Review to the California Legislature

HUMAN EMBRYONIC STEM CELL RESEARCH ACTIVITY IN CALIFORNIA

Review prepared by:

Human Stem Cell Research Program
Maternal, Child and Adolescent Health Division
Center for Family Health
California Department of Public Health

Pursuant to Health and Safety Code §125119.5(b)
(Senate Bill 1260, Ortiz, Session 2005-2006)

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I. EXECUTIVE SUMMARY

Human embryonic stem cell research offers the promise of new therapeutic treatments as well as potential cures for numerous debilitating diseases that gravely affect the health of our population. Recent California legislation on stem cell research has allowed research to flourish while still maintaining high ethical standards. Oversight has been achieved by mandating human embryonic stem cell research (hESC) projects be reviewed and approved by a Stem Cell Research Oversight Committee (SCRO) before project commencement. Further, hESC projects must follow research guidelines developed by the California Department of Public Health (CDPH), or the California Institute for Regenerative Medicine (CIRM) in the case of projects fully funded by CIRM.

Research projects that are not solely funded by CIRM fall under the jurisdiction of both CDPH and CIRM. Per California statute, the SCRO Committees that oversee these projects must report specific project information to CDPH. Through collaboration with the CDPH Human Stem Cell Research Advisory Committee, members of the public, and external stakeholders, CDPH developed reporting forms for SCRO Committees to use in reporting project information. Statute further stipulates that CDPH is to use these reports to develop biennial reviews for the Legislature detailing hESC research activity in California.

The first hESC research biennial review to the Legislature includes hESC research conducted between January 1, 2007 and June 30, 2008. This review was developed from SCRO Committee reports and offers a better understanding of hESC research activity occurring in the State. Fifteen SCRO Committees provided detailed reporting on 244 hESC research projects from 16 different institutions. Ten of the reporting institutions were either public or private universities, including eight University of California schools. Three of the institutions were research institutes and the remaining three entities were medical centers or hospitals. The types of research included somatic cell nuclear transfer, stem cell line derivation, and research involving the use of oocytes (eggs). The projects included research into adverse health outcomes, such as Alzheimer's disease, cancer, and heart disease. Some projects also investigated the mechanisms of cell function and differentiation of cardiovascular system-related and nervous system-related stem cells. Of the 244 projects, there were no reports of unanticipated problems, unforeseen issues, or serious instances of investigator noncompliance.

The data collection and analysis of hESC research by CDPH is currently a main source of consolidated information about stem cell research occurring in the State. While the 244 research project reports may not be representative of all hESC projects in California, they do provide an overview of the diversity of hESC research types and activities occurring in the State. Ongoing biennial reviews to the Legislature will build upon these early data and identify trends in research activity.

Review of Human Embryonic Stem Cell Research Activity in California (Pursuant to Health and Safety Code §125119.5(b))

II. INTRODUCTION

The ability of human embryonic stem cells to become all cell types of the body provides researchers a unique opportunity to use these cells to investigate disease systems and to work towards the development of therapies for some of the most common diseases affecting people today. However, the use of an embryo in developing hESC lines and the possible future use of these cells in humans for therapies makes hESC research highly politically sensitive and qualifies the need for oversight to ensure that this research is being conducted in a legally, ethically and socially acceptable manner.

The California Legislature has passed several bills related to oversight for hESC research. Most recently, Senate Bill (SB) 1260 (Ortiz, Session 2005-2006), effective January 1, 2007, requires that all research projects involving the derivation or use of hESCs be reviewed and approved by a SCRO Committee prior to being undertaken and on an annual basis thereafter. Additionally, each SCRO Committee is required to report to CDPH on the projects they review and oversee. As part of this legislation, the Department must annually review the reports provided by the SCRO Committees and use these reports to provide biennial reviews to the Legislature on hESC research activity in California. This is the first biennial review to the Legislature covering the reporting period of January 1, 2007 to June 30, 2008.[1]

III. BACKGROUND

On November 6, 1998, University of Wisconsin professor, James Thomson reported the first derivation of hESC lines. Human embryonic stem cells are derived from embryos that are typically four or five days old and consist of a hollow microscopic ball of cells called a blastocyst. Embryonic stem cells are pluripotent, meaning they can become all cell types of the body. Although some progress has been made recently in reprogramming adult stem cells to revert back to a more embryonic stem cell-like pluripotent state, true embryonic stem cells remain the gold standard and will continue to be a significant focus for research efforts. Human embryonic stem cell lines have the potential to yield information about human development, improve testing of new drugs, and generate cells and tissues for use in cell-based therapies for a range of diseases and conditions such as Parkinson's and Alzheimer's, spinal cord injuries, strokes, diabetes, and heart disease.

[1] The first round of reporting spans an eighteen month period from January 1, 2007, when SB 1260 first went into effect, to June 30, 2008. Subsequent reports will provide information on human embryonic stem cell research on an annual basis beginning July 1 through June 30.

Since the derivation of hESC lines in 1998, rapid developments in stem cell research have occurred. Although the use of hESCs for clinically approved cell-based therapies is believed to be many years away, it is important to address the ethical, legal and social issues surrounding hESC research and the expected use of hESCs for transplantation. Failure to adequately address these issues may delay or preclude research that will test whether interventions based on hESCs are safe and effective and undermine progress toward stem cell therapies.

Stem Cell Policy and Legislation

Although the field of hESC research is still young, California has a robust legislative history when it comes to human stem cells and closely related research. From early legislation addressing the morality and ethics of human cloning to more recent support for State-sponsored human stem cell research, California legislation has evolved alongside advances in this complex field, addressing the ethical, legal and social issues that emerge and providing oversight to protect the interests of Californians.

California legislation that has impacted the development of hESC research statewide includes the following:

- **SB1344 (Johnston, Session 1997-1998)—**This bill imposed a five-year moratorium on human cloning, as well as the purchase or sale of an ovum, zygote, embryo or fetus for the purpose of human cloning. It also authorized significant fines for violation of this ban.

- **SB 1230 (Alpert, Session 2001-2002)—**This legislation amended the ban on human cloning, banning human reproductive cloning specifically and extending this prohibition indefinitely. It also required the Department to develop an advisory committee comprised of bioethicists and representatives from medicine, biotechnology, genetics, law, religion and the public to advise the Legislature and Governor on human cloning and other issues relating to human biotechnology.

- **SB 253 (Ortiz, Session 2001-2002)—**The California Legislature first directly addressed the issue of human embryonic stem cells in 2002, passing a bill that declared the policy of the State shall be to permit research involving the derivation and use of hESCs, human embryonic germ cells, and human adult stem cells. This legislation also included provisions designed to protect human subjects involved in such research, including requirements for IRB oversight and informed consent regarding leftover embryo disposition, as well as a ban on the purchase or sale of embryonic or fetal tissue for research purposes.

- **SB 322 (Ortiz, Session 2003-2004)—**In 2003, Senator Ortiz authored SB 322 as a means to address the multidisciplinary and multifaceted issues involved in the burgeoning field of hESC research (Appendix A). At the time, there was a lack of well-deliberated guidelines as well as a void in both state and federal oversight of hESC research. The development of SB 322 was considered essential to fill that void and provide a set of ethically, legally and socially acceptable standards by which this research in California could continue with careful oversight.

  Sections 125118 - 125119.5 of the California Health and Safety Code enacted by SB 322, Chapter 506, Statutes of 2003, charged the Department to perform four primary tasks:

  1. Develop statewide guidelines for research involving the derivation or use of hESCs in California and revise them as needed.
  2. Establish a Human Stem Cell Research Advisory Committee consisting of 13 members representing specified professional specialties, including scientists, medical ethicists, legal experts, and representatives of religious organizations, for the purpose of developing the guidelines.
  3. Collect and review mandated status reports from all Institutional Review Boards (IRBs) in California regarding the status of reviewed projects and proposals involving hESC research.
  4. Report annually to the Legislature on hESC research activity in California.

  Sections 125118–125119.5 were to statutorily repeal effective January 1, 2007 unless a later enacted statute deleted or extended the repeal date.

- **SB 771 (Ortiz, Session 2003-2004)—**Also in 2003, the California Legislature adopted legislation requiring fertility treatment providers to provide their patients with a form that sets forth advanced written directives regarding embryo storage and disposition options, and requiring providers to convey specified information to all individuals wishing to donate embryos for research purposes (California Health and Safety Code, Sections 125300–125315). These informed consent requirements include statements that early human embryos will be used to derive human pluripotent stem cells for research, and that derived cell lines may be kept for many years. This bill also required the Department to establish and maintain an anonymous registry of embryos available for research if funding became available.

- **Proposition 71 (2004)—**In November of 2004, California voters approved the California Stem Cell Research and Cures Act by a wide margin (59% vs. 41%). This initiative authorized $3 billion in State general obligation bonds to provide funding for stem cell research and research facilities in California (Appendix B). This act established the California Institute for

Regenerative Medicine (CIRM) and provided the requirements for stem cell research funded by CIRM.

Proposition 71 also exempted CIRM and its grantees from the requirements in Health and Safety Code Sections 125118-125119.5 (enacted with SB 322 in 2003) and Sections 125300 and 125320, as well as "any other current or future state laws or regulations dealing with the study and research of pluripotent stem cells and/or progenitor cells." Proposition 71 further specified "in order to avoid duplication or conflicts in technical standards for scientific and medical research, with alternative state programs, the institute will develop its own scientific and medical standards to carry out the specific controls and intent of the act." Thus, while the Department (under SB 322) and CIRM (under Proposition 71) have similar mandates with respect to stem cell research, the two bodies are complementary in respect to their authority. CIRM has full authority in the monitoring and oversight of CIRM-funded research, and the Department has authority in the monitoring, reporting and oversight of research that receives funding from other sources.

The increased State funding for hESC research under Proposition 71 has promoted an influx of researchers and an expansion of research activity within California. Although some of this research may be fully funded by CIRM and thus subject only to CIRM oversight and regulations, research that falls under the monitoring authority of CDPH and its Human Stem Cell Research Program has also expanded from private research organizations moving to California and new organizations forming that conduct research not fully funded by CIRM. With continued CIRM funding for the development of new hESC research facilities and support for researcher training programs, research activity is likely to continue growing within the State.

- **Senate Joint Resolution 17 (Ortiz, Session 2005-2006)—**Further demonstrating California's support for hESC research, in 2005 the California Senate and Assembly memorialized Congress and the President of the United States to lift restrictions on federal funding for stem cell research. The joint resolution spoke against impairing the ability of researchers to conduct promising stem cell research applications, and advocated for the development of ethical guidelines for federally funded stem cell research and prohibitions on human cloning.

- **SB 1260 (Ortiz, Session 2005-2006)—**Recognizing the need for continued oversight of hESC research in California, SB 1260 was enacted in 2006, extending the provisions of SB 322 for developing guidelines and reviewing stem cell research not solely funded by CIRM (Appendix C). SB 1260 also established provisions in Health and Safety Code Sections 125119 and 125300 for developing SCRO Committees, and required that

all research projects involving the derivation or use of hESCs be reviewed and approved by a SCRO Committee prior to being undertaken and at least annually thereafter. Although SB 322 had required review and approval of hESC research by an IRB, based on guidelines issued by the National Academy of Sciences it was determined that special review bodies are needed to oversee hESC research due to the complexity and novelty of many of the issues involved in such research.

This legislation requires that SCRO Committees be established in accordance with existing standards, including national stem cell guidelines and those issued by CIRM. These standards require that SCRO Committees include representatives of the public and persons with expertise in developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical and legal issues in hESC research. SCRO Committee responsibilities include providing local oversight of all issues related to derivation and research use of hESC lines and facilitating the education of investigators regarding applicable guidelines and the types and levels of review required for proposed hESC research.

Under additional requirements of SB 1260 (encoded in Health and Safety Code §125119.3), SCRO Committees must consider and apply the guidelines developed by CDPH for human stem cell research, and must annually review and report to CDPH on the status of each hESC project they oversee. SB 1260 also provides added protections for women undergoing assisted oocyte production (AOP) or another method of oocyte retrieval for research purposes, with mandatory reporting to CDPH. This legislation indefinitely extended the requirements of CDPH for providing oversight of human stem cell research and AOP research in California, as encoded in Health and Safety Code Sections 125330-125355.

- **AB 34 and SB 962 (Portantino; Migden, Session 2007-2008)—**The most recent legislation pertaining to stem cells has focused on umbilical cord blood banking. AB 34 requires the Department to establish the Umbilical Cord Blood Collection Program by January 1, 2010 for the purpose of increasing the number of units donated from Californians and included in the national inventory. While the primary focus of this legislation is on cord blood availability for stem cell transplantation, the bill also includes provisions for making units available for research purposes. Complementing AB 34, SB 962 requires the Department to make cord blood available through CDPH for research purposes. Although both bills included provisions for private donations to fund the activities, money to support implementation of either has not yet been received.

Federal policy has also exerted a strong influence on the course of human stem cell research within California, and will continue to do so in the future. One key factor behind California's leadership in the field of hESC was the federal policy

set by Former President George W. Bush. On August 9, 2001, Bush issued an Executive Order that stipulated specific criteria must be met to receive federal funding for hESC research. These criteria restricted research to a limited number of cell lines already in existence at that time. Despite concerns within the research community about the quality and availability of existing cell lines, this policy prevented researchers from obtaining federal funding to develop new hESC lines better suited to their research needs. California's Proposition 71 was a direct response to the Bush policy. In the absence of federal support for this promising research, California voters placed their support behind this initiative and approved a large-scale hESC research funding role for the State.

With the election of President Barack Obama in November 2008, the political landscape for hESC research changed dramatically. On March 9, 2009, President Obama signed an Executive Order lifting the ban on federal funding for promising hESC research. President Obama also directed the National Institutes of Health to develop national guidelines for human stem cell research within 120 days. While the ultimate impact of the forthcoming federal funding and new national guidelines on California's hESC research is yet unclear, stem cell researchers statewide will benefit from a likely increase in the number of established stem cell lines being available for federal funding, as well as the potential for new research collaborations.

IV. STATE OVERSIGHT AND MONITORING

Human embryonic stem cell research offers the promise of new therapeutic treatments as well as potential cures for numerous debilitating diseases that gravely affect the health and well being of our population. California has been at the forefront of efforts to address the gap in federal funding and leadership for the advancement of hESC research. With its history of legislation conducive to human stem cell research and the passage of Proposition 71, California continues to be a model for other states throughout the nation.

Given the State's leadership in promoting human stem cell research, it is appropriate for the California government to also pursue an active role in the monitoring and regulation of hESC research activity to ensure ethically sound scientific progress. Careful oversight of this critical research supports the Department to protect and improve the health of all Californians by ensuring responsible scientific progress that protects the safety and may improve the future health of all Californians.

Human Stem Cell Research Advisory Committee

With the passage of SB 322, CDPH was required to establish a Human Stem Cell Research Advisory Committee to serve as an independent resource and consultant to the State on human stem cell research issues, specifically to assist in the

development of statewide guidelines for hESC research. The Department established the 13-member committee in 2005, with members recruited in accordance with the expertise laid out in statute. The first HSCR Advisory Committee meeting was convened in February 2006, and the committee met a total of four times in 2006.

