discussion: Professor Greely mentioned this was discussed at the previous meeting when the Committee determined the prohibition was only tangentially related to human stem cell research and therefore chose not to include it in the guidelines. Dr. Magnus reaffirmed that decision.

Decision: Reject comment with the understanding that this did not indicate the Committee endorses the prohibition.

*Specific comment 3:* Pages 7-8; the majority of SCRO members should not be research scientists and should include at least one community member.

Discussion: Professor Greely cited “include at least one nonscientist member of the public...” in the SCRO membership section of the guidelines as being equivalent to “at least one community member.” He then argued that a majority of members not being scientists was not consistent with CIRM regulations or National Academy of Sciences guidelines and that scientific expertise was necessary on a SCRO Committee. Dr. Martinez-Maza agreed a tremendous amount of scientific expertise was needed.

Decision: Reject change.

*Specific comment 4:* Page 8, lines 3-4; “permissible expenses, as defined in Section 2” was cut from CIRM regulations.

Decision: Accept deletion.

*Specific comment 5:* Page 8, lines 6-7; “In addition, a SCRO Committee shall have a patient advocate...” was deleted because it was included elsewhere in the CIRM regulations text.

Decision: Accept deletion.

*Specific comments 6 & 7:* Page 8, line 9; “professional or financial stake” was cut from CIRM regulations, and UCOP commented that this phrase was unclear and should only read “conflicting interest.”

Decision: The first comment resolves the second one. Accept both comments.

*Specific comment 8:* Page 8, line 10; "IRB" was deleted from CIRM regulations.

Decision: Accept deletion.

*Specific comment 9:* Page 9, line 17; change "the" to "a" so it is not implied there can be only one expert in assisted reproduction.

Decision: No objections. Accept change.

*Specific comment 10:* Page 10, line 23; change "confidentiality of the donor(s) is protected" to "privacy of the donor is protected and the confidentiality of identifiable information is maintained."

Discussion: Professor Greely thought the proposed language might be better but was hesitant to change it since the current language was consistent with the CIRM regulations. Professor Rao noted that UCOP made the recommendation because it more closely mirrors federal regulations. Dr. Lo suggested the Committee make a recommendation to CIRM to amend its regulations accordingly. Professor Greely wanted to hear UCOP's arguments during the public session of the teleconference before making a final decision. Dr. Magnus preferred the new language given its similarity with federal regulations and anticipated this would likely be language CIRM would adopt in the near future. Professor Rao further commented that the new language would offer broader protection because the donor, as well as identifiable information, would be protected.

Decision: Professor Greely suggested adopting the new language pending any comments from UCOP during the public session of the teleconference.

*Specific comment 11:* Page 12, lines 2-5; two sentences were cut from the CIRM regulations.

Decision: Accept deletion.

*Specific comment 12:* Page 14, Sections 6 & 7; language should be directly from SB 1260 Sections 125330-125355.

Discussion: Dr. Magnus explained that the order of the CIRM regulations, from which the guidelines are modeled, do not necessarily flow with the order of SB 1260. He recommended comparing the guidelines with Sections 125330-125355 to ensure all of the requirements are included. Professor Greely concurred and thought this would entail more than just inserting exact language into the text.

Decision: Accept the thrust of the comment, ensure the guidelines are consistent and include the requirements of the applicable Sections of SB 1260, and adapt the language to the structure of the guidelines.

*Specific comment 13:* Page 14, Sections 7 & 8; clarify which provisions apply to all covered stem cell research versus research only involving derivation of new stem cell lines.

Discussion: Professor Greely thought the Sections were clear but agreed it could only help to further clarify them and ensure all applicable SB 1260 provisions are included. Dr. Lo agreed strongly with clarifying the guidelines as much as possible since CIRM had experienced problems with some research institutions not understanding the CIRM regulations.

Decision: Professor Greely agreed to review the Sections again and clarify where necessary.

*Specific comment 14:* Page 14, line 11; include “knowingly” in sentence to read like the CIRM regulations “The research shall not ‘knowingly’ compromise the optimal reproductive success of the woman in infertility treatment.”

Discussion: Professor Rao suggested checking if this wording was consistent with SB 1260 before including the change.

Decision: Professor Greely agreed to verify whether adding “knowingly” would be consistent with SB 1260.

*Specific comment 15:* Page 14, lines 13-14; delete sentence as it does not allow institutions to negotiate research subject medical costs with commercial sponsors of the research; instead keep Section 8(c) on page 15.

