

**APPROVED MEETING MINUTES**  
**California Department of Public Health, Human Stem Cell Research Advisory Committee**  
**December 5, 2007**  
**Four Points Sheraton, Los Angeles International Airport**  
**10:00 AM – 1:00 PM PST**

**Attendance:**

California Department of Public Health (CDPH), Human Stem Cell Research (HSCR) Advisory Committee Members

Elliot Dorff, PhD  
Henry Greely, JD  
Bertram Lubin, MD (by phone)  
David Magnus, PhD  
Otoniel Martinez-Maza, PhD  
Margaret McLean, PhD (by phone)  
Gregory Stock, PhD

CDPH

Shabbir Ahmad, Manager, Human Stem Cell Research Program, CDPH  
Cindy Chambers, Human Stem Cell Research Program, CDPH  
Amber Christiansen, Human Stem Cell Research Program, CDPH  
Kate Cordell, Human Stem Cell Research Program, CDPH  
Heidi Mergenthaler, Human Stem Cell Research Program, CDPH (by phone)  
Patricia Rodriguez, CDPH Legal Counsel

Members of the Public

Geoff Lomax, PhD, CIRM (by phone)  
Emily Galpern, Center for Genetics and Society (by phone)  
Christine Hui, Cedar Sinai Medical Center (by phone)

**Definitions**

- The California Department of Public Health – CDPH, “The Department”
- The California Institute for Regenerative Medicine – CIRM
- Stem Cell Research Oversight Committee – SCRO Committee
- Human Stem Cell Research Advisory Committee – HSCR Advisory Committee, “The Committee”
- Guidelines for Human Stem Cell Research, pursuant to Health and Safety Code 125118 – HSCR Guidelines, “The Guidelines”
- The CIRM Medical and Ethical Standards Regulations – “CIRM Regulations”
- Human Embryonic Stem Cell – hESC
- Senate Bill 1260 – SB 1260
- Assisted Oocyte Production – AOP
- Institutional Review Board – IRB
- Body Mass Index – BMI

**Agenda Item #1: Welcome and Introductions**

Professor Henry Greely called the meeting to order and noted that the primary topic of discussion would be the draft reporting forms developed by CDPH for the purposes of SCRO Committees reporting information as mandated by SB 1260. Professor Greely stated the role of the Advisory

Committee was to give advice to CDPH on the forms and CDPH would make the ultimate decisions.

### **Agenda Item #2: Approval of Minutes**

The September 24, 2007 CDPH HSCR Advisory Committee meeting minutes were approved. They can be viewed at:

<http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-Sept24Minutes-12-2007.pdf>.

### **Agenda Item #3: Discussion and Feedback on Proposed Reporting Forms**

Professor Henry Greely began review of the forms by citing the specific statute from SB 1260 that outlines the reporting responsibilities of SCRO Committees. Health and Safety Code §125119.3(a) says, "Each stem cell research oversight committee that has reviewed human embryonic stem cell research pursuant to Section 125119 shall report to the Department annually on the number of human embryonic stem cell projects that the stem cell research oversight committee has reviewed, and the status and disposition of each of those projects, including the information collected pursuant to Section 125342." Section 125342 refers to requirements for research projects involving AOP or any alternative method of oocyte retrieval. Professor Greely felt the statute was unclear about how and by whom the AOP information is to be transmitted.

Professor Greely also inquired whether the Committee should advise CDPH to only include the information required in statute or whether it wanted to recommend data collection of additional information. Based on the public comments received from SCRO Committees, the SCRO Committees encouraged restricting reporting to the statutory requirements. Professor Greely noted the Committee could recommend this approach, or it could suggest collecting additional information if it was for a good reason. CDPH lawyers would have to determine if the Department has the authority to collect this information. Professor Greely asked Dr. Shabbir Ahmad for clarification on this issue.

Dr. Ahmad cited §125119.5.a, "The department shall at least annually review reports from stem cell research oversight committees..." and based on those, "may revise the guidelines developed pursuant to Section 125118 as it deems necessary." He noted that part of the intent in receiving the reports was to determine if revisions to the CDPH guidelines were necessary. Professor Greely concurred that the reports would provide evidence that CDPH and the Committee could use in assessing the need for guideline revisions. Dr. Ahmad continued by citing §125119.5.b, "the department shall provide a biennial review to the legislature on human embryonic stem cell research activity" and pointed out that the Department can only capture data for the legislative review through the reporting forms.