Although the provision in Health and Safety Code Section 125118.5 that had established the HSCR Advisory Committee was not continued in SB 1260, the Department's HSCR Program felt there was a need for the continued advisement of the expert Committee on the technical, legal and ethical issues surrounding human stem cell research, particularly as stem cell science evolves and new issues arise. The HSCR Advisory Committee members were re-nominated in January 2007 and continue to be actively engaged in the HSCR Program, assisting with any revisions that need to be made to the CDPH Guidelines for Human Stem Cell Research. The Department convened the HSCR Advisory Committee twice in 2007 to address emerging issues, and twice again in 2008.

CDPH Guidelines for Human Stem Cell Research

SB 322 also required the Department to develop statewide guidelines for hESC research. CDPH relied heavily on the HSCR Advisory Committee in the development of the initial guidelines and continues to utilize the Committee's expertise in updating the guidelines as needed.

Over the course of a year, the guidelines were developed through several productive HSCR Advisory Committee meetings, insightful comments from the public during committee meetings and public comment periods, and an emphasis on consistency with California law and existing stem cell research guidelines. The HSCR Advisory Committee forwarded its recommended guidelines to the Department in February of 2007. In July 2007, the first CDPH Guidelines for Human Stem Cell Research were approved and finalized for use by human stem cell research projects not fully funded by CIRM. These guidelines restate the statutory requirement, in Health and Safety Code §125119.3, that SCRO Committees reviewing these projects must report to CDPH on the status and disposition of hESC research in California.

California has emerged as a leader in stem cell research, and the guidelines for hESC research developed by the State will require continuous deliberation and modification to keep pace with this dynamic cutting edge field of scientific research, as well as to ensure the protection of human subjects and the ethical and scientific conduct of research in California. The CDPH Guidelines for Human Stem Cell Research have already been revised once, and will be revised again in the summer of 2009 to address newly developed research techniques.

SCRO Committee Reporting Form Development

Increased funding opportunities and the subsequent influx of stem cell researchers have increased exponentially the number of proposals and activities involving the derivation or use of hESCs in California. Without the reporting mandates of SB 1260, CDPH would have no way to summarize that research and would lack data on the diversity and extent of studies being conducted, the types of issues being studied and whether all research is following ethically sound guidelines.

To standardize the data collected by CDPH from the SCRO Committees, CDPH developed a reporting form that SCRO Committees could use to both fulfill the requirements of SB 1260 and provide meaningful data for inclusion in the Legislative Review. The reporting form development process included collaborating with the HSCR Advisory Committee, the human stem cell research community, and interested members of the public.

The first draft of the SCRO Committee reporting form developed by CDPH was presented to the HSCR Advisory Committee at the September 24, 2007 Committee meeting. The Committee discussed the contents of the reporting forms and provided feedback on some of the questions, as did the members of the public that were present at the meeting. CDPH considered the various suggestions and revised the form accordingly.

On December 5, 2007, the Committee met again to discuss the second draft of the reporting form and the public comments that CDPH had received on its website in regard to the draft reporting form. The members of the public that were also in attendance at the Committee meeting provided additional feedback on the revised draft reporting form.

The draft reporting form was revised a third time and posted to the CDPH website for public comments. After making final revisions to the reporting form and consulting with the Office of Legal Services (OLS), the final reporting form, HSCR1260-1, was posted to the CDPH website for use by SCRO Committees within California (Appendix D).

SCRO Committee Outreach

Unlike IRBs, SCRO Committees are not required to be federally registered. In order to notify the recently formed SCRO Committees about the mandates of Health and Safety Code §125119 and the reporting requirements of Health and Safety Code §125119.3, CDPH obtained a list of federally registered California IRBs, as well as addresses for biotech companies and universities within California that may be conducting hESC research.

Given their role in reviewing hESC research projects under SB 322, it was expected that IRBs potentially overseeing hESC research would be aware of the

new requirements to have such research reviewed and approved by a SCRO Committee. The Offices of Research at universities were selected for notification so that the information could be distributed to their SCRO Committees and the other appropriate parties within the universities.

On May 28, 2008, a letter was sent to notify all IRBs, universities, and public/private biotech companies potentially conducting hESC research in California that reporting forms had been developed and posted on the CDPH website for their use in fulfilling the requirements for mandated reporting as stated in SB 1260 and Health and Safety Code §125119.3 (Appendix E). The first round of reporting would span an eighteen month period from January 1, 2007, when SB 1260 first went into effect, to June 30, 2008. Subsequent reports from SCRO Committees would provide information on hESC research on an annual basis beginning July 1 through June 30.

CDPH Data Collection, Monitoring and Analysis

The collection of mandated progress reports from all SCRO Committees that have reviewed research proposals involving the derivation or use of hESCs is an essential component of the effective monitoring of stem cell research in California. By reviewing the SCRO Committee reports, CDPH has access to information regarding the ethical performance of projects and will be able to communicate with SCRO Committees on any issues of concern. Well-coordinated and unbiased oversight and reporting of this highly visible, sensitive research is essential and of great benefit to the Legislature, the Governor's Office, and the public by ensuring research in California is progressing in a legally, ethically and socially acceptable manner.

To ensure effective monitoring and oversight of hESC research in California, CDPH developed and implemented a system for ongoing data collection, monitoring and analysis. In accordance with Health and Safety Code §125119.3, CDPH has completed the following tasks for SCRO Committee reporting and data collection:

- Developed and maintained a database to store incoming reports regarding the status of each reviewed stem cell research project in California.
- Implemented SCRO Committee reporting and data collection methodology.
- Followed up with SCRO Committees to ensure compliance with mandated annual progress reports.

Tasks completed by CDPH in order to monitor and provide guidance for hESC research in accordance with Health and Safety Code §125119.5(a), have included:

- Review of all SCRO Committee reports to identify trends related to hESC research.

- Analysis of all relevant stem cell research projects and proposals in the State.
- Continuing research in ethical/legal/biomedical and social standards for oversight of hESC research to remain current in the state, national and international evolution of this field.
- Communication with SCRO Committees, as needed.
- Periodic solicitation of recommendations from the HSCR Advisory Committee regarding potential modification of the CDPH Guidelines for Human Stem Cell Research and ways to promote compliance with adopted standards.
- Modification or addition of existing guidelines as necessary.

Additionally, once data had been collected by CDPH on hESC research in California, in accordance with Health and Safety Code §125119.5(b), CDPH completed the following tasks for analyzing and reporting the data:

- Synthesis of SCRO Committee reported data into the required biennial review to the Legislature.
- Drafting, editing and preparation of final review.
- Distribution of the review to the Legislature.

Biennial reviews to the Legislature will help provide evidence from which to make informed decisions regarding the direction of stem cell policy in California. Additionally, the development and maintenance of a continuous monitoring system provides the ability to, at any time, describe the status of non-CIRM funded hESC research occurring within the State and allows for early changes in policy, guidelines and law if necessary.

V. FINDINGS

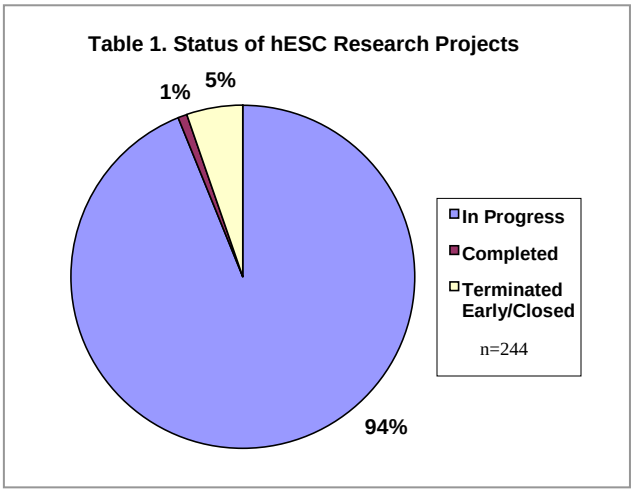
SCRO Committees are required to report on the number of hESC research projects they review each year; however, detailed reporting is only required for those projects not fully funded by CIRM.

- **Total number of projects**—SCRO Committees reported reviewing 272 hESC research projects between January 1, 2007 and June 30, 2008.
  Of these 272 projects, SCRO Committees included detailed reporting on 244 hESC research projects from 16 different institutions. The 28 projects for which data were not provided are presumably fully funded by CIRM and thus exempt from the CDPH reporting requirements; however, in the absence of requiring funding source data, this could not be confirmed.
- **Number of institutions reporting**—A total of 15 different SCRO Committees submitted data. Ten of the reporting institutions were either public or private universities, including eight University of California schools. Three of the institutions were research institutes and the remaining three entities were medical centers or hospitals. One SCRO Committee served as the oversight body for two different institutions.

A. Status of Research Projects

SCRO Committees were required to report whether the projects were still in progress, had been completed, or were terminated early or closed. Nearly all projects (94%) were still in progress at the end of the reporting period (Table 1).

A few projects (1%) had been completed and 5% were terminated early or closed. A project that was terminated early or closed does not necessarily imply that the project was discontinued due to improper research conduct or noncompliance. It could indicate, for example, that the project did not receive renewal funding or the researcher did not complete the project.



Due to statutory authority limitations, it was not possible to collect information on whether the projects were new or ongoing from previous years. However, as the Department collects data from future reporting periods, it will likely be able to follow the time trends of various projects.

One of the key elements of hESC research oversight includes monitoring whether ethical problems arise during a research project and responding to these issues. SCRO Committees are required to report on any unanticipated problems, unforeseen issues, or serious instances of investigator noncompliance. SCRO Committees reported that no issues or problems occurred this reporting period.

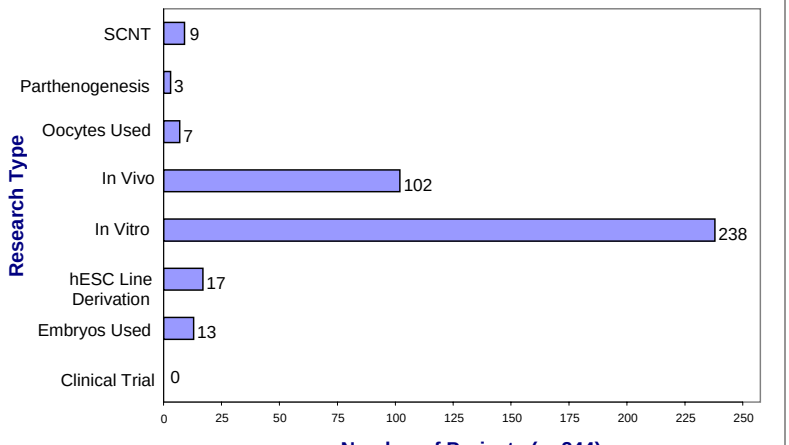
B. Types of Research

The status and activity of research projects was further determined using a designated list of eight types of research commonly cited in the stem cell scientific literature. These research types are not mutually exclusive and project types may fall within multiple categories. These terms are defined in Appendix F. The research types are:

- Research of hESCs *in vitro*
- Use of hESCs *in vivo* (non-human)
- Creation/Derivation of hESCs or cell lines
- Use of human oocytes for hESC research
- Use of human embryos for hESC research
- Somatic cell nuclear transfer (SCNT)
- Parthenogenesis; and
- Clinical trial.

Based on data from the SCRO Committee reports, two types of research were the most common. As seen in Table 2, nearly all (97.5%, n=238) of the research projects involve research of hESCs *in vitro*. Many (41.8%, n=102) of the projects involve research of hESCs *in vivo*. These two broader categories of hESC research are performed in laboratory glassware (*in vitro)* and living non-human beings (*in vivo*). As such, they encompass some of the other more specific research categories. Only a few projects did not involve research of hESCs *in vitro* or *in vivo*. One project was attempting to derive hESCs and the other two did not indicate a research category.

Table 2. Frequency of Human Embryonic Stem Cell Research Type



SCRO Committees reported that a total of 17 projects (7%) were involved in deriving new hESC lines. Deriving hESC lines can allow a researcher to develop a line with particular characteristics to help study a specific disease or better understand how cells differentiate. Of the thirteen (5.3%) projects involving the use of human embryos, most of these address the creation or derivation of stem cells or cell lines.

Nine, or 3.7%, of the projects involved SCNT. This process typically involves using fresh human or animal oocytes (eggs). Almost 3% (n=7) of all projects indicated they used, or plan to use, human oocytes. Among these, two projects plan to secure their oocytes from women who are donating oocytes strictly for research purposes. Generally, hESC research projects involving oocytes have had a limited source of human oocytes from assisted reproduction clinics. Retrieving oocytes from women strictly for research purposes continues to be an issue for ethical consideration due to the possible risks involved in oocyte retrieval through AOP. Mandatory reporting of demographic and health outcome information regarding the women involved in these projects will provide important and useful data on this sensitive issue. CDPH will review and present these data in an aggregated format and make the findings available to the public per Health and Safety Code §125342(b)(1).

The two least common types of research reported were parthenogenesis (n=3) and clinical trials (n=0). Like SCNT, parthenogenesis also requires using oocytes, which are chemically forced to begin replicating as if they had been fertilized. Although no clinical trials were reported for this reporting period, at least one

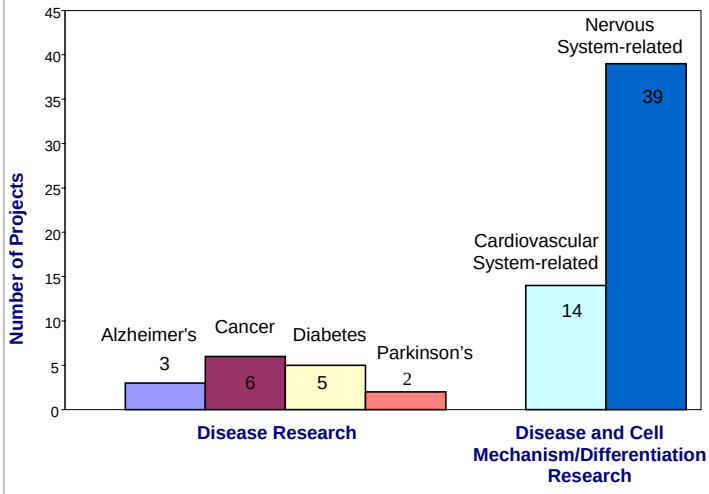
biotechnology company in California is expected to begin human clinical trials involving hESCs in 2009.

C. Research Project Activities

The research project titles were used to determine more specific information regarding the goals or focus of the research project activities. The project activities were divided into projects investigating specific diseases and projects investigating the mechanism of action for targeted cell types, which includes discovering the differentiation processes for specific cells types (Table 3).