Discussion: Professor Rao suggested using the language directly from SB 1260, which states that an IRB must “ensure the subject has access to and coverage for medically appropriate medical care that is required as a direct result of the procedure for research purposes, and the research program or project shall ensure the payment or coverage of resulting medical expenses be provided at no cost to the subject...” Professor Greely thought this language was superior and that the responsibility for any costs was left to the commercial entity and research institution to negotiate.

Decision: Use SB 1260 language.

*Specific comment 16:* Page 14, line 14 and page 15, line 23; language should match SB 1260 and read “...medical care at no cost to the donor that is required as a ‘direct result’ of that donation.”

Discussion: Professor Greely mentioned the Committee had discussed at the previous meeting retaining “direct and proximate” in this sentence, but suggested the language be changed in order to be consistent with SB 1260. Professor Rao and Dr. Lo agreed consistency with SB 1260 was preferable.

Decision: Remove “proximate” from sentence.

*Specific comment 17:* Page 16, Section 9; provide a definition of “clinical trial” in the Definitions Section.

Discussion: Professor Greely agreed this would be helpful. Dr. Magnus had already prepared a definition from various sources: “a scientifically designed and executed investigation of a medical intervention in humans that is aimed at determining the safety, efficacy, and pharmacological effect (including toxicity, side effects, incompatibilities, and interactions) of the intervention. This includes phases I, II, and III clinical trials under the FDA regulations.” Professor Greely thought this definition was a good starting point and Committee members suggested comparing this definition with the FDA definition for consistency.

Decision: Dr. Magnus will verify the “clinical trial” definition with the FDA definition and add it to the Definitions Section of the guidelines.

*Specific comments 18-19:* Page 16, Section 9; carefully delineate SCRO Committee and IRB responsibilities for clinical trials in such a way as to allow institutions flexibility in assigning responsibilities for certain aspects of review; include a list in the guidelines of the necessary elements of clinical trials review and then institutions can ensure these are carried out by a committee with appropriate expertise.

Discussion: Dr. Magnus noted the Committee had a substantial conversation about clinical trial review responsibilities at the last meeting. He explained the rationale for delineating some of the review elements was due to the expertise needed for stem cell trials and that without explicitly assigning some of these responsibilities, institutions may argue that IRBs already provide sufficient scientific review and therefore SCRO Committee review would be duplicative. He used the example of a recent set of stem cell trials in which two institutions with SCRO Committees decided to stop the trials while the institution without a SCRO Committee continued the trials.

Dr. Lo argued that because SCRO Committees are a new concept and in the process of being formed, institutions may differ in the types of expertise on the various review committees and in the relationships between the review bodies. So he cautioned not to be overly prescriptive in delineating review roles and thereby allow the institutions to determine what works best for them. Professor Greely countered that the language of the guidelines is more flexible than the CIRM regulations, for example, in that they do not require SCRO Committees perform the scientific review but only that they ensure scientific review has occurred. He also reiterated the concern for institutions deciding only standard IRB review is necessary for stem cell clinical trials. Dr. Lo offered that IRBs could appoint ad hoc members from a SCRO Committee in order to gain the necessary expertise for stem cell research review and that this decision should be left for IRBs to decide. Professor Greely asked if Dr. Lo meant he supported eliminating any requirement that a SCRO Committee necessarily be involved in clinical trials of covered stem cells. Dr. Lo emphasized that institutions do need stem cell expertise but that the presumption only a SCRO Committee will provide this was not necessarily the case at all institutions. Professor Greely pointed out that the CIRM regulations specifically require SCRO Committees perform scientific review because they are more likely to have the required expertise. While Dr. Lo agreed, he thought the main problem lay in prescribing specific duties for the SCRO Committees versus the IRBs.

Professor Greely concurred that institutions should be allowed to be efficient in determining review responsibilities for clinical trials, but was reluctant to not require SCRO Committee involvement in stem cell clinical trials.

Decision: Professor Greely proposed writing a sentence which encourages institutions to develop innovative and flexible ways to integrate SCRO Committee and IRB functions. In addition, he would clarify that SCRO Committees are not necessarily required to perform the scientific review of clinical trials but only that they ensure scientific review has occurred.

Dr. Magnus recommended the language not be so flexible that adequate expertise was not incorporated by institutions. Dr. Lubin reiterated that IRBs in general do not have the expertise to review stem cell research, so SCRO Committees are designed to provide that resource for the overall review process.