Professor Greely summarized by saying the reporting forms were for the purposes of collecting information that the Department would use in determining if guideline revisions were needed and in order to report to the Legislature on the status of hESC research activity in California. The Committee may want to consider recommending to the Department collecting information beyond the statute.

Dr. Elliot Dorff thought that the wording of the statute gave the Department the authority to request information not specifically mentioned in statute. For example, in several places the statute uses the phrase "this information shall include, but not be limited to..." In order to determine if additional information should be included, though, it is necessary to think about the goals of the reporting forms and how the information collected can help in regulating hESC research by ensuring it is safe and effective.

Professor Greely pointed out that the public comments from SCRO Committees expressed concern about the cost in time and effort needed to fill out the forms. These committees also

noted the potential confidentiality risks in collecting too much individual information in the forms. Professor Greely agreed with Dr. Dorff that the reporting forms would produce useful information for making decisions about regulations, but the drawbacks were the cost and efforts of the SCRO Committees in providing the information and the possible confidentiality risks to individuals (both AOP subjects and researchers).

In reference to the Committee considering collecting additional information, Dr. Gregory Stock felt the Committee had a responsibility in making recommendations to the Department, to determine what information is most valuable and least interfering with the data collection effort, in addition to indicating what information is prescribed in statute.

Professor Greely returned to the statute and cited §125119.3.a, "Each stem cell research oversight committee that has reviewed human embryonic stem cell research...shall report to the department annually on the number of human embryonic stem cell research projects that the Stem Cell Research Oversight Committee has reviewed and the status and disposition of each of those projects..." This part of the statute led to the development of reporting form HSCR1260-1. The remainder of that sentence in statute, "including the information collected pursuant to section 125342", which is the collection of information on research involving AOP, led to the development of Form HSCR1260-2. Professor Greely pointed out that most SCRO Committees would only need to fill out Form HSCR1260-1 since few research projects involve AOP.

### **Form HSCR 1260-1**

**Located at:** <http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-SCROForm-11-2007.xls>

Professor Greely noted there was a cover page with instructions. On page 2, he asked why the reporting timeframe was 18 months. Dr. Ahmad explained that the statute requires reporting from January 1, 2007 on, therefore, the Department must collect information dating back to January 2007 for the first biennial report, due at the end of 2008. This is a transitional reporting year and future reporting will be annually from July 1 to June 30.

Professor Greely then quickly outlined the types of questions about individual projects on pages 3 and 4 and opened the discussion for comments.

Dr. David Magnus was sympathetic to the SCRO Committees' public comments that this form should be in aggregate form rather than requiring particular information that is individuated for each research project protocol. He suggested the form be simplified by aggregating a majority of the data that the Department could then use in its legislative review.

Dr. Dorff agreed, but added that there should be more information about the progress/outcome of research projects so that the Legislature would have an idea of the various research results. Dr. Magnus thought this would be a tremendous amount of work that would not be possible for SCRO Committees to complete and he did not think this type of information was intended by the statutes. Dr. Dorff thought information about the potential (or lack thereof) of stem cell research would be useful to legislators and that reporting this information would only require a few sentences in the reporting form; or if the data were aggregated, then a paragraph or two could describe the overall results of various projects. Dr. Magnus pointed out that a project's status is often changing such that capturing this information would not be possible.

Dr. Stock commented that collecting this information is not a bad idea but that it is important to think about the quality of information that might come from this and how valuable the information might be overall. Dr. Martinez-Maza noted that if part of the intent was to provide the Legislature with this information, than it would be receiving most of the state's hESCR outcome information and in greater detail from the CIRM reports.

Dr. Bert Lubin asked if CIRM would be collecting similar information and if the forms include information about adverse events or complications. Professor Greely cited the statute (§125119.3.b) that requires SCRO Committees to “report to the department regarding unanticipated problems, unforeseen issues or serious continuing investigator noncompliance with the requirements or the determination of the SCRO Committee with respect to the review of human embryonic stem cell research projects, and the actions taken to respond to these situations.” Dr. Ahmad said CDPH would make sure all of these categories were included in Form HSCR1260-1.

