

Reporting on Human Embryonic Stem Cell Research and Research Involving Assisted Oocyte Production in California

Maternal, Child and Adolescent Health Division

Center For Family Health

California Department of Public Health

**July 25, 2008 CIRM Standards Working Group Meeting
Los Angeles, California**





Overview

1. Statutory Mandates
2. Reporting Form Development Process
3. Final Reporting Forms
4. Next Steps



Statutory Mandates – Human Embryonic Stem Cell Research

SB 1260 (Ortiz, 2006) Amended H&S Code §§125119, 125119.3, and 125119.5

Requirement for SCRO Committee review and approval of human embryonic stem cell (hESC) research, as well as continuing review at least once per year

- **§125119(a)(1):** All research projects involving the derivation or use of human embryonic stem cells shall be reviewed and approved by a stem cell research oversight committee prior to being undertaken.
- **§125119(b):** Not less than once per year, a stem cell research oversight committee shall conduct continuing review of human embryonic stem cell research projects reviewed and approved under this section.



Statutory Mandates – Human Embryonic Stem Cell Research

SB 1260 (Ortiz, 2006) Amended H&S Code §§125119, 125119.3, and 125119.5

Mandate for annual reporting by SCRO Committees

- **§125119.3(a):** 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 research 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.
- **§125119.3(b):** Each stem cell research oversight committee shall also report to the department regarding unanticipated problems, unforeseen issues, or serious continuing investigator noncompliance...



Statutory Mandates – Human Embryonic Stem Cell Research

SB 1260 (Ortiz, 2006) Amended H&S Code §§125119, 125119.3, and 125119.5

Requirement for annual Department review of reports and biennial Legislative review

- **§125119.5(a):** The department shall at least annually review reports from stem cell research oversight committees, and may revise the guidelines developed pursuant to Section 125118, as it deems necessary.
- **§125119.5(b):** The department shall provide a biennial review to the Legislature on human embryonic stem cell research activity. These biennial reviews shall be compiled from the reports from stem cell research oversight committees.



Statutory Mandates – Assisted Oocyte Production for Research

SB 1260 (Ortiz, 2006) Added Chapter 2 (commencing with §125330)

Institutional Review Board (IRB) requirements of research projects involving assisted oocyte production (AOP)

- §125341(a) – (h) includes:
 - Written summary of health risks
 - Informed consent requirements
 - Postprocedure medical examination
 - Coverage of medical expenses



Statutory Mandates – Assisted Oocyte Production for Research

SB 1260 (Ortiz, 2006) Added Chapter 2 (commencing with §125330)

Components of written record for subjects and oocytes

- **§125342(a):** A 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, but not be limited to, all of the following components:
 - (1) 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.
 - (2) Information regarding every oocyte that has been donated or used. This record should be sufficient to determine the provenance and disposition of those materials.
 - (3) A record of all adverse health outcomes, including, but not limited to, incidences and degrees of severity, resulting from the AOP or any alternative method of oocyte retrieval.



Statutory Mandates – Assisted Oocyte Production for Research

SB 1260 (Ortiz, 2006) Added Chapter 2 (commencing with §125330)

Subject privacy provisions

- **§125342(b)(1):** The information included in the written record pursuant to subdivision (a) shall not disclose personally identifiable information about subjects, and shall be confidential and is deemed protected by subject privacy provisions of law.

This information shall be reported to the State Department of Health Services, which shall aggregate the data and make it publicly available, as set forth in paragraph (2), in a manner that does not reveal personally identifiable information about the subjects.

- **§125342(b)(2):** The department shall provide public access to information which it is required to release pursuant to the California Public Records Act...



Statutory Mandates – hESC Research and AOP for Research

Reporting requirements not applicable to research projects fully funded by CIRM

- **Section 8:** This act shall not be construed to amend Proposition 71, approved by the voters at the November 2, 2004, general election.



Summary of Responsibilities

CDPH

- Annually review reports from SCRO Committees and IRBs
- Biennial review to Legislature
- Aggregate data from AOP reporting forms and publicly release

SCRO Committees

- Conduct annual review of projects
- Report annually to CDPH on each hESC project
- Review and forward to CDPH any AOP reporting forms

IRBs

- Ensure research involving AOP follows statutory requirements
- Review and forward to CDPH any AOP reporting forms, if no SCRO Committee

Researchers

- hESC research projects need SCRO Committee review and approval
- Follow statutory requirements for research involving AOP
- Ensure AOP reporting forms are completed for each subject; send forms to review committee



Reporting Form Development Process

1. Forms drafted based on interpretation of statutes
2. CDPH HSCR Advisory Committee meeting (Sept. 2007) – discussion and revision of forms
3. CDPH HSCR Advisory Committee meeting (Dec. 2007) – discussion and revision of forms
 - Public comments accepted
4. Public comment period for revised forms (Dec. 2007 – Jan 2008)
5. CDPH Office of Legal Services review (for multiple versions)
6. Beta testing by external reviewers – revisions made
7. Forms finalized and posted to website:
<http://www.cdph.ca.gov/programs/HSCR/Pages/HumanStemCellResearchReportingForms.aspx>