- **Cell mechanisms of action**—Research on cell mechanisms of action was the most common, representing approximately 77% of the projects in these two divided project areas. Within the mechanism of action category, there were approximately 39 (57%) projects studying cell mechanisms related to the nervous system. Examples of nervous system projects include research into motor neuron differentiation, modeling of neurological diseases, and strategies for treating spinal cord injuries using hESC derivatives. Three of these projects overlapped with the Alzheimer's and Parkinson's disease categories and two projects overlapped with the cardiovascular system-related category.

Table 3. Projects Involving Research on Specific Diseases and/or Cell Mechanisms



The next most frequent cell mechanism project type involved projects related to the cardiovascular system (20%, n=14). These projects included such objectives as developing hESC-based therapies following myocardial infarction and enhancing the production of hESC-derived cardiomyocytes.

- **Disease-related research**—Diseases commonly studied in stem cell research were identified from the project titles. The selected diseases were Alzheimer's, cancer, diabetes, and Parkinson's. Of the 64 projects for which research focus could be determined from the project title, 25% (n=16) indicated a focus on specific conditions. Research projects involving cancer and diabetes accounted for six and five of the projects,

respectively. Five projects involved research into Alzheimer's and Parkinson's disease.

While these data provide a glimpse into the predominant areas of research underway, current reporting requirements limit the comprehensiveness of these data. Project titles are limited by the amount of information that can be conveyed and the emphasis, or lack thereof, placed on including specific information in the title. As the disease-specific and cell mechanism data could only be based on the project titles, the data do not capture all projects for the disease and cell mechanism categories. Based on analysis of project titles, the research focus could only be categorized for 26% (n=64) of all the reported projects.

VI. CONCLUSION

Human embryonic stem cell research is thriving in California, and the recent legislation on stem cell research oversight and reporting requirements has allowed for a better understanding of hESC research activity in the State. The data collection and analysis by CDPH is currently a main source of consolidated information about stem cell research occurring in the State. Although research fully funded by CIRM is exempt from the current CDPH reporting requirements, SCRO Committee reports indicate that they provided data for a majority of the hESC research projects they reviewed during this period. While the 244 research project reports received by CDPH may not be representative of all hESC projects in California, they do provide an overview of the diversity of hESC research types and activities occurring in the State. Ongoing biennial reviews to the Legislature will build upon these early data and identify trends in research activity.

A. Limitations

While statute mandated the Department to collect information on hESC research projects,statute provides minimal specific language, and therefore limited authority, regarding the data required in the reports. Additionally, the Advisory Committee and public stakeholders expressed concern regarding the increased burden on SCRO Committees, which are composed of volunteer members. These factors limited the amount and type of data the Department collected.

While CDPH made every effort to inform and educate research institutions about the new oversight and reporting requirements for hESC projects, it is possible that some research not fully funded by CIRM was not reported to CDPH this reporting period. As this was the first reporting year, some researchers may not have learned of the new statutory reporting requirements for SCRO Committees and annual reporting to CDPH. Other researchers have indicated to the Department that they have had difficulty finding or assembling a SCRO Committee to review and approve their hESC research projects. These projects are likely reviewed by an IRB or animal review committee instead, as is required

by previous State law, but IRBs are not included in the hESC reporting mandate and no IRBs submitted hESC reporting forms to CDPH.

In preparation for the next annual reporting period (covering July 1, 2008 through June 30, 2009), CDPH will renew its outreach and education efforts to notify all SCRO Committees, universities, and public and private biotechnology companies that may be engaged in hESC research within the State about the requirement for SCRO Committee review and approval of all research projects involving the derivation or use of hESCs, as well as annual reporting on such projects to CDPH.

B. Recommendations

Human embryonic stem cell research remains a politically and ethically sensitive field. Over the past several years, the passage of California legislation that promotes hESC research and provides ethical guidance for how such research should be conducted demonstrates Californians' interest in supporting research advancements while maintaining high research standards. SCRO Committee reports on stem cell research projects in the State are a valuable tool for monitoring implementation of the existing standards and guidelines, and it is recommended that the Department continue to collect, review, and report on data from hESC research projects conducted in California.

As hESC research moves forward in California, CDPH will continue to play an active role in providing ethical guidance on emerging issues, monitoring ongoing research activity, and reporting to the Legislature in order to ensure that research is legally, ethically and socially acceptable. The above recommendations would facilitate these efforts and allow for a continued understanding of hESC research activity occurring in California.

Appendix A

SB 322 Legislation

Stem Cell Research

Senate Bill No. 322

CHAPTER 506

An act to add and repeal Sections 125118, 125118.5, 125119, 125119.3, and 125119.5 of the Health and Safety Code, relating to medical research.

[Approved by Governor September 24, 2003. Filed with Secretary of State September 25, 2003.]

LEGISLATIVE COUNSEL'S DIGEST

SB 322, Ortiz. Stem cell research.

Existing law states the policy of the state that research involving the derivation and use of human embryonic stem cells, human embryonic germ cells, and human adult stem cells from any source, including somatic cell nuclear transplantation, shall be permitted and that full consideration of the ethical and medical implications of this research be given, and that research involving the derivation and use of these cells shall be reviewed by an approved institutional review board.

This bill would require the State Department of Health Services, on or before January 1, 2005, to develop guidelines for research involving the derivation or use of human embryonic stem cells in the state, and would require the Director of Health Services to establish a Human Stem Cell Research Advisory Committee, comprised of specified members, for purposes of developing these guidelines. It would also authorize the department to contract with a public or private organization, to the extent permitted by state law, for assistance in developing the guidelines.

This bill would require all human embryonic stem cell research projects to be reviewed and approved by an institutional review board (IRB) that is established in accordance with federal regulations, as specified.

This bill would require an IRB to conduct continuing review of human stem cell research projects, as specified, and would authorize an IRB to require modifications to the plan or design of a continuing research project before permitting the research to continue. This bill would require IRBs to report to the department, as specified, and would require the department to report to the Legislature on human embryonic stem cell research activity.

This bill would repeal its provisions as of January 1, 2007.

The people of the State of California do enact as follows:

SECTION 1. (a) The Legislature finds and declares all of the following:

(1) Isolation of human embryonic stem cells represents a major step forward in human biology and has generated much interest among scientists and the public, particularly among patients and their advocates regarding the benefits of human embryonic stem cells and stem cell research.

(2) Because human embryonic stem cells can give rise to many different types of cells, such as muscle cells, nerve cells, heart cells, and others, they are enormously important to science and hold great promise for advances in health care.

(3) Research using human embryonic stem cells may help scientists generate cells and tissue that could be used for transplantation and may someday be used as replacement cells and tissue to treat many chronic diseases and conditions, including Parkinson's disease, spinal injury, stroke, burns, heart disease, diabetes, arthritis, and liver disease.

(4) Research involving human embryonic stem cells may also improve understanding of the complex events that occur during normal human development and what causes diseases and conditions including birth defects, pediatric brain injury, and cancer, and may improve the way new drugs are developed and tested for safety and efficacy.

(5) In view of the scientific and medical benefits that may result from research using human embryonic stem cells, it is essential that this research be supported and encouraged. However, in view of the ethical, legal, and social issues relevant to human embryonic stem cell research, it is essential that this research be subject to oversight that complements and goes beyond the oversight of human subject research provided by the Office for Human Research Protections within the United States Department of Health and Human Services.

(6) The National Institutes of Health currently has no comprehensive guidelines concerning the ethical, legal, and social issues involved with the derivation and use of human embryonic stem cells in medical research.

(b) Therefore, it is the intent of the Legislature that the State Department of Health Services develop guidelines for human embryonic stem cell research in California in order to ensure that this research is guided by ethical and legal standards.

SEC. 2. Section 125118 is added to the Health and Safety Code, to read:

125118. (a) On or before January 1, 2005, the department shall develop guidelines for research involving the derivation or use of human embryonic stem cells in California.

(b) In developing the guidelines specified in subdivision (a), the department may consider other applicable guidelines developed or in use in the United States and in other countries, including, but not limited to, the Guidelines for Research Using Human Pluripotent Stem Cells developed by the National Institutes of Health and published in August 2000, and corrected in November 2000.

(c) The department may contract with a public or private organization, to the extent permitted by state law, for assistance in developing the guidelines.

(d) This section shall remain in effect only until January 1, 2007, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2007, deletes or extends that date.

SEC. 3. Section 125118.5 is added to the Health and Safety Code, to read:

125118.5. (a) For purposes of developing the guidelines required by Section 125118, the director shall establish a Human Stem Cell Research Advisory Committee.

(b) The advisory committee shall consist of 13 members, as follows:

(1) Seven scientists with experience in biomedical research in the fields of cell differentiation, nuclear reprogramming, tissue formation and regeneration, stem cell biology, developmental biology, regenerative medicine, or related fields.

(2) Two medical ethicists.

(3) Two persons with backgrounds in legal issues related to human embryonic stem cell research, in vitro fertilization, or family law, as it applies to the donation of embryos and oocytes.

(4) Two persons who are members or leaders of religious organizations.

(c) This section shall remain in effect only until January 1, 2007, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2007, deletes or extends that date.

SEC. 4. Section 125119 is added to the Health and Safety Code, to read:

125119. (a) (1) All research projects involving the derivation or use of human embryonic stem cells shall be reviewed and approved by an institutional review board that is established in accordance with federal regulations, including Part 46 (commencing with Section 46.101) of Subchapter A of Subtitle A of Title 45 of the Code of Federal Regulations, prior to being undertaken. Any such institutional review board shall, in its review of human embryonic stem cell research projects, consider and apply the guidelines developed by the department pursuant to Section 125118. An institutional review board may require modifications to the plan or design of a proposed human

embryonic stem cell research project as a condition of approving the research project.

(2) For purposes of this article, "IRB" means an institutional review board described in paragraph (1).

(b) Not less than once per year, an IRB shall conduct continuing review of human embryonic stem cell research projects reviewed and approved under this section in order to ensure that the research continues to meet the standards for IRB approval. Pursuant to its review in accordance with this subdivision, an IRB may revoke its prior approval of research under this section and require modifications to the plan or design of a continuing research project before permitting the research to continue.

(c) This section shall remain in effect only until January 1, 2007, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2007, deletes or extends that date.

SEC. 5. Section 125119.3 is added to the Health and Safety Code, to read:

125119.3. (a) Each IRB 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 IRB has reviewed, and the status and disposition of each of those projects.

(b) Each IRB shall also report to the department regarding unanticipated problems, unforeseen issues, or serious continuing investigator noncompliance with the requirements or determinations of the IRB with respect to the review of human embryonic stem cell research projects, and the actions taken by the IRB to respond to these situations.

(c) This section shall remain in effect only until January 1, 2007, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2007, deletes or extends that date.

SEC. 6. Section 125119.5 is added to the Health and Safety Code, to read:

125119.5. (a) The department shall at least annually review reports from IRBs pursuant to Section 125120, and may revise the guidelines developed pursuant to Section 125118, as it deems necessary.

(b) The department shall report annually to the Legislature on human embryonic stem cell research activity. These annual reports shall be compiled from the reports from IRBs pursuant to Section 125120.

(c) This section shall remain in effect only until January 1, 2007, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2007, deletes or extends that date.

Appendix B

Proposition 71

California Stem Cell Research and Cures Initiative

TEXT OF PROPOSED LAWS
Proposition 71

This initiative measure is submitted to the people in accordance with the provisions of Section 8 of Article II of the California Constitution. This initiative measure expressly amends the California Constitution by adding an article thereto; and amends a section of the Government Code, and adds sections to the Health and Safety Code; therefore, new provisions proposed to be added are printed in *italic type* to indicate that they are new.

PROPOSED LAW

CALIFORNIA STEM CELL RESEARCH AND CURES INITIATIVE

SECTION 1. Title

This measure shall be known as the "California Stem Cell Research and Cures Act."

SEC. 2. Findings and Declarations

The people of California find and declare the following:

Millions of children and adults suffer from devastating diseases or injuries that are currently incurable, including cancer, diabetes, heart disease, Alzheimer's, Parkinson's, spinal cord injuries, blindness, Lou Gehrig's disease, HIV/AIDS, mental health disorders, multiple sclerosis, Huntington's disease, and more than 70 other diseases and injuries.

Recently medical science has discovered a new way to attack chronic diseases and injuries. The cure and treatment of these diseases can potentially be accomplished through the use of new regenerative medical therapies including a special type of human cells, called stem cells. These life-saving medical breakthroughs can only happen if adequate funding is made available to advance stem cell research, develop therapies, and conduct clinical trials.

About half of California's families have a child or adult who has suffered or will suffer from a serious, often critical or terminal, medical condition that could potentially be treated or cured with stem cell therapies.

In these cases of chronic illness or when patients face a medical crisis, the health care system may simply not be able to meet the needs of patients or control spiraling costs, unless therapy focus switches away from maintenance and toward prevention and cures.

Unfortunately, the federal government is not providing adequate funding necessary for the urgent research and facilities needed to develop stem cell therapies to treat and cure diseases and serious injuries. This critical funding gap currently prevents the rapid advancement of research that could benefit millions of Californians.

The California Stem Cell Research and Cures Act will close this funding gap by establishing an institute which will issue bonds to support stem cell research, emphasizing pluripotent stem cell and progenitor cell research and other vital medical technologies, for the development of life-saving regenerative medical treatments and cures.

SEC. 3. Purpose and Intent

It is the intent of the people of California in enacting this measure to:

Authorize an average of $295 million per year in bonds over a 10-year period to fund stem cell research and dedicated facilities for scientists at California's universities and other advanced medical research facilities throughout the state.

Maximize the use of research funds by giving priority to stem cell research that has the greatest potential for therapies and cures, specifically focused on pluripotent stem cell and progenitor cell research among other vital research opportunities that cannot, or are unlikely to, receive timely or sufficient federal funding, unencumbered by limitations that would impede the research. Research shall be subject to accepted patient disclosure and patient consent standards.

Assure that the research is conducted safely and ethically by including provisions to require compliance with standards based on national models that protect patient safety, patient rights, and patient privacy.

Prohibit the use of bond proceeds of this initiative for funding for human reproductive cloning.

Improve the California health care system and reduce the long-term health care cost burden on California through the development of therapies that treat diseases and injuries with the ultimate goal to cure them.

Require strict fiscal and public accountability through mandatory independent audits, open meetings, public hearings, and annual reports to the public. Create an Independent Citizen's Oversight Committee composed of representatives of the University of California campuses with medical schools; other California universities and California medical research institutions; California disease advocacy groups; and California experts in the development of medical therapies.

Protect and benefit the California budget: by postponing general fund payments on the bonds for the first five years; by funding scientific and medical research that will significantly reduce state health care costs in the future; and by providing an opportunity for the state to benefit from royalties, patents, and licensing fees that result from the research.

Benefit the California economy by creating projects, jobs, and therapies that will generate millions of dollars in new tax revenues in our state.

Advance the biotech industry in California to world leadership, as an economic engine for California's future.

SEC. 4. Article XXXV is added to the California Constitution, to read:

Article XXXV. Medical Research

SECTION 1. There is hereby established the California Institute for Regenerative Medicine.