Dr. Ahmad also further emphasized the section in statute (§125119.3.a) which mandates SCRO Committees to report on the status and disposition of *each* hESCR project that is reviewed. Dr. Magnus thought the information in the reports could still be captured either individually or in aggregate. Provided the number and description of all projects was included, he thought this would be consistent with the statutory requirements regardless of the specific format. Dr. Dorff remarked this was a creative interpretation of the statute, but Professor Greely felt it was not an impossible interpretation. He pointed out that the statutory language was ambiguous on this issue. Dr. Magnus continued, suggesting that reporting the information in aggregate would achieve the goals of the statute and help the Department in developing the final Legislative review because the information would already be compiled. Dr. Stock questioned if it would then be too difficult or time consuming to extract individual project data if it were needed/requested. Dr. Magnus reiterated the SCRO Committees’ public comments that they would prefer to report in aggregate form.

#### **Form HSCR1260-1: Pages 1 and 2**

Professor Greely suggested discussing the form question-by-question. No one had objections to information in pages 1 (instructions) and 2 (SCRO Committee information) of the form.

#### **Form HSCR1260-1: Page 3**

Dr. Magnus recommended compiling the information in pages 3 and 4 into aggregate form, similar to the example given by Steve Peckman in a public comment, and including how much of each type of hESC research was occurring. He also suggested adding the placement of embryonic stem cells into non-human animals as a type of research in Question 9 (page 3). Dr. Stock proposed keeping Questions 1-6 at the individual level and aggregating the remaining information. This would provide additional information about a project without increasing the burden on SCRO Committees. Dr. Martinez-Maza asked whether new methods of generating pluripotent stem cells should be included. Professor Greely agreed the Committee should address this type of research and suggested discussing it as part of Agenda Item #4 or #5.

In addition to Dr. Stock’s suggestion, Dr. Dorff wanted the forms to include a question about the goal of the research, which would only require a brief one-sentence response. Dr. Stock suggested this information might come from the project title, but Dr. Dorff thought the titles would be too scientific for legislators. Dr. Magnus felt this would be too time-consuming and that the Department would be responsible for communicating to the Legislature what research activity is occurring in the state. This issue was left for the Department to consider.

The Committee agreed to eliminate Questions 7 and 8. Professor Greely reiterated Dr. Magnus’ proposal to aggregate Question 9 by research type. He noted some projects will involve more than one type, in which case the total will be greater than 100%. If the question remained at the individual level, then there would be slightly more work for the SCRO Committees, but the research types could be linked with noncompliance issues and unanticipated problems (Questions 17 and 18, page 4). Dr. Stock felt Question 9 would be less useful individually because the Department would have to aggregate the information eventually. He also suggested removing Questions 5 and 6; he thought they would be out of date quickly and require a lot of work.

Dr. Ahmad noted that the forms included protocol date information in order to help identify the appropriate year of the projects since many of them will last several years, and therefore, be sending in several reports. The Committee considered aggregating Questions 5 and 6. Dr. Martinez-Maza pointed out that many projects are modified for minor reasons, so the "most recent review date" would not be very useful. Professor Greely felt Questions 5.1 and 5.2 could be useful and would also remind projects and SCRO Committees that project review is required annually. Overall, the Committee felt Question 6 was unnecessary, especially since Questions 17 and 18 would capture some of this information.

#### **Form HSCR 1260-1: Page 4**

For Question 10, Dr. Magnus asked why it was necessary to collect information about human oocytes when Form HSCR 1260-2 already includes this information. Dr. Ahmad clarified that if a research project only involves oocytes or embryos from IVF clinics initially retrieved for reproductive purposes, then Form HSCR 1260-2 would not need to be completed. Question 10 helps collect data about the source of the research materials, as well as links this form with the other form in the case of human oocytes retrieved for research purposes or the development of medical therapies.