Final Reporting Forms

Form HSCR1260-1: SCRO Committee

Form HSCR1260-2: Research Involving Oocyte Retrieval

- Both forms include an instructions page
 - Statutory authority
 - First round reporting period: January 1, 2007 – June 30, 2008
 - Reporting period: July 1 – June 30 (each year)
 - Due date: August 1 (each year)
 - Special Excel features
 - Email completed forms to stemcell@cdph.ca.gov
 - Supporting materials



Final Reporting Forms

Form HSCR1260-1: SCRO Committee

Stem Cell Research Oversight of Individual Projects

Form HSCR1260-1



Research Project 1

Research Project Identification

1.1. Research Protocol ID (assigned by SCRO Committee):

1.2. Initial Review Date:

1.3. Most Recent Review Date:

1.4. Research Project Title:

Research Project Disposition

2. Project Disposition

Research Project Status & Activity

3. This Research Project Involves: (answer all that apply & leave non-applicable fields blank)

<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>

- 3.1. Research of human embryonic stem cells *in vitro*
- 3.2. Use of human embryonic stem cells *in vivo* (non-human)
- 3.3. Creation/Derivation of human embryonic stem cells or cell lines
- 3.4. Use of human oocytes for hESC research
- 3.5. Use of human embryos for hESC research
- 3.6. Somatic cell nuclear transfer (SCNT)
- 3.7. Parthenogenesis
- 3.8. Clinical Trial..... 3.8.1. Phase
- 3.9. Other hESC Methods.... 3.9.1. Explain

Indicate from the drop-down list whether during this reporting year the project 1) is In Progress; 2) has been Completed; or 3) was Terminated Early, Closed or rolled into a new project.

Research using the National Institutes of Health (NIH) / federal hESC lines should be included.

At this time, reporting on research using induced pluripotent stem (iPS) cells is not required.



Final Reporting Forms

Form HSCR1260-1: SCRO Committee

The oocytes from these women may include oocytes that fail to fertilize, are immature, or are otherwise deemed inappropriate for clinical use.

This includes women who are donating oocytes from a single oocyte retrieval procedure for both clinical and research purposes.

The SCRO Committee and Research Project must ensure that Form HSCR1260-2 has been completed for each female subject included in 6.2 and 6.3.

Provenance of Every Human Oocyte Donated or Used	
4. Does this project protocol include the use of human oocytes?	
<input type="text"/>	(If not, skip to question 7)
5. If this project includes the use of human oocytes, did the project plan to procure oocytes from:	
<input type="text"/>	5.1. Female <i>In Vitro</i> Fertilization (IVF) patients/donors
<input type="text"/>	5.2. Female donors specifically for research or the development of medical therapies
<input type="text"/>	5.3. Other.....5.3.1. Explain <input type="text"/>
If answered yes for 5.2 or 5.3, Form HSCR1260-2 must be completed for every oocyte donated or used.	
6. For projects that have existed >1 year, please specify the accumulative total numbers of women from whom oocytes were procured (this includes current and previous reporting years).	
<input type="text"/>	6.1. Number of female IVF patients/donors
<input type="text"/>	6.2. Number of female donors specifically for research or the development of medical therapies
<input type="text"/>	6.3. Other.....6.3.1. Explain <input type="text"/>
<input type="text"/>	6.4. Has Form HSCR1260-2 been completed for every subject included in 6.2 and 6.3?
Research Project Issues & Response (If none, skip 7-10)	
7. Describe any unforeseen issues or unanticipated problems. (limit of 1000 characters ? 200 words)	
8. Describe any serious investigator noncompliance issues. (limit of 1000 characters ? 200 words)	
9. Describe response of SCRO Committee to these situations. (limit of 1000 characters ? 200 words)	
10. If any issues or problems were reported in questions 7 or 8, please provide a brief summary, description or abstract of this research project. (limit of 3,000 characters ? 500 words)	



Final Reporting Forms

Form HSCR1260-2: Research Involving Oocyte Retrieval

Most women undergoing ovarian stimulation will have at least mild symptoms of ovarian hyperstimulation; therefore, only moderate and severe adverse health outcomes are included here.

Patients considered to have moderate symptoms should also have a normal hematological profile. More severe cases will include an abnormal profile.

Patients considered to have moderate symptoms should also have a normal hematological profile. More severe cases will include an abnormal profile.