SEC. 2. The institute shall have the following purposes:

(a) To make grants and loans for stem cell research, for research facilities, and for other vital research opportunities to realize therapies, protocols, and/or medical procedures that will result in, as speedily as possible, the cure for, and/or substantial mitigation of, major diseases, injuries, and orphan diseases.

(b) To support all stages of the process of developing cures, from laboratory research through successful clinical trials.

(c) To establish the appropriate regulatory standards and oversight bodies for research and facilities development.

SEC. 3. No funds authorized for, or made available to, the institut shall be used for research involving human reproductive cloning.

SEC. 4. Funds authorized for, or made available to, the institute shall be continuously appropriated without regard to fiscal year, be available and used only for the purposes provided in this article, and shall not be subject to appropriation or transfer by the Legislature or the Governor for any other purpose.

SEC. 5. There is hereby established a right to conduct stem cell research which includes research involving adult stem cells, cord blood stem cells, pluripotent stem cells, and/or progenitor cells. Pluripotent stem cells are cells that are capable of self-renewal, and have broad potential to differentiate into multiple adult cell types. Pluripotent stem cells may be derived from somatic cell nuclear transfer or from surplus products of in vitro fertilization treatments when such products are donated under appropriate informed consent procedures. Progenitor cells are multipotent or precursor cells that are partially differentiated, but retain the ability to divide and give rise to differentiated cells.

SEC. 6. Notwithstanding any other provision of this Constitution or any law, the institute, which is established in state government, may utilize state issued tax-exempt and taxable bonds to fund its operations, medical and scientific research, including therapy development through clinical trials, and facilities.

SEC. 7. Notwithstanding any other provision of this Constitution, including Article VII, or any law, the institute and its employees are exempt from civil service.

SEC. 5. Chapter 3 (commencing with Section 125290.10) is added to Part 5 of Division 106 of the Health and Safety Code, to read:

CHAPTER 3. CALIFORNIA STEM CELL RESEARCH AND CURES BOND ACT

Article 1. California Stem Cell Research and Cures Act

125290.10. General—Independent Citizen's Oversight Committee (ICOC)

This chapter implements Article XXXV of the California Constitution, which established the California Institute for Regenerative Medicine (institute).

125290.15. Creation of the ICOC

There is hereby created the Independent Citizen's Oversight Committee, hereinafter, the ICOC, which shall govern the institute and is hereby vested with full power, authority, and jurisdiction over the institute.

125290.20. ICOC Membership; Appointments; Terms of Office

(a) ICOC Membership

The ICOC shall have 29 members, appointed as follows:

(1) The Chancellors of the University of California at San Francisco, Davis, San Diego, Los Angeles, and Irvine, shall each appoint an executive officer from his or her campus.

(2) The Governor, the Lieutenant Governor, the Treasurer, and the Controller shall each appoint an executive officer from the following three categories:

(A) A California university, excluding the five campuses of the University of California described in paragraph (1), that has demonstrated success and leadership in stem cell research, and that has:

(i) A nationally ranked research hospital and medical school; this criteria will apply to only two of the four appointments.

(ii) A recent proven history of administering scientific and/or medical research grants and contracts in an average annual range exceeding one hundred million dollars ($100,000,000).

(iii) A ranking, within the past five years, in the top 10 United States universities with the highest number of life science patents or that has research or clinical faculty who are members of the National Academy of Sciences.

(B) A California nonprofit academic and research institution that is not a part of the University of California that has demonstrated success and leadership in stem cell research, and that has:

(i) A nationally ranked research hospital or that has research or clinical faculty who are members of the National Academy of Sciences.

(ii) A proven history in the last five years of managing a research budget in the life sciences exceeding twenty million dollars ($20,000,000).

(C) A California life science commercial entity that is not actively engaged in researching or developing therapies with pluripotent or progenitor stem cells, that has a background in implementing successful experimental medical therapies, and that has not been awarded, or applied for, funding by the institute at the time of appointment. A board member of that entity with a successful history of developing innovative medical therapies may be appointed in lieu of an executive officer.

(D) Only one member shall be appointed from a single university, institution, or entity. The executive officer of a California university, a nonprofit research institution or life science commercial entity who is appointed as a member, may from time to time delegate those duties to an executive officer of the entity or to the dean of the medical school, if applicable.

(3) The Governor, the Lieutenant Governor, the Treasurer, and the Controller shall appoint members from among California representatives of California regional, state, or national disease advocacy groups, as follows:

(A) The Governor shall appoint two members, one from each of the following disease advocacy groups: spinal cord injury and Alzheimer's disease.

(B) The Lieutenant Governor shall appoint two members, one from each of the following disease

advocacy groups: type II diabetes and multiple sclerosis or amyotrophic lateral sclerosis.

(C) The Treasurer shall appoint two members, one from each of the following disease groups: type I diabetes and heart disease.

(D) The Controller shall appoint two members, one from each of the following disease groups: cancer and Parkinson's disease.

(4) The Speaker of the Assembly shall appoint a member from among California representatives of a California regional, state, or national mental health disease advocacy group.

(5) The President pro Tempore of the Senate shall appoint a member from among California representatives of a California regional, state, or national HIV/AIDS disease advocacy group.

(6) A chairperson and vice chairperson who shall be elected by the ICOC members. Within 40 days of the effective date of this act, each constitutional officer shall nominate a candidate for chairperson and another candidate for vice chairperson. The chairperson and vice chairperson shall each be elected for a term of six years. The chairperson and vice chairperson of ICOC shall be full or part time employees of the institute and shall meet the following criteria:

(A) Mandatory Chairperson Criteria

(i) Documented history in successful stem cell research advocacy.

(ii) Experience with state and federal legislative processes that must include some experience with medical legislative approvals of standards and/or funding.

(iii) Qualified for appointment pursuant to paragraph (3), (4), or (5) of subdivision (a).

(iv) Cannot be concurrently employed by or on leave from any prospective grant or loan recipient institutions in California.

(B) Additional Criteria for Consideration:

(i) Experience with governmental agencies or institutions (either executive or board position).

(ii) Experience with the process of establishing government standards and procedures.

(iii) Legal experience with the legal review of proper governmental authority for the exercise of government agency or government institutional powers.

(iv) Direct knowledge and experience in bond financing.

The vice chairperson shall satisfy clauses (i), (iii), and (iv) of subparagraph

(A). The vice chairperson shall be selected from among individuals who have attributes and experience complementary to those of the chairperson, preferably covering the criteria not represented by the chairperson's credentials and experience.

(b) Appointment of ICOC Members

(1) All appointments shall be made within 40 days of the effective date of this act. In the event that any of the appointments are not completed within the permitted timeframe, the ICOC shall proceed to operate with the appointments that are in place, provided that at least 60 percent of the appointments have been made.

(2) Forty-five days after the effective date of the measure adding this chapter, the State Controller and the Treasurer, or if only one is available within 45 days, the other shall convene a meeting of the appointed members of the ICOC to elect a chairperson and vice chairperson from among the individuals nominated by the constitutional officers pursuant to paragraph (6) of subdivision (a).

(c) ICOC Member Terms of Office

(1) The members appointed pursuant to paragraphs (1), (3), (4), and (5) of subdivision (a) shall serve eight-year terms, and all other members shall serve six-year terms. Members shall serve a maximum of two terms.

(2) If a vacancy occurs within a term, the appointing authority shall appoint a replacement member within 30 days to serve the remainder of the term.

(3) When a term expires, the appointing authority shall appoint a member within 30 days. ICOC members shall continue to serve until their replacements are appointed.

125290.25. Majority Vote of Quorum

Actions of the ICOC may be taken only by a majority vote of a quorum of the ICOC.

125290.30. Public and Financial Accountability Standards

(a) Annual Public Report

The institute shall issue an annual report to the public which sets forth its activities, grants awarded, grants in progress, research accomplishments, and future program directions. Each annual report shall include, but not be limited to, the following: the number and dollar amounts of research and facilities grants; the grantees for the prior year; the institute's administrative expenses; an assessment of the availability of funding for stem cell research from sources other than the institute; a summary of research findings, including promising new research areas; an assessment of the relationship between the institute's grants and the overall strategy of its research program; and a report of the institute's strategic research and financial plans.

(b) Independent Financial Audit for Review by State Controller

The institute shall annually commission an independent financial audit of its activities from a certified public accounting firm, which shall be provided to the State Controller, who shall review the audit and annually issue a public report of that review.

(c) Citizen's Financial Accountability Oversight Committee

There shall be a Citizen's Financial Accountability Oversight Committee chaired by the State Controller. This committee shall review the annual financial audit, the State Controller's report and evaluation of that audit, and the financial practices of the institute. The State

Controller, the State Treasurer, the President pro Tempore of the Senate, the Speaker of the Assembly, and the Chairperson of the ICOC shall each appoint a public member of the committee. Committee members shall have medical backgrounds and knowledge of relevant financial matters. The committee shall provide recommendations on the institute's financial practices and performance. The State Controller shall provide staff support. The committee shall hold a public meeting, with appropriate notice, and with a formal public comment period. The committee shall evaluate public comments and include appropriate summaries in its annual report. The ICOC shall provide funds for the

per diem expenses of the committee members and for publication of the annual report.

(d) Public Meeting Laws

(1) The ICOC shall hold at least two public meetings per year, one of which will be designated as the institute's annual meeting. The ICOC may hold additional meetings as it determines are necessary or appropriate.

(2) The Bagley-Keene Open Meeting Act, Article 9 (commencing with Section 11120) of Chapter 1 of Part 1 of Division 3 of Title 2 of the Government Code, shall apply to all meetings of the ICOC, except as otherwise provided in this section. The ICOC shall award all grants, loans, and contracts in public meetings and shall adopt all governance, scientific, medical, and regulatory standards in public meetings.

(3) The ICOC may conduct closed sessions as permitted by the Bagley-Keene Open Meeting Act, under Section 11126 of the Government Code. In addition, the ICOC may conduct closed sessions when it meets to consider or discuss:

(A) Matters involving information relating to patients or medical subjects, the disclosure of which would constitute an unwarranted invasion of personal privacy.

(B) Matters involving confidential intellectual property or work product, whether patentable or not, including, but not limited to, any formula, plan, pattern, process, tool, mechanism, compound, procedure, production data, or compilation of information, which is not patented, which is known only to certain individuals who are using it to fabricate, produce, or compound an article of trade or a service having commercial value and which gives its user an opportunity to obtain a business advantage over competitors who do not know it or use it.

(C) Matters involving prepublication, confidential scientific research or data.

(D) Matters concerning the appointment, employment, performance, compensation, or dismissal of institute officers and employees. Action on compensation of the institute's officers and employees shall only be taken in open session.

(4) The meeting required by paragraph (2) of subdivision (b) of Section 125290.20 shall be deemed to be a special meeting for the purposes of Section 11125.4 of the Government Code.

(e) Public Records

(1) The California Public Records Act, Article 1 (commencing with Section 6250) of Chapter 3.5 of Division 7 of Title 1 of the Government Code, shall apply to all records of the institute, except as otherwise provided in this section.

(2) Nothing in this section shall be construed to require disclosure of any records that are any of the following:

(A) Personnel, medical, or similar files, the disclosure of which would constitute an unwarranted invasion of personal privacy.

(B) Records containing or reflecting confidential intellectual property or work product, whether patentable or not, including, but not limited to, any formula, plan, pattern, process, tool, mechanism, compound, procedure, production data, or compilation of information, which is not patented, which is known only to certain individuals who are using it to fabricate, produce, or compound an article of trade or a service having commercial value and which gives its user an opportunity to obtain a business advantage over competitors who do not know it or use it.

(C) Prepublication scientific working papers or research data.

(f) Competitive Bidding

(1) The institute shall, except as otherwise provided in this section, be governed by the competitive bidding requirements applicable to the University of California, as set forth in Article 1 (commencing with Section 10500) of Chapter 2.1 of Part 2 of Division 2 of the Public Contract Code.

(2) For all institute contracts, the ICOC shall follow the procedures required of the Regents by Article 1 (commencing with Section 10500) of Chapter 2.1 of Part 2 of Division 2 of the Public Contract Code with respect to contracts let by the University of California.

(3) The requirements of this section shall not be applicable to grants or loans approved by the ICOC.

(4) Except as provided in this section, the Public Contract Code shall not apply to contracts let by the institute.

(g) Conflicts of Interest

(1) The Political Reform Act, Title 9 (commencing with Section 81000) of the Government Code, shall apply to the institute and to the ICOC, except as provided in this section and in subdivision (e) of Section 125290.50.

(A) No member of the ICOC shall make, participate in making, or in any way attempt to use his or her official position to influence a decision to approve or award a grant, loan, or contract to his or her employer, but a member may participate in a decision to approve or award a grant, loan, or contract to a nonprofit entity in the same field as his or her employer.

(B) A member of the ICOC may participate in a decision to approve or award a grant, loan, or contract to an entity for the purpose of research involving a disease from which a member or his or her immediate family suffers or in which the member has an interest as a representative of a disease advocacy organization.

(C) The adoption of standards is not a decision subject to this section.

(2) Service as a member of the ICOC by a member of the faculty or administration of any system of the University of California shall not, by itself, be deemed to be inconsistent, incompatible, in conflict with, or inimical to the duties of the ICOC member as a member of the faculty or administration of any system of the University of California and shall not result in the automatic vacation of either such office. Service as a member of the ICOC by a representative or employee of a disease advocacy organization, a nonprofit academic and research institution, or a life science commercial entity shall not be deemed to be inconsistent, incompatible, in conflict with, or inimical to the duties of the ICOC member as a representative or employee of that organization, institution, or entity.

(3) Section 1090 of the Government Code shall not apply to any grant, loan, or contract made by the ICOC except where both of the following conditions are met:

(A) The grant, loan, or contract directly relates to services to be provided by any member of the ICOC or the entity the member represents or financially benefits the member or the entity he or she represents.

(B) The member fails to recuse himself or herself from making, participating in making, or in any way

attempting to use his or her official position to influence a decision on the grant loan or contract.

(h) Patent Royalties and License Revenues Paid to the State of California

The ICOC shall establish standards that require that all grants and loan awards be subject to intellectual property agreements that balance the opportunity of the State of California to benefit from the patents, royalties, and licenses that result from basic research, therapy development, and clinical trials with the need to assure that essential medical research is not unreasonably hindered by the intellectual property agreements.

(i) Preference for California Suppliers

The ICOC shall establish standards to ensure that grantees purchase goods and services from California suppliers to the extent reasonably possible, in a good faith effort to achieve a goal of more than 50 percent of such purchases from California suppliers.

125290.35. Medical and Scientific Accountability Standards

(a) Medical Standards

In order to avoid duplication or conflicts in technical standards for scientific and medical research, with alternative state programs, the institute will develop its own scientific and medical standards to carry out the specific controls and intent of the act, notwithstanding subdivision (b) of Section 125300, Sections 125320, 125118, 125118.5, 125119, 125119.3 and 125119.5, or any other current or future state laws or regulations dealing with the study and research of pluripotent stem cells and/or progenitor cells, or other vital research opportunities, except Section 125315. The ICOC, its working committees, and its grantees shall be governed solely by the provisions of this act in the establishment of standards, the award of grants, and the conduct of grants awarded pursuant to this act.

