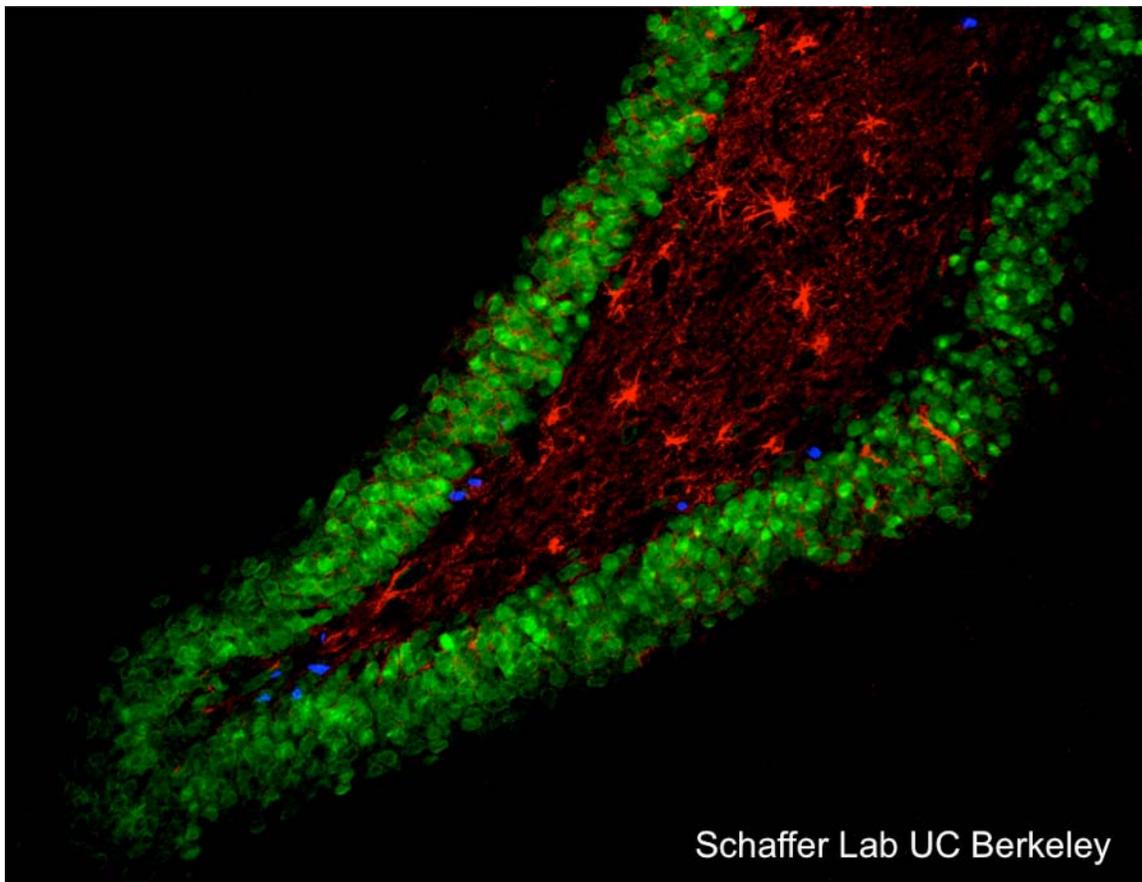


***Advancing the Effective Research Oversight:
2010 Regional Workshops on Regulatory
Compliance***



Schaffer Lab UC Berkeley

**Workshop Summary
May 2010**

Background:

CIRM's mission is to support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of therapies and cures for chronic disease and injury. Pursuant to our obligation to assure that research is conducted safely and ethically, CIRM is committed to the ongoing evaluation and improvement of its [Medical and Ethical Standards Regulations](#) through an evidence-based policy development process. Such a process is essential in a rapidly evolving field such as stem cell research.

Numerous national bodies, including the Institute of Medicine, Department of Health and Human Services Office of Inspector General, and Office for Human Research Protection, recommend evaluation to support the development of scientific and ethically responsible research.^{1 2 3} Evidence-based evaluation can serve to identify challenging compliance issues among the regulated community, refine best practices, promote consistency, and create sustainable feedback mechanisms for policy development. Figure 1 illustrates CIRM's model for evidence-based policy evaluation and development.

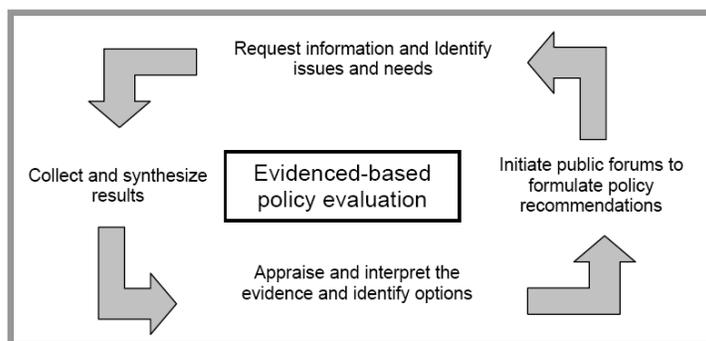


Figure 1: Adapted from Heller et. al. *Public Health* 117(2003)

