CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Advancing Effective Research Oversight: CIRM's Evaluation Initiative

Introduction:

CIRM's mission is to support and advance stem cell research and regenerative medicine under the highest medical and ethical standard for the discovery and development of therapies and cures. CIRM has recently developed Medical and Ethical Standards (MES) regulations to govern research funded by the institute.[1] Consistent with the recommendations of the National Academies Committee on Guidelines for Human Embryonic Stem Cell Research the MES regulations are intended to ensure that human stem cell research advances in a scientifically and ethically responsible manner.[2] They require institutions to develop a system of oversight to promote the incorporation of ethical principles in the design and conduct of studies, to ensure that independent scientific review occurs—as well as considerations of financial conflicts of interest—and to make sure that mechanisms are in place for continuing review and monitoring of protocols.[3]

The regulations achieve these objectives through a combined approach that incorporates existing state and Federal oversight mechanisms and creates new requirements tailored to the rapidly advancing field of human stem cell research. The new requirements emphasize scientific and ethical review of studies, acceptable research materials, informed consent, and additional protections for research donors. The CIRM MES regulations are designed to be compatible with the CIRM Grants Administration Policy and intellectual property regulations. Collectively, these regulations represent a mutually reinforcing set of requirements intended to ensure CIRM-funded research is conducted under the highest standards.

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[1] The Office of Administrative Law approved the CIRM regulation on 10/10/06 with an effective date of 11/22/06.

[2] *Guidelines for Human Embryonic Stem Cell Research* Committee on Guidelines for Human Embryonic Stem Cell Research, National Research Council. http://www.nap.edu/catalog/11278.html.

[3] This oversight framework is recommended by the Institute of Medicine of the National Academies. 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.

In accordance with the California Administrative Procedure Act, the MES regulations predominantly adopt performance standards rather than prescriptive standards.[4] A prescriptive standard described an exact method for compliance. In contrast, a performance standard describes an objective with the criteria stated for achieving the objective.[5] The MES regulations encourage the development of best practices by requiring intuitions to achieve a number of objectives (e.g. scientific and ethical review and informed consent).

The CIRM Evaluation Initiative:

Pursuant to our obligation to assure that research is conducted safely and ethically, CIRM is committed to the ongoing evaluation of its MES Regulations through an evidence-based evaluation 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.[6] [7] [8] 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. As part of our commitment to advancing high ethical and medical standards, CIRM has designed an evaluation initiative intended to perform the following functions:

- Evaluation: Request information from stem cell research institutions regarding their experience implementing the MES regulations. The focus of this evaluation is the identification of issues and needs that have emerged during implementation.

- Communication: Convene meetings with institutions to facilitate peer learning and quality improvement. Synthesize the results of evaluation findings and determine the extent to which there is commonality between institutions with regard to implementation issues.

- Collaboration: Promote collaboration among participants, including other government agencies, to enhance the evidentiary basis for identifying best-practices.[9] Develop consensus findings with regard to best practices for addressing common issues. Present these findings to the Standards Working

[4] California Government Code, section 11346**.2(b)(3)(A)**.
[5] California Government Code, section 11342**.**570.
[6] 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.
[7] Department of Health and Human Services Office of Inspector General, Institutional Review Boards: A Time for Reform. June 1998, OEI-01-97-00193.
[8] Office for Human Research Protections (OHRP) Division of Assurances and Quality Improvement Objectives and Overview of the OHPR Quality Improvement Program April 15, 2002.
[9] CIRM contemplates coordination with the California Department of Health Services and the National Academies Committee on Guidelines for Human Embryonic Stem Cell Research. Both organizations are committed to the development of policies to support ethically responsible stem cell research.

Group and the Independent Citizens Oversight Committee to inform policy development. These findings may also inform Communities of Science and Public Responsibility initiatives described in the *CIRM Scientific Strategic Plan*.[10]