Dr. Magnus asked whether this information should be aggregate by indicating how many protocols involve procuring oocytes from IVF patients, etc. Dr. Ahmad explained that the question establishes the provenance of the research materials. Dr. Magnus thought it would be redundant to collect information in 10.1 because the answer to that question would be clear if Form 2 was not also completed. Dr. Ahmad noted that there could be an alternate source of the materials that would need to be explained. Dr. Magnus was concerned about how difficult this information would be for SCRO Committees to collect and the possibility that protocols might have a combination of sources for oocytes/embryos. He emphasized that at the time of protocol review, this information is not available. Dr. Stock suggested using a check box to indicate if oocytes were retrieved specifically for research and thus would indicate that Form 2 would need to be completed. Professor Greely returned to Dr. Magnus' point about oocyte/embryo information not being available at the time of protocol review, but that it would be available when the project was renewed. He also was not clear on the rationale for including the list of unique clinic patient identifiers (Question 10.2.2).

Dr. Margaret McLean interjected that she had to leave the conference call, and inquired if Question 11 was necessary since projects fully funded by CIRM would not need to fill out the form. With Dr. McLean's departure, Professor Greely mentioned that the Committee no longer met quorum but they could continue to advise the Department even though they could not formally vote on decisions/recommendations.

The Committee suggested removing Questions 11 and 12 because most SCRO Committees will not have specific funding information and it would not necessarily be available at the time of protocol review. Additionally, they felt that, while interesting, the information would have limited value and could possibly change within a reporting year. Professor Greely pointed out that if the Legislature is interested in more specific funding information, then the Department could ask SCRO Committees directly for this information and they would typically be eager to comply.

For Questions 13, 14, and 15, Dr. Magnus initially suggested the information about locations and sources of collaborators and research materials should be aggregated, but then ultimately felt that this type of information would be available in the literature and did not need to be in the form. Dr. Stock thought Question 13 might be useful in aggregate form and would be easy to answer, but Dr. Magnus noted that this information could change throughout the project. Dr. Stock inquired whether the intent of the question was to get a sense of where, or if, research is shifting geographically. Based on §125119.3.b, Professor Greely offered that Question 13 could also be helpful in obtaining information if there are problems with certain research projects. If the

information would be easy to access in the literature and may change over time, Dr. Stock wondered whether the information would really be helpful to collect.

Dr. Ahmad explained that the Department included these questions as a means of determining provenance of the research materials and reiterated §125346 that "All oocytes procured outside of this state for research taking place in this state shall meet these same standards." Dr. Magnus emphasized that there was a difference between a research requirement and the SCRO Committee reporting requirements. He also noted that sources of oocytes are very limited.

In relation to individual project versus aggregate reporting, Pat Rodriguez pointed out that §125119.3.a states "Each SCRO Committee that has reviewed hESCR pursuant to Section 125119 shall report to the department annually on...the status and disposition of *each* of those projects, including the information collected pursuant to Section 125342." This may indicate that there is a requirement to report individually in order to satisfy the statute. Professor Greely argued that it depends on where you decide to include the "information collected" to and where you attach that to the clause that has "each." He also mentioned that the questions the Committee suggested be aggregated (e.g. Question 9) were not related to status and disposition, which would apply to "each" project. Pat Rodriguez added that in §125342, the legislation was very clear about the requirement that the department take the information collected about oocyte retrieval and aggregate this data. So the legislation did use "aggregate" specifically in the oocyte retrieval section but did not use it in the SCRO Committee reporting information section. Dr. Stock pointed out that the Committee's recommendations were to capture individual information on Question 1-5, cut 7 and 8, aggregate 9, cut 11-15, and 17-18 would be individualized. Professor Greely summarized that the Committee's advice was to use the broader statutory language of what is required to be reported and some of the information will be individually reported.

For Question 16, Dr. Magnus thought it was too much information for a SCRO Committee to provide. Dr. Dorff offered that a summary could come directly from the principal investigator, but Dr. Magnus argued that this would not be in lay terms. Dr. Stock suggested including this question in the forms researchers must fill out for SCRO Committee review, allowing the information to be copied into the Department's form. Professor Greely thought writing a brief two-sentence lay description would be easy for SCRO Committees to do for each project. On the other hand, some SCRO Committees may give vague, and therefore, meaningless descriptions. Dr. Magnus further argued that writing the description would be more complicated than it sounded and that reporting this information was not required in statute. Dr. Dorff thought the question fell under "disposition" of the project. Dr. Martinez-Maza mentioned that the UCLA IRBs have to write short summaries, which they ask the investigators to complete. For SCRO Committees then, a brief summary would need to be added to the existing SCRO Committee forms. There was concern about developing summaries for past projects dating back to January 1, 2007, but Dr. Stock suggested only requiring summaries for new applications and renewals. Dr. Magnus reiterated that the SCRO Committees' public comments felt this information was not supported by statute. Dr. Ahmad pointed out that the intent of the legislature is to know about hESC research activity and that Question 16 would help capture general information about this activity that the project title alone could not.