In 2007, CIRM published [Advancing Effective Research Oversight: CIRM's Evaluation Initiative](#). This report detailed findings from two regional workshops attended by individuals with responsibility for institutional research compliance and stem cell research oversight. The findings from this report

were taken into consideration by CIRM's [Medical and Ethical Standards Working Group](#) and served as the basis for subsequent policy recommendations. In 2009, CIRM convened a two-day workshop attended by institutional officials responsible for research oversight. The 2009 workshop focused on the following topics:

- Current state and national issues related to regulatory compliance;
- Initiatives designed to support ethics in stem cell research;
- Potential future challenges posed by translational research.

¹ Responsible Research: A Systems Approach to Protecting Research Participants. Daniel D. Federman, Kathi E. Hanna, and Laura Lyman Rodriguez, Editors Committee on Assessing the System for Protecting Human Research Participants. Institute of Medicine of the National Academies.

² Department of Health and Human Services Office of Inspector General, Institutional Review Boards: A Time for Reform. June 1998, OEI-01-97-00193.

³ Office for Human Research Protections (OHRP) Division of Assurances and Quality Improvement Objectives and Overview of the OHRP Quality Improvement Program April 15, 2002.

The workshop culminated with the publication of [Advancing the Field: Institutional Approaches Supporting Ethics in Stem Cell Research](#).

2010 Regional Workshops Activities:

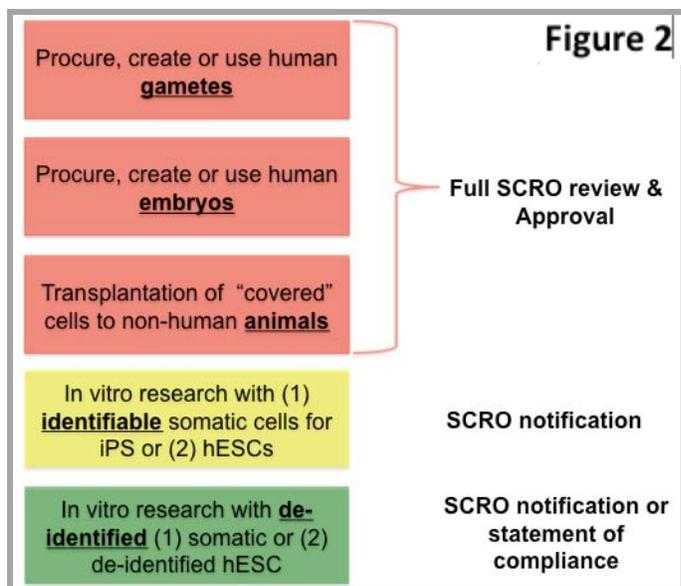
In March and April 2010, CIRM sponsored three regional workshops – San Francisco, Los Angeles and San Diego. The 2010 workshops included the following topics:

- **A review of amendments to CIRM’s Medical and Ethical Standards**
- **Discussion of compliance issues in multi-institutional collaborations**
- **A description of the CIRM Compliance Program (compliance site visits)**
- **Discussion of financial administration issues and reporting requirements**

42 participants from CIRM grantee institutions attended the three workshops.

MES Regulatory Amendments:

CIRM described recent amendments to the Medical and Ethical Standards Regulations – many of which are based on the recommendations of the 2009 workshop report. A major focus was changes to section 100070 governing review by and notification of SCRO committees. Figure 2 illustrates the SCRO committee review requirements for different types of research.



Participants felt the amendments served their stated purpose of clarifying review and notification requirements. Questions were raised regarding the requirement for SCRO notification of human subjects research (identifiable cells). Participants noted that such research must be reviewed by an IRB. CIRM recognizes the role of the IRB, and indicated SCRO committee notification provides an opportunity for the committee to evaluate the informed consent protocol against CIRM regulatory requirements.

Participants also noted there are some discrepancies between the CIRM MES regulations and the *California Department of Public Health Guidelines for Human Stem Cell Research*. Two differences include (1) review of research involving non-human animals and (2) SCRO notification requirements. CIRM requires research involving the transplantation of pluripotent cells to a non-human animal to be reviewed by the SCRO committee. The CDPH guidelines require review of research introducing pluripotent cells or cells differentiated from human pluripotent cells into non-human animals. CIRM facilitated discussion between grantees and members of the CDPH advisory committee. The CDPH committee believes the expanded scope of the CDPH guidelines is appropriate. Participants emphasized the value of compatibility between the CIRM regulations and state guidelines, but acknowledged this deviation was minor and did not present operational difficulties for SCRO committees.