(b) The ICOC shall establish standards as follows:

(1) Informed Consent

Standards for obtaining the informed consent of research donors, patients, or participants, which initially shall be generally based on the standards in place on January 1, 2003, for all research funded by the National Institutes of Health, with modifications to adapt to the mission and objectives of the institute.

(2) Controls on Research Involving Humans Standards for the review of research involving human subjects which initially shall be generally based 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.

(3) Prohibition on Compensation

Standards prohibiting compensation to research donors or participants, while permitting reimbursement of expenses.

(4) Patient Privacy Laws

Standards to assure compliance with state and federal patient privacy laws.

(5) Limitations on Payments for Cells

Standards limiting payments for the purchase of stem cells or stem cell lines to reasonable payment for the removal, processing, disposal, preservation, quality control, storage, transplantation, or implantation or legal transaction or other administrative costs associated with these medical procedures and specifically including any required payments for medical or scientific technologies, products, or processes for royalties, patent, or licensing fees or other costs for intellectual property.

(6) Time Limits for Obtaining Cells

Standards setting a limit on the time during which cells may be extracted from blastocysts, which shall initially be 8 to 12 days after cell division begins, not counting any time during which the blastocysts and/or cells have been stored frozen.

125290.40. ICOC Functions

The ICOC shall perform the following functions:

(a) Oversee the operations of the institute.

(b) Develop annual and long-term strategic research and financial plans for the institute.

(c) Make final decisions on research standards and grant awards in California.

(d) Ensure the completion of an annual financial audit of the institute's operations.

(e) Issue public reports on the activities of the institute.

(f) Establish policies regarding intellectual property rights arising from research funded by the institute.

(g) Establish rules and guidelines for the operation of the ICOC and its working groups.

(h) Perform all other acts necessary or appropriate in the exercise of its power, authority, and jurisdiction over the institute.

(i) Select members of the working groups.

(j) Adopt, amend, and rescind rules and regulations to carry out the purposes and provisions of this chapter, and to govern the procedures of the ICOC. Except as provided in subdivision (k), these rules and regulations shall be adopted in accordance with the Administrative Procedure Act (Government Code, Title 2, Division 3, Part 1, Chapter 4.5, Sections 11371 et seq.).

(k) Notwithstanding the Administrative Procedure Act (APA), and in order to facilitate the immediate commencement of research covered by this chapter, the ICOC may adopt interim regulations without compliance with the procedures set forth in the APA. The interim regulations shall remain in effect for 270 days unless earlier superseded by regulations adopted pursuant to the APA.

(l) Request the issuance of bonds from the California Stem Cell Research and Cures Finance Committee and loans from the Pooled Money Investment Board.

(m) May annually modify its funding and finance programs to optimize the institute's ability to achieve the objective that its activities be revenue-positive for the State of California during its first five years of operation without jeopardizing the progress of its core medical and scientific research program.

(n) Notwithstanding Section 11005 of the Government Code, accept additional revenue and real and personal property, including, but not limited to, gifts, royalties, interest, and appropriations that may be used to supplement annual research grant funding and the operations of the institute.

125290.45. ICOC Operations

(a) Legal Actions and Liability

(1) The institute may sue and be sued.

(2) Based upon ICOC standards, institute grantees shall indemnify or insure and hold the institute harmless against any and all losses, claims, damages, expenses, or

liabilities, including attorneys' fees, arising from research conducted by the grantee pursuant to the grant,
and/or, in the alternative, grantees shall name the institute as an additional insured and submit proof of such insurance.
(3) Given the scientific, medical, and technical nature of the issues facing the ICOC, and notwithstanding Section 11042 of the Government Code, the institute is authorized to retain outside counsel when the ICOC determines that the institute requires specialized services not provided by the Attorney General's office.
(4) The institute may enter into any contracts or obligations which are authorized or permitted by law.
(b) Personnel
(1) The ICOC shall from time to time determine the total number of authorized employees for the institute, up to a maximum of 50 employees, excluding members of the working groups, who shall not be considered institute employees. The ICOC shall select a chairperson, vice chairperson and president who shall exercise all of the powers delegated to them by the ICOC. The following functions apply to the chairperson, vice chairperson, and president:
(A) The chairperson's primary responsibilities are to manage the ICOC agenda and work flow including all evaluations and approvals of scientific and medical working group grants, loans, facilities, and standards evaluations, and to supervise all annual reports and public accountability requirements; to manage and optimize the institute's bond financing plans and funding cash flow plan; to interface with the California Legislature, the United States Congress, the California health care system, and the California public; to optimize all financial leverage opportunities for the institute; and to lead negotiations for intellectual property agreements, policies, and contract terms. The chairperson shall also serve as a member of the Scientific and Medical Accountability Standards Working Group and the Scientific and Medical Research Facilities Working Group and as an ex-officio member of the Scientific and Medical Research Funding Working Group. The vice chairperson's primary responsibilities are to support the chairperson in all duties and to carry out those duties in the chairperson's absence.
(B) The president's primary responsibilities are to serve as the chief executive of the institute; to recruit the highest scientific and medical talent in the United States to serve the institute on its working groups; to serve the institute on its working groups; to direct ICOC staff and participate in the process of supporting all working group requirements to develop recommendations on grants, loans, facilities, and standards as well as to direct and support the ICOC process of evaluating and acting on those recommendations, the implementation of all decisions on these and general matters of the ICOC; to hire, direct, and manage the staff of the institute; to develop the budgets and cost control programs of the institute; to manage compliance with all rules and regulations on the ICOC, including the performance of all grant recipients; and to manage and execute all intellectual property agreements and any other contracts pertaining to the institute or research it funds.
(2) Each member of the ICOC except, the chairperson, vice chairperson, and president, shall receive a per diem of one hundred dollars ($100) per day (adjusted annually for cost of living) for each day actually spent in the discharge of the member's duties, plus reasonable and necessary travel and other expenses incurred in the performance of the member's duties.
(3) The ICOC shall establish daily consulting rates and expense reimbursement standards for the non-ICOC members of all of its working groups.
(4) Notwithstanding Section 19825 of the Government Code, the ICOC shall set compensation for the chairperson, vice chairperson, and president and other officers, and for the scientific, medical, technical, and administrative staff of the institute within the range of compensation levels for executive officers and scientific, medical, technical, and administrative staff of medical schools within the University of California system and the nonprofit academic and research institutions described in paragraph (2) of subdivision (a) of Section 125290.20.
125290.50. Scientific and Medical Working Groups-General
(a) The institute shall have, and there is hereby established, three separate scientific and medical working groups as follows:
(1) Scientific and Medical Research Funding Working Group.
(2) Scientific and Medical Accountability Standards Working Group.
(3) Scientific and Medical Research Facilities Working Group.
(b) Working Group Members
Appointments of scientific and medical working group members shall be made by a majority vote of a quorum of the ICOC, within 30 days of the election and appointment of the initial ICOC members. The working group members' terms shall be six years except that, after the first six-year terms, the members' terms will be staggered so that one-third of the members shall be elected for a term that expires two years later, one-third of the members shall be elected for a term that expires four years later, and one-third of the members shall be elected for a term that expires six years later. Subsequent terms are for six years. Working group members may serve a maximum of two consecutive terms.
(c) Working Group Meetings
Each scientific and medical working group shall hold at least four meetings per year, one of which shall be designated as its annual meeting.
(d) Working Group Recommendations to the ICOC
Recommendations of each of the working groups may be forwarded to the ICOC only by a vote of a majority of a quorum of the members of each working group. If 35 percent of the members of any working group join together in a minority position, a minority report may be submitted to the ICOC. The ICOC shall consider the recommendations of the working groups in making its decisions on applications for research and facility grants and loan awards and in adopting regulatory standards.
Each working group shall recommend to ICOC rules, procedures, and practices for that working group.
(e) Conflict of Interest

(1) The ICOC shall adopt conflict of interest rules, based on standards applicable to members of scientific review committees of the National Institutes of Health, to govern the participation of non-ICOC working group members.

(2) The ICOC shall appoint an ethics officer from among the staff of the institute.

(3) Because the working groups are purely advisory and have no final decisionmaking authority, members of the working groups shall not be considered public officials, employees, or consultants for purposes of the Political Reform Act (Title 9 (commencing with Section 81000)
of the Government Code), Sections 1090 and 19990 of the Government Code, and Sections 10516 and 10517 of the Public Contract Code.

(f) Working Group Records

All records of the working groups submitted as part of the working groups' recommendations to the ICOC for approval shall be subject to the Public Records Act. Except as provided in this subdivision, the working groups shall not be subject to the provisions of Article 9 (commencing with Section 11120) of Chapter 1 of Part 1 of Division 3 of Title 2 of the Government Code, or Article 1 (commencing with Section 6250) of Chapter 3.5 of Division 7 of Title 1 of the Government Code.

125290.55. Scientific and Medical Accountability Standards
Working Group

(a) Membership

The Scientific and Medical Accountability Standards Working Group shall have 19 members as follows:

(1) Five ICOC members from the 10 groups that focus on diseasespecific areas described in paragraphs (3), (4), and (5) of subdivision (a) of Section 125290.20.

(2) Nine scientists and clinicians nationally recognized in the field of pluripotent and progenitor cell research.

(3) Four medical ethicists.

(4) The Chairperson of the ICOC.

(b) Functions

The Scientific and Medical Accountability Standards Working Group shall have the following functions:

(1) To recommend to the ICOC scientific, medical, and ethical standards.

(2) To recommend to the ICOC standards for all medical, socioeconomic, and financial aspects of clinical trials and therapy delivery to patients, including, among others, standards for safe and ethical procedures for obtaining materials and cells for research and clinical efforts for the appropriate treatment of human subjects in medical research consistent with paragraph (2) of subdivision (b) of Section 125290.35, and to ensure compliance with patient privacy laws.

(3) To recommend to the ICOC modification of the standards described in paragraphs (1) and (2) as needed.

(4) To make recommendations to the ICOC on the oversight of funded research to ensure compliance with the standards described in paragraphs (1) and (2).

(5) To advise the ICOC, the Scientific and Medical Research Funding Working Group, and the Scientific and Medical Research Facilities Working Group, on an ongoing basis, on relevant ethical and regulatory issues.

125290.60. Scientific and Medical Research Funding Working Group

(a) Membership

The Scientific and Medical Research Funding Working Group shall have 23 members as follows:

(1) Seven ICOC members from the 10 disease advocacy group members described in paragraphs (3), (4), and (5) of subdivision (a) of Section 125290.20.

(2) Fifteen scientists nationally recognized in the field of stem cell research.

(3) The Chairperson of the ICOC.

(b) Functions

The Scientific and Medical Research Funding Working Group shall perform the following functions:

(1) Recommend to the ICOC interim and final criteria, standards, and requirements for considering funding applications and for awarding research grants and loans.

(2) Recommend to the ICOC standards for the scientific and medical oversight of awards.

(3) Recommend to the ICOC any modifications of the criteria, standards, and requirements described in paragraphs (1) and (2) above as needed.

(4) Review grant and loan applications based on the criteria, requirements, and standards adopted by the ICOC and make recommendations to the ICOC for the award of research, therapy development, and clinical trial grants and loans.

(5) Conduct peer group progress oversight reviews of grantees to ensure compliance with the terms of the award, and report to the ICOC any recommendations for subsequent action.

(6) Recommend to the ICOC standards for the evaluation of grantees to ensure that they comply with all applicable requirements. Such standards shall mandate periodic reporting by grantees and shall authorize the Scientific and Medical Research Funding Working
Group to audit a grantee and forward any recommendations for action to the ICOC.

(7) Recommend its first grant awards within 60 days of the issuance of the interim standards.

(c) Recommendations for Awards

Award recommendations shall be based upon a competitive evaluation as follows:

(1) Only the 15 scientist members of the Scientific and Medical Research Funding Working Group shall score grant and loan award applications for scientific merit. Such scoring shall be based on scientific merit in three separate classifications—research, therapy development, and clinical trials, on criteria including the following:

(A) A demonstrated record of achievement in the areas of pluripotent stem cell and progenitor cell biology and medicine, unless the research is determined to be a vital research opportunity.

(B) The quality of the research proposal, the potential for achieving significant research, or clinical results, the timetable for realizing such significant results, the importance of the research objectives, and the innovativeness of the proposed research.

(C) In order to ensure that institute funding does not duplicate or supplant existing funding, a high priority shall be placed on funding pluripotent stem cell and progenitor cell research that cannot, or is unlikely to,

receive timely or sufficient federal funding, unencumbered by limitations that would impede the research. In this regard, other research categories funded by the National Institutes of Health shall not be funded by the institute.

(D) Notwithstanding subparagraph (C), other scientific and medical research and technologies and/or any stem cell research proposal not actually funded by the institute under subparagraph (C) may be funded by the institute if at least two-thirds of a quorum of the members of the Scientific and Medical Research Funding Working Group recommend to the ICOC that such a research proposal is a vital research opportunity.

125290.65. Scientific and Medical Facilities Working Group

(a) Membership

The Scientific and Medical Research Facilities Working Group shall have 11 members as follows:

(1) Six members of the Scientific and Medical Research Funding Working Group.

(2) Four real estate specialists. To be eligible to serve on the Scientific and Medical Research Facilities Working Group, a real estate specialist shall be a resident of California, shall be prohibited from receiving compensation from any construction or development entity providing specialized services for medical research facilities, and shall not provide real estate facilities brokerage services for any applicant for, or any funding by the Scientific and Medical Research Facilities
Working Group and shall not receive compensation from any recipient of institute funding grants.

(3) The Chairperson of the ICOC.

(b) Functions

The Scientific and Medical Research Facilities Working Group shall perform the following functions:

(1) Make recommendations to the ICOC on interim and final criteria, requirements, and standards for applications for, and the awarding of, grants and loans for buildings, building leases, and capital equipment; those standards and requirements shall include, among others:

(A) Facility milestones and timetables for achieving such milestones.

(B) Priority for applications that provide for facilities that will be available for research no more than two years after the grant award.

(C) The requirement that all funded facilities and equipment be located solely within California.

(D) The requirement that grantees comply with reimbursable building cost standards, competitive building leasing standards, capital equipment cost standards, and reimbursement standards and terms recommended by the Scientific and Medical Facilities Funding Working Group, and adopted by the ICOC.

(E) The requirement that grantees shall pay all workers employed on construction or modification of the facility funded by facilities grants or loans of the institute, the general prevailing rate of per diem wages for work of a similar character in the locality in which work on the facility is performed, and not less than the general prevailing rate of per diem wages for holiday and overtime work fixed as provided in Chapter 1 (commencing with Section 1720) of Part 7 of Division 2 of the Labor Code.

(F) The requirement that grantees be not-for-profit entities.