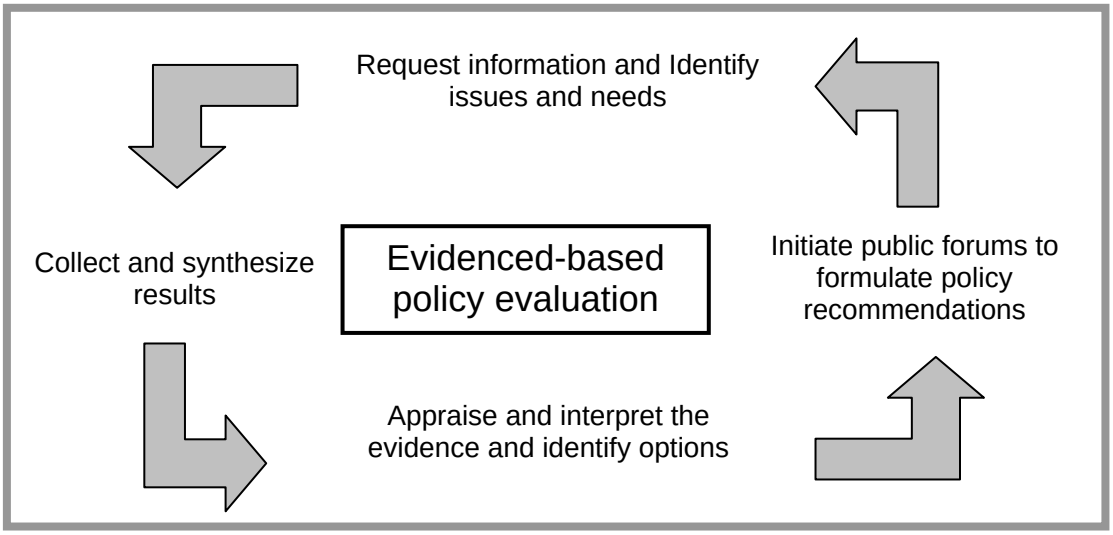

Figure 1: Adapted from Heller et. al. *Public Health* 117(2003)

Preliminary Formative Evaluation

Formative evaluation is concerned largely with determining the effectiveness or worth of steps taken during the developmental phase of a program. In this context, the *program* refers to individual institution's program of oversight for CIRM-funded research. The CIRM MES regulations establish a framework for such a program (e.g. creation of stem cell research oversight committees and research review requirements). We anticipate initial oversight efforts will center on the implementation of this framework. A major objective of the formative evaluation is to identify issues that have emerged during program implementation and development. The preliminary formative evaluation will be conducted through interviews with institutional officials, participation in meetings and workshops, and review of existing materials (e.g. interviews, conferences, e-mail list-serves, and workshop proceedings).

Communication

Developing best-practices in the context of research oversight involves individuals working together within and between institutions to improve systems and processes with the intent of securing superior possible outcomes.[11] Communication between institutions

[10] see http://www.cirm.ca.gov/strat/

[11] 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.

may be particularly useful for understanding common issues related to program implementation and identifying best-practices. CIRM will strive to facilitate communication aimed at achieving these outcomes by facilitating forums to disseminate evaluation findings and consider methods for achieving best outcomes.

Collaboration

Through collaboration, a core CIRM value, the evidentiary basis for improving program outcomes can be developed. CIRM seeks to facilitate collaboration among California research institutions at sponsored forums to develop, further refine, disseminate, and continually evaluate best practices to address issues identified in the formative evaluation. CIRM will also collaborate with national stakeholders such as the Board on Life Sciences of the National Academies. Lessons learned from these collaborative efforts will be communicated in public forums to the Standards Working Group and the Independent Citizens Oversight Committee to inform the Communities of Science and Public Responsibility initiative in the *CIRM Scientific Strategic Plan* and broader policy development.

Timeline & Activities:

As suggested by figure 1, evidence-based policy development is an iterative process designed to continually re-evaluate needs and options. The first iteration of the process is designed to coincide with the implementation of the MES regulations and the Scientific Excellence through Exploration and Development (SEED) Grant Program and the Comprehensive Research Grant Program. In early 2007, there will be a substantial increase in the number of CIRM-sponsored research studies subject to review and approval. The following timeline is designed to benefit from the knowledge gained from this review process.

Phase	Timeline	Objective	Activities
Evaluative phase	11/2006–3/2007	• Identify issues and needs	Key informant interviews Attend and/or review conference proceedings
Communication	2/2007–4/2007	• Understand extent of needs • Synthesize evidence	Conduct 2-3 regional forums Partner with NAS/IOM and other state, national, and international organizations
Collaboration	5/2007	• Identify options and best practices • Report to SWG and ICOC • Incorporate into policy and programming	Convene annual CIRM Standards Working Group (SWG) public meeting Present evidence and policy options in public forum Provide report to the ICOC