CIRM requires SCRO committees to be notified of research involving identifiable somatic cells or in vitro research with de-identified somatic cells with the intent of deriving a pluripotent cell line. There is no such notification requirement in the state guidelines. The CDPH advisory committee believes the SCRO committee should be primarily focused on hESC research.⁴ This more limited scope is consistent with the charge of the state advisory committee. The expanded notification requirements in the MES regulations are appropriate given CIRM is a funding agency. CIRM requires SCRO committees to provide documentation of compliance with any required regulatory review. CIRM also believes it is valuable to have a single (“go to”) committee that provide assurance of compliance with regulatory requirements.

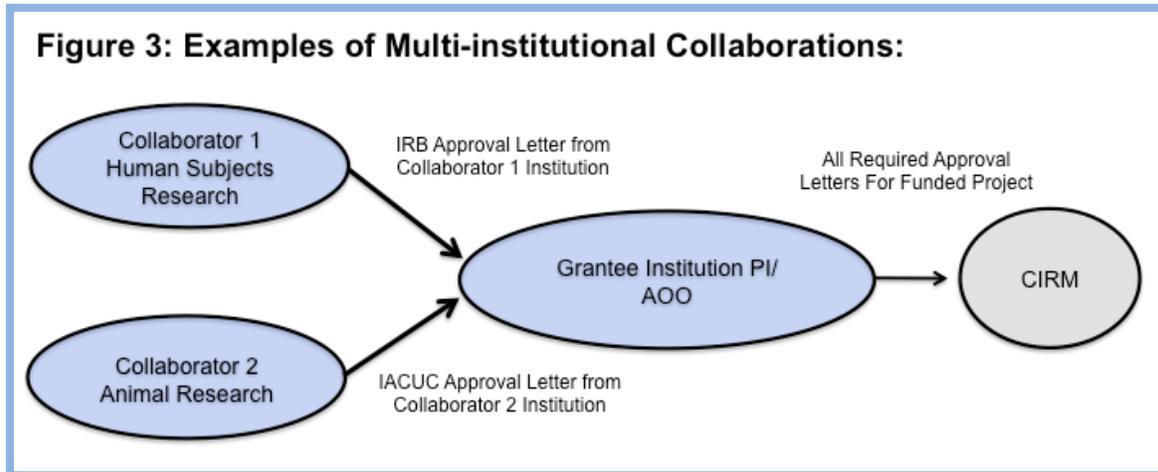
Another important amendment, that served to align the CIRM regulations with the CDPH guidelines, involved section 100080. Section 100080 was revised to allow the use of embryos for which the oocyte donor was paid provided the embryo was created for reproductive purposes and the person(s) in fertility treatment have determined it is no longer needed for reproductive use. This amendment also aligns the CIRM regulations with the NIH Guidelines for Human Embryonic Stem Cell Research. Participants indicated that this revision was important because it removes regulatory uncertainty in research supported by multiple funding agencies.

Multi-institutional Collaborations:

CIRM discussed the issue of compliance assurance for collaborative research projects involving multiple institutions. CIRM indicated that the grantee (as defined by the CIRM Grants Administration Policy) is responsible for submitting all required reviews and approvals within the scope of the collaborative research project. For example, if a collaborating institution is performing human subject research, the grantee is responsible for providing notice of IRB approval to

⁴ See <http://www.cdph.ca.gov/services/boards/HSCR/Documents/MO-HSCR-May21Transcript-09-2009.pdf>

CIRM. Figure 3 illustrates this example. Participants indicated that the CIRM policy is consistent with how multi-institutional collaboratives are administered.



CIRM Compliance Program:

The CIRM compliance program is designed to evaluate and support grantee compliance with the institute's regulations and contracts. The program includes site visits to grantee institutions. During site visits CIRM staff perform (1) a regulatory review to evaluate compliance with CIRM Medical and Ethical Standards Regulations and Grants Administration Policy (2) a financial review to evaluate expenditure reporting. The CIRM presented its compliance program protocol and discussed results from 12 site visits to date.

- Among academic research centers (SCRO) oversight structure is consistent with CIRM regulations.
- Reviews of specific applications by SCRO is consistent with regulatory requirements.
- CIRM has provided recommendations to two institutions regarding the need for more explicit procedures and policies to govern their SCRO operations.
- CIRM did identify one patent that had not been reported; grantee has now submitted required disclosure report.
- CIRM has worked with two grantee institutions to ensure compliance with AALAC (animal care accreditation) requirements.
- Site visits generally result in ongoing communications between CIRM and institutions regarding good regulatory practice.

CIRM Grants Administration:

CIRM provided a grants management update at the workshops. The update focused on grants management issue related to regulatory compliance. Staff emphasized the important of providing regulatory assurance documents. Staff also informed participants of the need to submit approval letters consistent with [CIRM guidance](#). There was discussion among participants and CIRM staff about a range of budgeting issues.

Conclusion:

The 2010 workshops were designed to inform participants of changes to CIRM policy. Many of these changes are based on recommendations from the report [Advancing the Field: Institutional Approaches Supporting Ethics in Stem Cell Research](#). Participants were supportive of policies governing research oversight and acceptable research materials. In the interest of supporting regulatory consistency, CIRM will continue to coordinate with state, particularly the CDPH, federal and international agencies and policymaking organizations.