(G) The requirement that awards be made on a competitive basis, with the following minimum requirements:

(i) That the grantee secure matching funds from sources other than the institute equal to at least 20 percent of the award. Applications of equivalent merit, as determined by the Scientific and Medical Research Funding Working Group, considering research opportunities to be conducted in the proposed research facility, shall receive priority to the extent that they provide higher matching fund amounts. The Scientific and Medical Research Facilities Working Group may recommend waiving the matching fund requirement in extraordinary cases of high merit or urgency.

(ii) That capital equipment costs and capital equipment loans be allocated when equipment costs can be recovered in part by the grantee from other users of the equipment.

(2) Make recommendations to the ICOC on oversight procedures to ensure grantees' compliance with the terms of an award.

125290.70. Appropriation and Allocation of Funding

(a) Moneys in the California Stem Cell Research and Cures Fund shall be allocated as follows:

(1) (A) No less than 97 percent of the proceeds of the bonds authorized pursuant to Section 125291.30, after allocation of bond proceeds to purposes described in paragraphs (4) and (5) of subdivision (a) of Section 125291.20, shall be used for grants and grant oversight as provided in this chapter.

(B) Not less than 90 percent of the amount used for grants shall be used for research grants, with no more than the following amounts as stipulated below to be committed during the first 10 years of grant making by the institute, with each year's commitments to be advanced over a period of one to seven years, except that any such funds that are not committed may be carried over to one or more following years. The maximum amount of research funding to be allocated annually as follows: Year 1, 5.6 percent; Year 2, 9.4 percent; Year 3, 9.4 percent; Year 4, 11.3 percent; Year 5, 11.3 percent; Year 6, 11.3 percent; Year 7, 11.3 percent; Year 8, 11.3 percent; Year 9, 11.3 percent; and Year 10, 7.5 percent.

(C) Not more than 3 percent of the proceeds of bonds authorized by Section 125291.30 may be used by the institute for research and research facilities implementation costs, including the development, administration, and oversight of the grant making process and the operations of the working groups.

(2) Not more than 3 percent of the proceeds of the bonds authorized pursuant to Section 125291.30 shall be used for the costs of general administration of the institute.

(3) In any single year any new research funding to any single grantee for any program year is limited to no more than 2 percent of the total bond authorization under this chapter. This limitation shall be considered separately for each new proposal without aggregating any prior year approvals that may fund research activities. This requirement shall be determinative, unless 65 percent of a quorum of the ICOC approves a higher limit for that grantee.

(4) Recognizing the priority of immediately building facilities that ensure the independence of the scientific and medical research of the institute, up to 10 percent of the proceeds of the bonds authorized pursuant to Section 125291.30, net of costs described in paragraphs (2),
(4), and (5) of subdivision (a) of Section 125291.20 shall be allocated for grants to build scientific and medical research facilities of nonprofit entities which are intended to be constructed in the first five years.
(5) The institute shall limit indirect costs to 25 percent of a research award, excluding amounts included in a facilities award, except that the indirect cost limitation may be increased by that amount by which the grantee provides matching funds in excess of 20 percent of the grant amount.
(b) To enable the institute to commence operating during the first six months following the adoption of the measure adding this chapter, there is hereby appropriated from the General Fund as a temporary start-up loan to the institute three million dollars ($3,000,000) for initial administrative and implementation costs. All loans to the institute pursuant to this appropriation shall be repaid to the General Fund within 12 months of each loan draw from the proceeds of bonds sold pursuant to Section 125291.30.
(c) The institute's funding schedule is designed to create a positive tax revenue stream for the State of California during the institute's first five calendar years of operations, without drawing funds from the General Fund for principal and interest payments for those first five calendar years.

Article 2. California Stem Cell Research and Cures Bond Act of 2004

125291.10. This article shall be known, and may be cited, as the California Stem Cell Research and Cures Bond Act of 2004.
125291.15. As used in this article, the following terms have the following meaning:
(a) "Act" means the California Stem Cell Research and Cures Bond Act constituting Chapter 3 (commencing with Section 125290.10) of Part 5 of Division 106.
(b) "Board" or "institute" means the California Institute for Regenerative Medicine designated in accordance with subdivision (b) of Section 125291.40.
(c) "Committee" means the California Stem Cell Research and Cures Finance Committee created pursuant to subdivision (a) of Section 125291.40.
(d) "Fund" means the California Stem Cell Research and Cures Fund created pursuant to Section 125291.25.
(e) "Interim debt" means any interim loans pursuant to subdivision (b) of Section 125290.70, and Sections 125291.60 and 125291.65, bond anticipation notes or commercial paper notes issued to make deposits into the fund and which will be paid from the proceeds of bonds issued pursuant to this article.
125291.20. (a) Notwithstanding Section 13340 of the Government Code or any other provision of law, moneys in the fund are appropriated without regard to fiscal years to the institute for the purpose of (1) making grants or loans to fund research and construct facilities for research, all as described in and pursuant to the act, (2) paying general administrative costs of the institute (not to exceed 3 percent of the net proceeds of each sale of bonds), (3) paying the annual administration costs of the interim debt or bonds after December 31 of the fifth full calendar year after this article takes effect, (4) paying the costs of issuing interim debt, paying the annual administration costs of the interim debt until and including December 31 of the fifth full calendar year after this article takes effect, and paying interest on interim debt, if such interim debt is incurred or issued on or prior to December 31 of the fifth full calendar year after this article takes effect, and (5) paying the costs of issuing bonds, paying the annual administration costs of the bonds until and including December 31 of the fifth full calendar year after this article takes effect, and paying interest on bonds that accrues on or prior to December 31 of the fifth full calendar year after this article takes effect (except that such limitation does not apply to premium and accrued interest as provided in Section 125291.70). In addition, moneys in the fund or other proceeds of the sale of bonds authorized by this article may be used to pay principal of or redemption premium on any interim debt issued prior to the issuance of bonds authorized by this article. Moneys deposited in the fund from the proceeds of interim debt may be used to pay general administrative costs of the institute without regard to the 3 percent limit set forth in (2) above, so long as such 3 percent limit is satisfied for each issue of bonds.
(b) Repayment of principal and interest on any loans made by the institute pursuant to this article shall be deposited in the fund and used to make additional grants and loans for the purposes of this act or for paying continuing costs of the annual administration of outstanding bonds.
125291.25. The proceeds of interim debt and bonds issued and sold pursuant to this article shall be deposited in the State Treasury to the credit of the California Stem Cell Research and Cures Fund, which is hereby created in the State Treasury, except to the extent that proceeds of the issuance of bonds are used directly to repay interim debt.
125291.30. Bonds in the total amount of three billion dollars ($3,000,000,000), not including the amount of any refunding bonds issued in accordance with Section 125291.75, or as much thereof as is necessary, may be issued and sold to provide a fund to be used for carrying out the purposes expressed in this article and to be used and sold for carrying out the purposes of Section 125291.20 and to reimburse the General Obligation Bond Expense Revolving Fund pursuant to Section 16724.5 of the Government Code. The bonds, when sold, shall be and shall constitute a valid and binding obligation of the State of California, and the full faith and credit of the State of California is hereby pledged for the punctual payment of both the principal of, and interest on, the bonds as the principal and interest become due and payable.
125291.35. The bonds authorized by this article shall be prepared, executed, issued, sold, paid, and redeemed as provided in the State General Obligation Bond Law (Chapter 4 (commencing with Section 16720) of Part 3 of Division 4 of Title 2 of the Government Code), and all of the provisions of that law except Section 16727 apply to the bonds and to this article and are hereby incorporated in this article as though set forth in full in this article.

125291.40. (a) Solely for the purpose of authorizing the issuance and sale, pursuant to the State General Obligation Bond Law, of the bonds and interim debt authorized by this article, the California Stem Cell Research and Cures Finance Committee is hereby created. For purposes of this article, the California Stem Cell Research and Cures Finance Committee is "the committee" as that term is used in the State General Obligation Bond Law. The committee consists of the Treasurer, the Controller, the Director of Finance, the Chairperson of the California Institute for Regenerative Medicine, and two other members of the Independent Citizens Oversight Committee (as created by the act) chosen by the Chairperson of the California Institute for Regenerative Medicine, or their designated representatives. The Treasurer shall serve as chairperson of the committee. A majority of the committee may act for the committee.

(b) For purposes of the State General Obligation Bond Law, the California Institute for Regenerative Medicine is designated the "board."

125291.45. (a) The committee shall determine whether or not it is necessary or desirable to issue bonds authorized pursuant to this article in order to carry out the actions specified in this article and, if so, the amount of bonds to be issued and sold. Successive issues of bonds may be authorized and sold to carry out those actions progressively, and it is not necessary that all of the bonds authorized to be issued be sold at any one time. The bonds may bear interest which is includable in gross income for federal income tax purposes if the committee determines that such treatment is necessary in order to provide funds for the purposes of the act.

(b) The total amount of the bonds authorized by Section 125291.30 which may be issued in any calendar year, commencing in 2005, shall not exceed three hundred fifty million dollars ($350,000,000). If less than this amount of bonds is issued in any year, the remaining permitted amount may be carried over to one or more subsequent years.

(c) An interest-only floating rate bond structure will be implemented for interim debt and bonds until at least December 31 of the fifth full calendar year after this article takes effect, with all interest to be paid from proceeds from the sale of interim debt or bonds, to minimize debt service payable from the General Fund during the initial period of basic research and therapy development, if the committee determines, with the advice of the Treasurer, that this structure will result in the lowest achievable borrowing costs for the state during that five-year period considering the objective of avoiding any bond debt service payments, by the General Fund, during that period. Upon such initial determination, the committee may delegate, by resolution, to the Treasurer such authority in connection with issuance of bonds as it may determine, including, but not limited to, the authority to implement and continue this bond financing structure (including during any time following the initial five-year period) and to determine that an alternate financing plan would result in significant lower borrowing costs for the state consistent with the objectives related to the General Fund and to implement such alternate financing plan.

125291.50. There shall be collected each year and in the same manner and at the same time as other state revenue is collected, in addition to the ordinary revenues of the state, a sum in an amount required to pay the principal of, and interest on, the bonds maturing each year. It is the duty of all officers charged by law with any duty in regard to the collection of the revenue to do and perform each and every act that is necessary to collect that additional sum.

125291.55. Notwithstanding Section 13340 of the Government Code, there is hereby appropriated from the General Fund in the State Treasury, for the purposes of this article, an amount that will equal the total of the following:

(a) The sum annually necessary to pay the principal of, and interest on, bonds issued and sold pursuant to this article, as the principal and interest become due and payable.

(b) The sum necessary to carry out Section 125291.60 appropriated without regard to fiscal years.

125291.60. The Director of Finance may authorize the withdrawal from the General Fund of an amount or amounts, not to exceed the amount of the unsold bonds that have been authorized by the committee, to be sold for the purpose of carrying out this article. Any amount withdrawn shall be deposited in the fund. Any money made available under this section shall be returned to the General Fund, plus an amount equal to the interest that the money would have earned in the Pooled Money Investment Account, from money received from the sale of bonds for the purpose of carrying out this article.

125291.65. The institute may request the Pooled Money Investment Board to make a loan from the Pooled Money Investment Account in accordance with Section 16312 of the Government Code for the purposes of carrying out this article. The amount of the request shall not exceed the amount of the unsold bonds that the committee, by resolution, has authorized to be sold for the purpose of carrying out this article. The institute shall execute any documents required by the Pooled Money Investment Board to obtain and repay the loan. Any amounts loaned shall be deposited in the fund to be allocated by the institute in accordance with this article.

125291.70. All money deposited in the fund that is derived from premium and accrued interest on bonds sold shall be reserved in the fund and shall be available for transfer to the General Fund as a credit to expenditures for bond interest.

125291.75. The bonds may be refunded in accordance with Article 6 (commencing with Section 16780) of Chapter 4 of Part 3 of Division 4 of Title 2 of the Government Code, which is a part of the State General Obligation Bond Law. Approval by the voters of the state for the issuance of the bonds described in this article includes the approval of the issuance of any bonds issued to refund any bonds originally issued under this article or any previously issued refunding bonds.

125291.80. Notwithstanding any provision of this article or the State General Obligation Bond Law, if the Treasurer sells bonds pursuant to this article that include a bond counsel opinion to the effect that the interest on the bonds is excluded from gross income for federal tax purposes, subject to designated conditions,

the Treasurer may maintain separate accounts for the investment of bond proceeds and the investment earnings on those proceeds. The Treasurer may use or direct the use of those proceeds or earnings to pay any rebate, penalty, or other payment required under federal law or to take any other action with respect to the investment and use of bond proceeds required or desirable under federal law to maintain the tax-exempt status of those bonds and to obtain any other advantage under federal law on behalf of the funds of this state.

125291.85. Inasmuch as the proceeds from the sale of bonds authorized by this article are not "proceeds of taxes" as that term is used in Article XIII B of the California Constitution, the disbursement of these proceeds is not subject to the limitations imposed by that article.

Article 3. Definitions

125292.10. As used in this chapter and in Article XXXV of the California Constitution, the following terms have the following meanings:

(a) "Act" means the California Stem Cell Research and Cures Bond Act constituting Chapter 3 (commencing with Section 125290.10) of Part 5 of Division 106 of the Health and Safety Code.

(b) "Adult stem cell" means an undifferentiated cell found in a differentiated tissue in an adult organism that can renew itself and may, with certain limitations, differentiate to yield all the specialized cell types of the tissue from which it originated.

(c) "Capitalized interest" means interest funded by bond proceeds.

(d) "Committee" means the California Stem Cell Research and Cures Finance Committee created pursuant to subdivision (a) of Section 125291.40.

(e) "Constitutional officers" means the Governor, Lieutenant Governor, Treasurer, and Controller of California.

(f) "Facilities" means buildings, building leases, or capital equipment.

(g) "Floating-rate bonds" means bonds which do not bear a fixed rate of interest until their final maturity date, including commercial paper notes.

(h) "Fund" means the California Stem Cell Research and Disease Cures Fund created pursuant to Section 125291.25.

(i) "Grant" means a grant, loan, or guarantee.

(j) "Grantee" means a recipient of a grant from the institute. All University of California grantee institutions shall be considered as separate and individual grantee institutions.

(k) "Human reproductive cloning" means the practice of creating or attempting to create a human being by transferring the nucleus from a human cell into an egg cell from which the nucleus has been removed for the purpose of implanting the resulting product in a uterus to initiate a pregnancy.

(l) "Indirect costs" mean the recipient's costs in the administration, accounting, general overhead, and general support costs for implementing a grant or loan of the institute. NIH definitions of indirect costs will be utilized as one of the bases by the Scientific and Medical Research Standards Working Group to create a guideline for recipients on this definition, with modifications to reflect guidance by the ICOC and this act.

(m) "Institute" means the California Institute for Regenerative Medicine.

(n) "Interim standards" means temporary standards that perform the same function as "emergency regulations" under the Administrative Procedure Act (Government Code, Title 2, Division 3, Part 1, Chapter 4.5, Sections 11371 et seq.) except that in order to provide greater opportunity for public comment on the permanent regulations, remain in force for 270 days rather than 180 days.