Dr. Geoff Lomax returned to an earlier discussion about the information CIRM provides about its projects. He mentioned that CIRM develops a compilation of (grant) awards and research abstracts approved for funding and then provides a summary of the projects. He was not sure if a lay summary was required, but CIRM staff use the summary provided by researchers and modify it for the public to an approximate 500-word abstract.

In summary, the Committee suggested that Questions 1-5 (removing 5.3), 16 (not retroactive), 17, and 18 collect individual project data, and that Question 9 collect aggregate data.

**Form HSCR1260-2: Page 1**

(Located at: <http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-OocyteForm-11-2007.xls>)

No one had objections to information in page 1 (instructions).

**Form HSCR1260-2: Page 2**

Professor Greely mentioned someone might question how much IRB contact information is needed but that it would not hurt to collect it.

Dr. Ahmad and Professor Greely clarified that this form would be transmitted to the Department by a SCRO Committee and that (per §125342.a) any “research program or project that involves AOP or any alternative method of oocyte retrieval shall ensure that a written record is established and maintained to include” specific information about each AOP subject. Dr. Magnus agreed that the forms should be transmitted by SCRO Committees to help with compliance. Professor Greely further clarified that the researcher would collect specific information about each subject and then send this information to the corresponding SCRO Committee, which would send it on to the Department.

**Form HSCR1260-2: Page 3**

Dr. Magnus recommended removing “height” and “weight” from the list of demographics. Professor Greely noted that §125342.a.1 says “The demographics of subjects, including, but not limited to, their age, race, primary language, ethnicity, income bracket, education level, and the first three digits of the ZIP code of current residence.” So the statute uses “but not limited to” in relation to demographics. Dr. Magnus felt that keeping height and weight in addition to the other variables might compromise subject confidentiality. Cindy Chambers explained that these were included to calculate BMI because there are risks associated with both very small or very large women undergoing AOP. Dr. Magnus noted how easy it is to identify individuals using these types of data. While Professor Greely agreed re-identifying individuals can be very easy, he suggested this may not be a problem because statute says the information collected for each subject (per §125342.b.1) “shall be reported to the state which shall aggregate the data and make it publicly available in a manner that does not reveal personally identifiable information.” Dr. Ahmad further noted that in the public health field if you have fewer than five cases in a particular area, then you do not report the information for confidentiality purposes. So the Department would take this into consideration before releasing any subject data.

Professor Greely continued with the form and the Demographics section and noted that “born in the US” was also not required in statute, although the concern about these women being exploited was understandable. After comments about using ranges for the variables to help reduce identifiability, Kate Cordell clarified that most of the variables had dropdown menus with ranges. The Committee suggested increasing the income bracket range.

For Questions 4-7, Professor Greely noted these related to the statute (§125342.a.2) that states, “This record should be sufficient to determine the provenance and disposition of those materials” and that provenance could mean where the materials came from or it could mean whether they were ethically derived. Dr. Magnus suggested cutting these questions as the researchers would already be required by their SCRO Committees and IRBs to abide by these, so answering the questions again in this form would be duplicative. Professor Greely noted that the questions served as a regulatory reminder and that because of the sensitivity involved in oocyte procurement, written consent is also required. Dr. Martinez-Maza pointed out that other states or countries may not be fully aware of California’s oocyte research donor requirements, but would

still be required to follow them if sending oocytes to a researcher/collaborator in California. However, this scenario is not likely since oocyte freezing technology is not well developed and it is not anticipated there will be many oocyte research donors. Dr. Stock agreed that the questions were highly redundant. The SCRO Committees could not aggregate this data since a record is required for each subject.