Adverse Health Outcomes	
Hormone Treatment (Oocyte Production/Ovarian Stimulation)	
<p>▲ 6. Select "Yes" if the subject experienced moderate and severe adverse health outcomes as a result of ovarian stimulation for AOP:</p> <p>Moderate:</p> <p><input type="checkbox"/> 6.1. Discomfort, abdominal fluid buildup</p> <p><input type="checkbox"/> 6.2. Nausea/vomiting</p> <p>Severe:</p> <p><input type="checkbox"/> 6.3. Grade A</p> <p><input type="checkbox"/> 6.4. Grade B</p> <p><input type="checkbox"/> 6.5. Grade C</p>	
Oocyte Retrieval (Surgical Procedure)	
<p>7. Select "Yes" if the subject experienced any of the following adverse health outcomes as a result of the oocyte retrieval surgery:</p> <p><input type="checkbox"/> 7.1. Vaginal bleeding</p> <p><input type="checkbox"/> 7.2. Intra-abdominal bleeding</p> <p><input type="checkbox"/> 7.3. Intestinal injuries (e.g., damage to uterus or ureter)</p> <p><input type="checkbox"/> 7.4. Inflammation of the peritoneum (peritonitis)</p> <p><input type="checkbox"/> 7.5. Severe pain (requiring hospitalization)</p> <p><input type="checkbox"/> 7.6. Ovarian torsion</p> <p><input type="checkbox"/> 7.7. Infection</p> <p><input type="checkbox"/> 7.8. Surgery (required to correct one or more adverse health outcome)</p>	
Other Issues Related to Adverse Health Outcomes	
<p>8. Indicate if the subject experienced any of the following:</p> <p><input type="checkbox"/> 8.1. Unplanned pregnancy (resulting from this donation)</p> <p><input type="checkbox"/> 8.2. Adverse psychological outcomes (e.g., psychological distress or regret)?</p> <p><input type="checkbox"/> 8.3. Other moderate or severe adverse health outcomes not included in 6-7 above?</p> <p>8.3.1 If other, please explain (limit 500 characters):</p> <div style="border: 1px solid black; height: 40px; width: 100%;"></div>	



Final Reporting Forms

Form HSCR1260-2: Research Involving Oocyte Retrieval

Grade A: Severe cases have enlarged ovaries, clearly evidenced abdominal swelling, shortness of breath, nausea and vomiting, but blood chemistry is normal. Patients with Grade A severe hyperstimulation syndrome are generally treated as outpatients.

Grade B: Cases are more severe than Grade A. The concentration of red blood cells is markedly increased due to fluid loss from the blood vessels. The white blood cell count may be higher than normal. The blood flow to the kidneys may be less than normal, leading to a buildup of creatinine and a decreased production of urine. These patients may require hospitalization and should be monitored closely.

Grade C: Patients have serious complications, such as a blood clot or kidney failure. They need hospitalization and appropriate treatment.

Adverse Health Outcomes

Hormone Treatment (Oocyte Production/Ovarian Stimulation)

6. Select "Yes" if the subject experienced moderate and severe adverse health outcomes as a result of ovarian stimulation for AOP:

Moderate:

<input type="checkbox"/>	6.1. Discomfort, abdominal fluid buildup
<input type="checkbox"/>	6.2. Nausea/vomiting

Severe:

<input type="checkbox"/>	6.3. Grade A
<input type="checkbox"/>	6.4. Grade B
<input type="checkbox"/>	6.5. Grade C

Oocyte Retrieval (Surgical Procedure)

7. Select "Yes" if the subject experienced any of the following adverse health outcomes as a result of the oocyte retrieval surgery:

<input type="checkbox"/>	7.1. Vaginal bleeding
<input type="checkbox"/>	7.2. Intra-abdominal bleeding
<input type="checkbox"/>	7.3. Intestinal injuries (e.g., damage to uterus or ureter)
<input type="checkbox"/>	7.4. Inflammation of the peritoneum (peritonitis)
<input type="checkbox"/>	7.5. Severe pain (requiring hospitalization)
<input type="checkbox"/>	7.6. Ovarian torsion
<input type="checkbox"/>	7.7. Infection
<input type="checkbox"/>	7.8. Surgery (required to correct one or more adverse health outcome)

Other Issues Related to Adverse Health Outcomes

8. Indicate if the subject experienced any of the following:

<input type="checkbox"/>	8.1. Unplanned pregnancy (resulting from this donation)
<input type="checkbox"/>	8.2. Adverse psychological outcomes (e.g., psychological distress or regret)?
<input type="checkbox"/>	8.3. Other moderate or severe adverse health outcomes not included in 6-7 above?
	8.3.1 If other, please explain (limit 500 characters):
<input style="width: 100%; height: 40px;" type="text"/>	



Next Steps

Next Steps

- CDPH HSCR Program will review completed forms, develop biennial review for Legislature and publicly release aggregated AOP data by the end of 2008
- CDPH HSCR Program is in the process of developing regulations for the reporting forms