(o) "Life science commercial entity" means a firm or organization, headquartered in California, whose business model includes biomedical or biotechnology product development and commercialization.

(p) "Medical ethicist" means an individual with advanced training in ethics who holds a Ph.D., MA, or equivalent training and who spends or has spent substantial time (1) researching and writing on ethical issues related to medicine, and (2) administering ethical safeguards during the clinical trial process, particularly through service on institutional review boards.

(q) "Pluripotent cells" means cells that are capable of self-renewal, and have broad potential to differentiate into multiple adult cell types. Pluripotent stem cells may be derived from somatic cell nuclear transfer or from surplus products of in vitro fertilization treatments when such products are donated under appropriate informed consent procedures. These excess cells from in vitro fertilization treatments would otherwise be intended to be discarded if not utilized for medical research.

(r) "Progenitor cells" means multipotent or precursor cells that are partially differentiated but retain the ability to divide and give rise to differentiated cells.

(s) "Quorum" means at least 65 percent of the members who are eligible to vote.

(t) "Research donor" means a human who donates biological materials for research purposes after full disclosure and consent.

(u) "Research funding" includes interdisciplinary scientific and medical funding for basic research, therapy development, and the development of pharmacologies and treatments through clinical trials. When a facility's grant or loan has not been provided to house all elements of the research, therapy development, and/or clinical trials, research funding shall include an allowance for a market lease rate of reimbursement for the facility. In all cases, operating costs of the facility, including, but not limited to, library and communication services, utilities, maintenance, janitorial, and security, shall be included as direct research funding costs. Legal costs of the institute incurred in order to negotiate standards with federal and state governments and research institutions; to implement standards or regulations; to resolve disputes; and/or to carry out all other actions necessary to defend and/or advance the institute's mission shall be considered direct research funding costs.

(v) "Research participant" means a human enrolled with full disclosure and consent, and participating in clinical trials.

(w) "Revenue positive" means all state tax revenues generated directly and indirectly by the research and facilities of the institute are greater than the debt service on the state bonds actually paid by the General Fund in the same year.

(x) "Stem cells" mean nonspecialized cells that have the capacity to divide in culture and to differentiate into more mature cells with specialized functions.

(y) "Vital research opportunity" means scientific and medical research and technologies and/or any stem cell research not actually funded by the institute under subparagraph (C) of paragraph (1) of subdivision (c) of Section 125290.60 which provides a substantially superior research opportunity vital to advance medical science as determined by at least a two-thirds vote of a quorum of the members of the Scientific and Medical Research Funding Working Group and recommended as such by that working group to the ICOC. Human reproductive cloning shall not be a vital research opportunity.

SEC. 6. Section 20069 of the Government Code is amended to read:

(a) "State service" means service rendered as an employee or officer (employed, appointed or elected) of the state, *the California Institute for Regenerative Medicine and the officers and employees of its governing body,* the university, a school employer, or a contracting agency, for compensation, and only while he or she is receiving compensation from that employer therefore, except as provided in Article 4 (commencing with Section 20990) of Chapter 11.

(b) "State service," solely for purposes of qualification for benefits and retirement allowances under this system, shall also include service rendered as an officer or employee of a county if the salary for the service constitutes compensation earnable by a member of this system under Section 20638.

SEC. 7. Severability

If any provision of this act, or part thereof, is for any reason held to be invalid or unconstitutional, the remaining provisions shall not be affected, but shall remain in full force and effect, and to this end the provisions of this act are severable.

SEC. 8. Amendments

The statutory provisions of this measure, except the bond provisions, may be amended to enhance the ability of the institute to further the purposes of the grant and loan programs created by the measure, by a bill introduced and passed no earlier than the third full calendar year following adoption, by 70 percent of the membership of both houses of the Legislature and signed by the Governor, provided that at least 14 days prior to passage in each house, copies of the bill in final form shall be made available by the clerk of each house to the public and news media.

Appendix C

SB 1260 Legislation

Reproductive Health and Research

Senate Bill No. 1260

CHAPTER 483

An act to amend Sections 125118, 125119, 125119.3, 125119.5, and 125300 of, and to add Chapter 2 (commencing with Section 125330) to Part 5.5 of Division 106 of, the Health and Safety Code, relating to reproductive health.

[Approved by Governor September 26, 2006. Filed with Secretary of State September 26, 2006.]

LEGISLATIVE COUNSEL'S DIGEST

SB 1260, Ortiz Reproductive health and research.

The California Stem Cell Research and Cures Act, an initiative measure approved by the voters at the November 2, 2004, general election (Proposition 71), establishes the California Institute for Regenerative Medicine, the purpose of which is, among other things, to make grants and loans for stem cell research, for research facilities, and for other vital research opportunities to realize therapies, protocols, and medical procedures that will result in the cure for, or substantial mitigation of, diseases and injuries.

Existing law establishes the Independent Citizen's Oversight Committee (ICOC), composed of appointed members, that is required to perform various functions and duties with regard to the operation of the institute, including, but not limited to, establishing standards applicable to research funded by the institute.

Existing law prohibits amendment of Proposition 71 by the Legislature unless the amendment is approved by the voters, or the amendment is accomplished by a bill introduced after the first 2 full calendar years and approved by a vote of 70% of both houses.

Existing law, which is not applicable to research funded under Proposition 71, and which would be repealed on January 1, 2007, requires the State Department of Health Services to, among other things, develop guidelines for research involving the derivation or use of embryonic stem cells, and to report annually to the Legislature.

This bill would delete the repeal date of those provisions, thus indefinitely extending their duration. The bill would also revise the department's reporting duties, by requiring biennial reviews rather than annual reports to the Legislature.

Existing law requires research projects involving the derivation or use of human embryonic stem cells to be reviewed and approved by an

institutional review board established in accordance with federal regulations.

This bill would revise a related declaration of state policy, would require these research projects to instead be reviewed and approved by a stem cell research oversight committee established substantially in accordance with specified guidelines, and would make these provisions applicable also to research projects involving human adult stem cells.

Existing law applicable to fertility treatment requires that a physician and surgeon provide a patient with prescribed information and obtain the patient's informed consent prior to providing the fertility treatment.

This bill, with certain exceptions, would require a physician and surgeon, prior to obtaining informed consent from a subject for assisted oocyte production, as defined, or other method of ovarian retrieval for purposes of retrieving eggs for research or for developing medical therapies, to provide the subject with a standardized written summary of health and consumer issues and to obtain the subject's written and oral informed consent for the procedure.

Existing law prohibits a person from knowingly, for valuable consideration, purchasing or selling embryonic or cadaveric fetal tissue for research purposes.

This bill would prohibit human oocytes or embryos from being acquired, sold, offered for sale, received, or otherwise transferred for valuable consideration for medical research or development of medical therapies, and would prohibit payment in excess of the amount of reimbursement of expenses to be made to any research subject to encourage her to produce human oocytes for the purposes of medical research.

The bill would declare that it is not to be construed to amend Proposition 71.

The People of the State of California do enact as follows:

SECTION 1. The Legislature finds and declares all of the following:
(a) The purpose of this act is to create protections for research subjects and it should not be construed to affect any other form of medical care.
(b) Scientific research can be most effectively achieved by establishing protocols to protect, respect, and promote human health, safety, dignity, autonomy, and rights in conducting research.
(c) This act seeks to support the requirements already in current law upholding the principle of voluntary and informed consent and to tailor them to this new area of pioneering research that utilizes human oocytes.

(d) The potential for exploitation of the reproductive capabilities of women for commercial gain raises health and ethical concerns that justify the prohibition of payment for human oocytes.

SEC. 2. Section 125118 of the Health and Safety Code is amended to read:

125118. (a) The State Department of Health Services shall develop guidelines for research involving the derivation or use of human embryonic stem cells in California.

(b) In developing the guidelines specified in subdivision (a), the department may consider other applicable guidelines developed or in use in the United States and in other countries, including, but not limited to, the Guidelines for Research Using Human Pluripotent Stem Cells developed by the National Institutes of Health and published in August 2000, and corrected in November 2000, and the Guidelines for Human Embryonic Stem Cell Research issued by the National Research Council and Institute of Medicine of the National Academies in 2005.

SEC. 3. Section 125119 of the Health and Safety Code is amended to read:

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. Any stem cell research oversight committee shall, in its review of human embryonic stem cell research projects, consider and apply the guidelines developed by the department pursuant to Section 125118. A stem cell research oversight committee may require modifications to the plan or design of a proposed human embryonic stem cell research project as a condition of approving the research project.

(2) A stem cell research oversight committee for purposes of this article shall be established substantially in accordance with Guidelines for Human Embryonic Stem Cell Research issued by the National Research Council and the Institute of Medicine of the National Academies in 2005. This committee shall be established in accordance with standards issued by the California Institute for Regenerative Medicine (CIRM) as authorized by Article XXXV of the California Constitution. 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.

(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 in order to ensure that the research continues to meet the standards for stem cell research oversight committee approval. Pursuant to its review in accordance with this subdivision, a stem cell research oversight committee may revoke its prior approval of research under this section and require modifications to the plan or design of a continuing research project before permitting the research to continue.

(c) A stem cell research oversight committee may provide scientific and ethical review of research consistent with this article.

SEC. 4. Section 125119.3 of the Health and Safety Code is amended to read:

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.

(b) Each stem cell research oversight committee shall also report to the department regarding unanticipated problems, unforeseen issues, or serious continuing investigator noncompliance with the requirements or determinations of the stem cell research oversight committee with respect to the review of human embryonic stem cell research projects, and the actions taken by the stem cell research oversight committee to respond to these situations.

SEC. 5. Section 125119.5 of the Health and Safety Code is amended to read:

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.

(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.

SEC. 6. Section 125300 of the Health and Safety Code is amended to read:

125300. The policy of the State of California shall be that research involving the derivation and use of human embryonic stem cells, human embryonic germ cells, and human adult stem cells, including somatic cell nuclear transplantation, shall be reviewed by a stem cell research oversight committee.

SEC. 7. Chapter 2 (commencing with Section 125330) is added to Part 5.5 of Division 106 of the Health and Safety Code, to read:

CHAPTER 2. Procuring of Oocytes for Research

125330. The following definitions shall apply to this chapter:

(a) "Assisted oocyte production" or "AOP" means surgical extraction of oocytes following pharmaceutically induced manipulation of oocyte production through the use of ovarian stimulation.

(b) "Oocyte" means a female egg or egg cell of a human female.

(c) "Subject" means any person undergoing AOP or any alternative method of ovarian retrieval for research or for the development of medical therapies, including those who would not meet the definition of "subject" under 45 C.F.R. 46.102.

(d) "Alternate method of oocyte retrieval" means a method of oocyte retrieval that does not involve the pharmaceutically induced manipulation of oocyte production.

(e) "Institutional review board" means a body established in accordance with federal regulations, including Part 46 (commencing with Section 46.101) of Subchapter A of Subtitle A of Title 45 of the Code of Federal Regulations.

125335. (a) Prior to obtaining informed consent from a subject for AOP or any alternative method of ovarian retrieval on a subject for the purpose of procuring oocytes for research or the development of medical therapies, a physician and surgeon shall provide to the subject a standardized medically accurate written summary of health and consumer issues associated with AOP and any alternative methods of oocyte retrieval. The failure to provide to a subject this standardized medically accurate written summary constitutes unprofessional conduct within the meaning of Chapter 5 (commencing with Section 2000) of Division 2 of the Business and Professions Code.

(b) The summary shall include, but not be limited to, medically accurate disclosures concerning the potential risks of AOP or any alternative method of oocyte retrieval, including the risks associated with the surgical procedure and with using the drugs, medications, and hormones prescribed for ovarian stimulation during the AOP process or any alternative method of oocyte retrieval.

(c) For purposes of subdivision (a), "written summary of health and consumer issues" means the guide published and updated by the American Society for Reproductive Medicine entitled, "Assisted Reproductive Technology: A Guide for Patients" or an alternative written medically accurate document prepared by a recognized authority on oocyte retrieval for medical research that also meets the criteria included in this section. This alternative document may be one that has been approved and recommended by the State Department of Health Services pursuant to Section 125118 and shall include all of the following:

(1) The document shall adhere to simplified reading standards, including, but not limited to, those generally accepted and required for government publications. The document shall be written in layperson's language and shall be made available in languages spoken by subjects in the study if their proficiency is largely in a language other than English. All information in the document shall be conveyed to the subject orally in easy to understand and nontechnical terms.

(2) The document shall include additional resources for, or list additional sources of, medical information on health and safety issues surrounding oocyte retrieval.

125340. (a) Prior to providing AOP or any alternative method of ovarian retrieval to a subject for the purposes of medical research or development of medical therapies, a physician and surgeon shall obtain written and oral informed consent for the procedure from the subject. Informed consent for the purposes of this chapter shall comply with the informed consent requirements of the Protection of Human Subjects in Medical Experimentation Act (Chapter 1.3 (commencing with Section 24170) of Division 20).

(b) The failure to obtain written informed consent from the subject constitutes unprofessional conduct within the meaning of Chapter 5 (commencing with Section 2000) of Division 2 of the Business and Professions Code. Nothing in this section shall be construed to relieve the physician and surgeon from other existing duties under the law, including, but not limited to, the duty to obtain a subject's informed consent after fully explaining the proposed procedure. The requirement that a physician and surgeon provide the standardized written summary pursuant to Section 125335 is in addition to, and does not supplant, other existing legal requirements regarding informed consent, including, but not limited to, compliance with the Protection of Human Subjects in Medical Experimentation Act (Chapter 1.3 (commencing with Section 24170) of Division 20.

(c) This chapter shall not affect the suitability or availability of oocytes procured for research before January 1, 2007, if the oocytes were donated pursuant to protocols or standards that are generally recognized and accepted by national or international scientific bodies.

(d) Any written document required pursuant to this section shall adhere to simplified reading standards, including, but not limited to, those generally accepted and required for government publications, and in layperson's language. The document shall be made available in languages spoken by subjects in the study if their proficiency is largely in a language other than English. All information in the written informed consent document shall also be conveyed to the subject orally in easy to understand and nontechnical terms.

125341. An institutional review board (IRB) that reviews and approves medical and scientific research shall require all of the following of any research program or project that comes under its review that involves AOP or any alternative method of oocyte retrieval:

(a) That it include a written summary as required under Section 125335 that would include information on health risks and potential adverse consequences of the procedure and describe the manner in which the subject will receive and review this written summary.

(b) That it obtain informed consent in compliance with the Protection of Human Subjects in Medical Experimentation Act (Chapter 1.3 (commencing with Section 24170) of Division 20), including informed consent for information obtained pursuant to Section 125342.

(c) That it provide the subject with an objective and accurate statement about the existing state of the research for which the subject is providing oocytes.

(d) That it perform psychological and physical screening, in accordance with the appropriate standard of care, for all subjects prior to the oocyte retrieval procedure.