For Questions 8-14, Professor Greely thought Question 9 referred to the disposition of every oocyte, Question 10 was a more broad interpretation of provenance and that alternative methods may be more prevalent in the future. Dr. Stock felt Question 11 regarding expense reimbursement might be difficult to ascertain. It was noted that not all the questions could be filled out initially. Dr. Magnus emphasized that the form should follow statute as closely as possible with regard to reporting requirements. He suggested removing Questions 10 and 12-14, and supported keeping 11 for safety reasons. Dr. Ahmad noted that Question 13 refers to a medical procedure that is required in statute, but researchers are not required to report the information. It is a regulatory reminder question.

Dr. Stock asked if the subjects would be signing these forms to verify the information is correct. If the forms were verified by subjects, then including questions like 4-7 may have some benefit. Dr. Ahmad replied that signatures were not required. Dr. Stock recommended the SCRO Committees have the researchers sign the forms as verification. There was discussion about who was responsible for completing the different parts of the form. Department staff indicated that the intent was to have oocyte procurement facilities fill out the form. The Committee agreed this would work and thought the facilities may have to coordinate with the researchers regarding the use of the oocytes (Question 9). Because oocytes have to be used immediately, the Committee felt it would not be difficult to know the type of research in which the oocytes would be used.

In light of the SCRO Committees' public comments, Professor Greely agreed that Questions 4-7 should be cut. While the "date of retrieval" (Question 8) is not required in statute, it helps distinguish between the different oocyte retrieval procedures if a woman donates twice in one year. Dr. Magnus suggested using only month and year for donor confidentiality purposes.

Professor Greely recalled that Question 3.7, referring to donor parity, was not in statute. Department staff explained that this was included based on a previous public comment about concern for nulliparous women donating oocytes. It was suggested to change the dropdown for parity to 0 and 1+. Compared to Question 10 and 12-14, Professor Greely thought there was a stronger argument for safety reasons to retain Question 11.

#### **Form HSCR1260-2: Page 4**

For time concerns, Professor Greely moved the discussion to the final page of the form. He noted there were various public comments about the clarity of the adverse health outcomes. Kate Cordell indicated there were several mouse-over comments and dropdown menus on the form. There were concerns about the length of time the donors would need to be followed to determine if there were adverse outcomes related to the procedure, but it was noted that the form was collecting data on the known adverse outcomes, not on all adverse outcomes.

Emily Galpern suggested that the Demographics section use US Census categories. Dr. Ahmad noted that the form has to follow the California Department of Finance categories. She also mentioned Susan Burke-Fogel's suggestions to add questions about disclosing professional/financial interest in the outcome of a research project and providing the research donor with a statement about the existing state of the research. The Committee noted those issues were required by the review committees so it would be redundant to require reporting on them. Emily Galpern emphasized the importance of Question 10 for safety purposes in case a particular method of oocyte retrieval was leading to certain adverse health outcomes.

Based on an earlier comment, Dr. Lomax clarified that CIRM regulations do not require a physical and psychological screening be performed prior to oocyte donation (Question 7). Dr. Lomax also pointed out the likely difference in time costs and burden for SCRO Committees that are housed in institutions/universities versus Committees that are contracted for oversight.

### **CDPH Timeline**

Dr. Ahmad indicated the Department would be revising the forms in December and posting them again for public comment and Committee review in January. The forms will then need internal approval and should be ready for distribution by March or April.

### **Agenda Items 4 and 5: Discussion of Existing Guidelines and Topics for Future Meetings**

Professor Greely suggested getting feedback via email from the Committee regarding possible changes to the guidelines and/or legislation that would eliminate the need for SCRO Committee review of non-hESC research. The Committee may also need to revise the guidelines and/or legislation based on new methods of creating pluripotent cells and in regard to specific issues of confidentiality. Dr. Magnus mentioned the need to discuss old legislation stemming from the UCI fertility clinic scandal that has now become problematic and may be in violation of federal law. Dr. Martinez-Maza recommended discussing whether SCRO Committees should be overseeing pluripotent stem cells that are not derived from embryos or oocytes.

Professor Greely and Dr. Ahmad will determine whether a Committee teleconference will be necessary for the next round of revisions to the forms.

Dr. Magnus suggested the Committee consider changing the makeup of the Committee and whether it would be helpful to add or replace members.

The Committee also agreed it was easier for most members to meet in northern California.

**Meeting adjourned.**