*Specific comment 20:* Page 16, Section 9; include a requirement for clinical trials to register with a national registry such as [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

Discussion: Dr. Lo explained the benefit of a clinical trials registry is that trials must register from the onset, they cannot publish an article unless they are registered, and negative results must be disclosed in the registry. He mentioned [www.clinicaltrials.gov](http://www.clinicaltrials.gov) is an NIH website and that other organizations, such as the World Health Organization, are beginning to establish similar registries. These registries allow for greater transparency through public disclosure of basic trial information without compromising proprietary information.

Professor Rao wondered if by recommending now that researchers register clinical trial information, this would help fulfill the public comment requests for extensive data reporting until the Committee could more thoroughly address these comments at the next meeting. If there were no objections, Professor Greely thought it would be a non-controversial

recommendation for stem cell trials to register with [www.clinicaltrials.gov](http://www.clinicaltrials.gov). Dr. Lo noted that currently the registry only requires basic trial information, but this may change as the specific information to be collected is under debate. Dr. Lubin questioned whether it was premature to include this requirement. Dr. Lo and Professor Greely clarified that the recommendation would be only for clinical trials involving covered cells, and a couple companies have already announced they will be beginning such trials this year.

Decision: Add recommendation for clinical trials involving covered stem cells to register with [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

*Specific comment 21:* Page 17, line 5; change wording to “donors of the biological materials used to produce the covered cells used in the trial.”

Decision: Professor Greely agreed the terminology needed to be broader and accepted the change.

*Specific comment 22:* Page 18, line 2; change “involved” to “that involve.”

Decision: Accept change.

*Specific comment 23:* Page 18, line 8; insert “adequate” to read “an IRB shall require that any clinical trials involving hESCs and their derivatives shall have an ‘adequate’ Data Safety Monitoring Board.”

Decision: Accept insertion.

*Specific comment 24:* Page 18, line 21; correct typo by removing “8” from “Title 45 Code of Federal Regulations Part ‘8’ 46.”

Decision: Accept change.

*Specific comment 25:* Page 21, line 1; correct typo by removing “additional” from “In addition, the following ‘additional’ requirements shall apply.”

Decision: Accept change.

*Specific comment 26:* Page 21, line 2; identify what “subdivision (a)” is referring to.

Decision: Professor Greely and Dr. Magnus agreed to determine the reference of “subdivision (a).”

*Specific comment 27:* Page 21, line 23; change “the research will not benefit them” to “the research is not intended to benefit them.”

Decision: Accept change.

*Specific comment 28:* Page 22, lines 4-5; two sentences were cut from the CIRM Record Keeping Section.

Decision: Professor Greely would ensure the information was not specified in SB 1260 before making the change in the guidelines.

## **Discussion Summary**

Professor Greely summarized the discussion noting that the Committee was adopting most of the recommended changes, Professor Greely would be drafting new language for some of the

comments, and Dr. Magnus would be preparing a definition for “clinical trial”. After the changes are made, the guidelines will be emailed to the Committee for any final comments or changes before being officially submitted to CDHS.

### **Public Comment Session**

Professor Greely opened the discussion to the public. Emily Galpern of the Center for Genetics and Society appreciated the Committee considering her organization’s comments regarding guideline consistency with SB 1260. She highlighted that SB 1260 addresses financial and professional conflict of interest for physicians performing assisted oocyte production, so it should be clear that cutting this language from the guidelines does not also refer to research involving oocyte retrieval. She also suggested retaining in the guidelines the prohibition of genetically modified human embryos.

Professor Greely agreed to ensure the guidelines do not imply financial and professional conflict of interest issues do not apply to research involving oocyte retrieval. Ms. Galpern also informed the Committee that Nicole Vasquez of Senator Ortiz’s office had been on the teleconference earlier. Professor Rao followed up by noting that CIRM was retaining “conflict of interest” and only removing “professional and financial stake.” Because SB 1260 uses “financial or professional stake,” she suggested using “a conflict of interest, including professional or financial...” Professor Greely reiterated that CIRM’s language change only applies to SCRO Committee members, and while the conflict of interest issue for oocyte retrieval physicians is addressed in SB 1260, it is not actually included in the guidelines. He used this as an example of the broader concern that some research projects may only comply with the guidelines without recognizing that SB 1260 includes other specific research mandates.

There were no other public comments.

Dr. Magnus recommended that in the absence of UCOP feedback on the confidentiality language, the Committee should accept the language change for now. The Committee agreed.

### **Agenda Item #3: Remaining Business Items**

Professor Greely noted the Committee had been extended and therefore would have future meetings. For the next meeting, the proposed additional disclosure and data collection items would be on the agenda. Professor Greely anticipated completing the guideline revisions by the end of the year.

**Adjournment:** 3:45 PM.