(e) That it ensure that after conducting AOP or any alternative method of oocyte retrieval on a subject, the subject be given a postprocedure medical examination at a time within the standard of care to determine if the subject has experienced an adverse health effect that is a result of the

procedure. The subject shall be informed that she has the right to a second opinion if she has any medical concerns.

(f) That it ensure that 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. The research program or project shall ensure that payment or coverage of resulting medical expenses be provided at no cost to the subject and that a summary of the arrangements the procuring entity has made for coverage or payment for medical care related to AOP or any alternative method of oocyte retrieval is provided to the subject prior to the procedure.

(g) That it provide a summary informing the subject that oocytes may not be sold or transferred for valuable consideration except as set forth in Section 125350.

(h) That it provide disclosure if the physician and surgeon and his or her immediate family members have any professional interest in the outcome of the research or of the oocyte retrieval procedure and, if so, that it provide disclosure that he or she carries the interest of both the subject and the success of the research.

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.

(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.

(2) The department shall provide public access to information which it is required to release pursuant to the California Public Records Act (Chapter 3.5 (commencing with Section 6250) of Division 7 of Title 1 of the Government Code). The department shall disseminate the information to the general public via governmental and other Web sites in a manner that is understandable to the average person. The information shall be made available to the public when the biennial review pursuant to Section 125119.5 is provided to the Legislature.

125343. Any employee who works in the unit conducting stem cell research using human oocytes, persons who report to, or are supervised by, the principal investigator or key personnel of the project, or both, along with the principal investigator and the key personnel of the project, and the immediate family members of any of the above persons are prohibited from being a subject in the research.

125344. The physician and surgeon performing the AOP or any alternative method of oocyte retrieval shall not have a financial interest in the outcome of the research.

125345. Pursuant to guidelines adopted by the Research Council and Institute of Medicine of the National Academies, researchers shall offer subjects an opportunity to document their preferences regarding future uses of their donated materials. The consent process shall fully explore whether subjects have objections to any specific forms of research to ensure that their wishes are honored.

125346. Any procedures for procuring oocytes in this state for research or the development of medical therapies shall meet all of the standards for subjects included in this chapter. All oocytes procured outside of this state for research taking place in this state shall meet these same standards. All egg extractions for research shall be approved by an institutional review board pursuant to Section 125341.

125350. No human oocyte or embryo shall be acquired, sold, offered for sale, received, or otherwise transferred for valuable consideration for the purposes of medical research or development of medical therapies. For purposes of this section, "valuable consideration" does not include reasonable payment for the removal, processing, disposal, preservation, quality control, and storage of oocytes or embryos.

125355. No payment in excess of the amount of reimbursement of direct expenses incurred as a result of the procedure shall be made to any subject to encourage her to produce human oocytes for the purposes of medical research.

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

Appendix D

Form HSCR1260-1

Human Embryonic Stem Cell Research Reporting Form
Form HSCR1260-1

Reporting Period: January 1, 2007 - June 30, 2008
Due Date: August 1, 2008

California Requirements for Research Involving Human Embryonic Stem Cell Research

Statutory Authority:
Pursuant to Health and Safety Code §125119, at least once per year a Stem Cell Research Oversight (SCRO) Committee must conduct continuing review of each human embryonic stem cell (hESC) research project in California under its purview and report to the California Department of Public Health (CDPH) on each project. This mandate does not apply to research projects that are fully funded by the California Institute for Regenerative Medicine (CIRM).

CDPH is required to develop a biennial Legislative review on human embryonic stem cell research activities occurring in California (Health and Safety Code §125119(5)(b)). CDPH will compile the information from the workbooks to complete the biennial review.

Instructions

Sending the Form to CDPH:

After a workbook has been completed, please save a copy of the workbook on your computer. You may print out a copy of the workbook for your files. Please email each workbook as an attachment to stemcell@cdph.ca.gov (an active link is below for your convenience). Due to some electronic transmission size restrictions, a separate email should be sent for each workbook. If you experience any issues with reporting in this manner, please contact stemcell@cdph.ca.gov for an alternative method of sending the information to CDPH. (If you have to report on >50 projects and you store your data in a database, a flat file option may be available. Please contact CDPH for further details.)

stemcell@cdph.ca.gov

Trouble Shooting Macro Settings:

** Note, if navigation buttons or checkboxes are not operable, then macro security settings are set too high. Please reset macro security to **MEDIUM** level by selecting from the menu:*
***Tools > Options** > **Security** (tab) > **Macro Security** (button) > **Medium** (toggle)*
and then close and reopen this form.

Macintosh users may experience difficulties using macros and fill-in fields. Please contact CDPH for use of an alternative format.

Additional Reporting via Form HSCR1260-2:

If you answer positively to project questions 4-6 (procurement of oocytes) for any projects in the report, then additional reporting in form HSCR1260-2 will be required. The SCRO Committees and the research projects are responsible for ensuring that form HSCR1260-2 is completed and accounts for every oocyte donated or used for the project. The CDPH Oocyte Retrieval Reporting Form **(form HSCR1260-2)** collects information specified in Health and Safety Code §125330 and Chapter 2 (commencing with §125330) and a link to that form has been provided below for your convenience.

Form HSCR1260-2

Project Reporting:

This report should be completed by a SCRO Committee. Reporting is required for all projects that involve the derivation or use of human embryonic stem cells (hESCs) for each reporting year that the project is active. In the reporting year of project completion, the SCRO Committee should report a "Complete" disposition of the project after a final review. In addition, if that project also involves the use of human oocytes, a continuing or final report on oocyte provenance, via IVF patients or donors contributing material to the project, should be completed for each project as detailed in project questions 4 through 6, and the SCRO Committee and research project should ensure that form HSCR1260-2 has been completed for every donor subject counted in question 6.2 and 6.3 (see the "Additional Reporting via Form HSCR1260-2" section below for further information).

Using the Reporting Form:

This workbook is designed to collect information from one SCRO Committee for up to 10 hESC projects. This workbook is limited to 10 projects due to size restrictions when transmitting information electronically. Please use additional workbooks as needed in order to report on all hESC projects reviewed within the reporting time frame. There is one worksheet in each workbook to capture SCRO Committee information, and there are 10 worksheets dedicated to individual project reporting. Please fill out the SCRO Committee worksheet in each workbook and as many project worksheets as are needed. Leave any remaining project worksheets empty.

Filling in the Fields:

Many of the fields in this workbook have mouse-over comment instructions and/or definitions. To view mouse-over comments, place your mouse cursor over fields that have red triangles in the upper right hand corner. A comment box will appear with further instructions or definitions. Move your cursor away to hide the comment box.

In addition, many fields have drop-down lists from which to select your answer. If a drop-down list is present, it will become visible when you click on the field to enter a response. A small box with a down arrow will appear at the right of the field. Select the down-arrow to view the answer list and make your selection.

To cut and paste text into fields, double click on the desired field and a blinking cursor will appear, then perform the paste procedure. A single mouse click on the field will result in an error message.

Supporting Materials

CDPH Human Stem Cell Research Webpage
http://www.cdph.ca.gov/programs/HSCR/Pages/default.aspx

Guidelines for Human Stem Cell Research Pursuant to California Health and Safety Code §125118
http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-HSCRGuidelines-08-2007.pdf

Human Stem Cell Research Reporting Forms
http://www.cdph.ca.gov/programs/HSCR/Pages/HumanStemCellResearchReportingForms.aspx

Please send all inquiries to:
stemcell@cdph.ca.gov

SCRO Committee Information
Form HSCR1260-1

1.1 SCRO Committee Name (e.g., Company or Institutional Affiliation):			
1.2. SCRO Committee ID (if assigned)			
2. SCRO Committee Contact Information:			
2.1. Name			
2.2. Address 1			
2.3. Address 2			
2.4. Address 3			
2.5. Address 4			
2.6. - 2.8 City, State, Zip			
2.9. Phone			
2.10. Fax			
2.11. Email			
3. Number of Human Embryonic Stem Cell (hESC) Projects[a] Reviewed by this SCRO Committee: (reviewed between January 1, 2007- June 30, 2008)			

[a] Only projects involving hESC require reporting in this form.

Stem Cell Research Oversight of Individual Projects
Form HSCR1260-1

Research Project 1

Research Project Identification

1.1. Research Protocol ID (assigned by SCRO
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)

- 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

Provenance of Every Human Oocyte Donated or Used

4. Does this project protocol include the use of human oocytes?
(If not, skip to question 7)

5. If this project includes the use of human oocytes, did the project plan to procure oocytes

- 5.1. Female *in Vitro* Fertilization (IVF) patients/donors
- 5.2. Female donors specifically for research or the development of medical therapies
- 5.3. Other.....5.3.1. Explain

If answered yes for 5.2 or 5.3, Form HSCR1260-2 must be completed for every oocyte

6. <u>For projects that have existed >1 year</u>, please specify the accumulative total numbers of women from whom oocytes were procured (this includes current and previous reporting

- 6.1. Number of female IVF patients/donors
- 6.2. Number of female donors specifically for research or the development of medical therapies
- 6.3. Other.....6.3.1. Explain
- 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. <u>Describe any unforeseen issues or unanticipated problems.</u> (limit of 1000 characters = 200 words)

8. <u>Describe any serious investigator noncompliance issues.</u> (limit of 1000 characters = 200 words)

9. <u>Describe response of SCRO Committee to these situations.</u> (limit of 1000 characters = 200 words)

10. If any issues or problems were reported in questions 7 or 8, please provide a brief summary.

Appendix E

CDPH Notification Letter on Research Review and Reporting Requirements

State of California—Health and Human Services Agency

Department of Public Health

CDPH

Mark B Horton, MD, MSPH
Director

ARNOLD SCHWARZENEGGER
Governor

May 29, 2008

Dear Colleague,

This letter is being sent to California Institutional Review Boards, university offices of research, and various companies in an effort to educate and inform those parties affected by new research guidelines and State legislation concerning **human stem cell research**.

In September 2006, the California Legislature passed Senate Bill 1260 (SB 1260, Ortiz, Chapter 483, Statutes of 2006), which addresses research involving **human embryonic stem cells** and **human oocyte procurement**. This law **does not** apply to human embryonic stem cell research that is fully funded by the California Institute for Regenerative Medicine (CIRM). However, if a project is partially funded by CIRM, those non-CIRM funded components of the project must abide by the mandates of SB 1260.

Scope of New Statutory Mandates
SB 1260 amended California Health and Safety Code §125118–125119.5, §125300 and added Chapter 2 (commencing with §125330) to Part 5.5 of Division 106 to include specific reporting and review requirements for research involving the derivation or use of human embryonic stem cells as well as for procurement of human oocytes for research or the development of medical therapies.

Human Embryonic Stem Cell Research (hESC)
The amended California Health and Safety Code §125119 and §125300 mandate that any hESC research project must be reviewed and receive approval by a Stem Cell Research Oversight (SCRO) Committee prior to being undertaken. This mandate supersedes previous statutory language that required Institutional Review Board (IRB) review and approval for hESC research in California (enacted by SB 253, Ortiz, 2002). [Note: Institutional review and approval may still be necessary for some projects per federal regulations or institution policy (e.g., if research involves human subjects)]. SCRO Committees are required to review the research projects at least annually and report annually to the California Department of Public Health (CDPH) on the status and disposition of each project (**Form HSCR1260-1**, version May 2008).

Human Oocyte Procurement for Research
Enacted statutes commencing with California Health and Safety Code §125330 specify new mandates for research projects involving assisted oocyte production (AOP) or alternative methods of human oocyte retrieval for research or the development of medical therapies. The mandates apply to oocytes retrieved after January 1, 2007.

IRBs are charged with ensuring that various informed consent provisions and subject protections are provided for research subjects donating oocytes for research purposes.

Research projects involving AOP must ensure a written record is maintained of subject demographics, adverse health outcomes, and the provenance and disposition of every oocyte

Maternal, Child and Adolescent Health Program, Center for Family Health
1615 Capitol Ave, MS 8300, PO Box 997420 , Sacramento, CA 95899-7420
(916) 650-0300 I stemcell@cdph.ca.gov
Internet Address: http://www.cdph.ca.gov/programs/HSCR/Pages/default.aspx

donated or used as detailed in **Form HSCR1260-2** (version May 2008). The research projects or clinics/facilities should submit this record to their IRB or SCRO Committee, as determined by their review committee, who will then transmit the information to CDPH.

The information included in the records is deemed confidential and protected by subject privacy provisions of law.

CDPH Guidelines for Human Stem Cell Research

Per Health and Safety Code §125118, CDPH has developed and issued comprehensive statewide guidelines for most human stem cell research: http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-HSCRGuidelines-08-2007.pdf. The guidelines are principally consistent with established state and national standards. They outline ethical stem cell research practices, SCRO Committee and institutional review committee functions and responsibilities, as well as offer direction for clinical trials involving human progenitor stem cells. The guidelines are a living document and may be amended as the field of stem cell research evolves. Any future revisions to the guidelines will be posted to the CDPH Human Stem Cell Research website.

Annual Reporting and Reporting Forms

Annual reporting is required on any hESC research project not fully funded by CIRM and any human oocyte procured after January 1, 2007 for research or the development of medical therapies. Reporting forms have been developed for both SCRO Committees overseeing hESC research (**Form HSCR1260-1**) and research projects involving human oocyte retrieval (**Form HSCR1260-2**). Reporting for the first year includes research conducted from January 1, 2007 – June 30, 2008. The forms are provided to help facilitate compliance with the mandates of Health and Safety Code Sections 125118–125119.5, 125300 and125330 et. seq. The completed forms are due to CDPH by **August 1, 2008**. Subsequent annual reports are due August 1 immediately following the reporting period (July 1 - June 30).

The guidelines, reporting forms for hESC research and research involving human oocyte procurement, applicable statue in the Health and Safety Code, and other helpful information can be found at: http://www.cdph.ca.gov/programs/HSCR/Pages/default.aspx.

Sincerely,

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Appendix F

Glossary

Clinical trial—a scientifically designed and executed investigation of a medical intervention in humans that is aimed at determining the safety, efficacy, and pharmacological effects (including toxicity, side effects, incompatibilities, and interactions) of the intervention.

Differentiation—the process whereby an undifferentiated embryonic cell acquires the features of a specialized cell such as a heart, liver, or muscle cell.

Embryonic stem cell line—embryonic stem cells which have been cultured under *in vitro* conditions that allow proliferation without differentiation for months to years.

In vitro—in a laboratory dish or test tube, or in an artificial environment.

In vivo—in the living body of a plant or animal.

Parthenogenesis—artificial activation of an egg in the absence of a sperm; the egg is "tricked" into behaving as if it has been fertilized.

Proliferation—expansion of cells by the continuous division of single cells into two identical daughter cells.

Somatic cell—any body cell other than gametes (egg or sperm).

Somatic cell nuclear transfer (SCNT)—a technique that combines an enucleated egg (nucleus removed) and the nucleus of a somatic cell to make an embryo.

Reference: National Institutes of Health Stem Cell Information. http://stemcells.nih.gov/info/glossary.asp. Retrieved November 13, 2008.