**MEMORANDUM**

**TO:** Members of the Science Subcommittee of the ICOC

**FROM:** Legal Team

**RE:** **Item 3:** Consideration of adoption of the interim Grants Administration Policy for Clinical Stage Programs

**DATE:** March 16, 2015

## Executive Summary

The mission of CIRM is to accelerate the development of stem cell therapies to patients with unmet medical needs. To better serve this mission, CIRM is overhauling the manner in which it does business, referred to as "CIRM 2.0" in previous communications with the Independent Citizens Oversight Committee ("ICOC"). CIRM will implement a more streamlined process for awarding and administering grants that will include frequent and predictable submission opportunities followed by rapid review, quick funding decisions, streamlined contracting and the prompt initiation of research. Post-award, CIRM intends to become a more active partner with its recipients to further increase the probability of timely success.

In December, the ICOC approved the concept plan for a trio of program announcements to expedite support for the clinical stage candidate stem cell therapies that demonstrate scientific excellence. Under this initiative, CIRM will provide funding for eligible projects that are completing late stage preclinical development through any stage of clinical trial activity.

To accomplish this, CIRM has established an open call for proposals and will accept applications on a monthly basis for three complementary award types. As part of the process of implementing these proposals, CIRM must adopt a new Grants Administration Policy ("GAP") to govern these awards.

In January of this year, the Science Subcommittee reviewed a prior draft of the GAP attached to this memorandum and recommended the ICOC adopt this interim policy. At the subsequent Board meeting the team presented the draft as an informational item, and used the ensuing time to accomplish further refinements. Substantively, this draft is virtually the same as the draft reviewed in January. The primary changes have been to make more clear and concise the certification and reporting obligations, and delete redundant regulatory requirements.

## I. Background

CIRM's Grant Administration Policy for Academic and Nonprofit Institutions – the GAP – sets out the detailed rules for management of CIRM awards. The GAP is generally modeled on the NIH's Grants Policy Statement, with differences that reflect CIRM's distinct role and mission.

The GAP was adopted by the ICOC in December 2006. On three subsequent occasions, the ICOC adopted amendments intended to further clarify certain provisions, simplify some requirements, and incorporate several modifications based on experience with the GAP.

The CIRM team regards the proposed interim GAP as the starting point for drafting a final policy that will govern clinical stage projects. In light of the fact that the deadline for the first round of applications falls at the end of this month, and to ensure that rules are in place to govern the application, review and administrative process, CIRM must avail itself of its statutory authority to adopt the GAP on an interim basis, to be followed by the permanent regulatory adoption procedure as administered by the Office of Administrative Law. With the approval of this interim policy by the ICOC, the CIRM team will initiate the formal rulemaking process. Accordingly, this subcommittee and the ICOC will have additional occasions to review and comment upon the final GAP.

## II. Interim GAP Components

The proposed interim GAP follows the same basic template of the existing policy that applies to currently active and former grants. This policy is chronologically organized to govern the grant-making process, addressing the primary areas of the application and review process, the pre-award and award requirements, and the rules governing payment and use of funds as the grant is funded. In creating this interim GAP, the CIRM team reviewed each aspect of the existing policy through the lens of the new Clinical Stage Programs and its requirements. The result is a policy designed to attract more high quality applications, reduce the cycle time from application to project start, accelerate progression of funded projects, and provide for more efficient administration of the projects.

A. Part I. General Information (pp. 7-13)

This section contains introductory information regarding CIRM's mission, a glossary of terms used in the policy and generally describes the roles and responsibilities of key individuals in the grantee organization. To eliminate potential confusion and to conform with the structural reorganization at CIRM, the prior CIRM team roles are eliminated. Another important conforming change is the description of the role of the Clinical Advisory Panel ("CAP"). A combination of the CDAP and Accelerated Development Pathway concepts, CAPs will provide real-time course correction and will focus more on acceleration opportunities than pure evaluation. CAPs will be tailored for the needs of each project and will consist of CIRM and external members, more nimbly sized than prior CDAP panels. CAPs will meet on a quarterly basis (instead of annually with CDAP) and examine all relevant information regarding project progression, possible roadblocks, and avenues for progression. The CAPs will report to the Grants Working Group ("GWG") and CIRM on a regular basis.

B. Part II. Grant Application and Review Process (pp. 13-18)

As in Part I, Part II has been tightened to remove unnecessary restrictions or processes not vital to successful implementation of late-stage clinical projects. The eligibility section has been drafted to reflect that applicants will undergo a background

check to ensure no prior or pending records of fraud or misuse of funds (p. 13).

One of the key features of the new approach approved by the Board will be the performance of a key external budget review as soon as the application is received (p. 14). This new review will examine the proposed budget to identify where proposed costs diverge from established market rates and where opportunities for budget tightening may be found. To incentivize efficient budgeting, where CIRM determines that a budget differs significantly from market rates, the applicant will be required to make conforming adjustments of the budget before the application will be brought forward for review by the GWG. This budget review is in addition to existing budget analysis by the CIRM team, GWG or ICOC.

Because CIRM's strategy is to prioritize funding projects that score very highly during scientific review at the GWG, the recommendation tiers described in the "Application Review" section (III.D.) now reflect this goal (pp. 14-15).

The GAP is also streamlined with respect to criteria for review of research applications (p. 15). Preserving flexibility for modification in a given program announcement or RFA, the GAP now distills the primary criteria to four: 1) project significance/impact; 2) rationale; 3) project plan/design; and 4) feasibility. These four criteria will assist the agency to identify and promote projects that show a promise of success and are structured soundly.

Finally, in light of the rolling nature of the programs that will allow unsuccessful applicants in many instances to reapply with improvements to their applications, CIRM will limit the grounds for appeal of Scientific Review to those based on demonstrable conflicts of interest (as defined in the conflict of interest policy applicable to GWG members) (pp. 15-16).

C. Part III. Pre-Award and Award

A key bottleneck that has prolonged the grant-making process at CIRM is in the area of pre-award activities after the ICOC has approved an award but before the Notice of Grant Award has been issued and research begun. Instead of consuming several months for this step, CIRM's goal is to reduce this period of time to just 45 days. Accordingly, this section of the GAP places emphasis on efficient administration of the contracting process. Rather than require submission of extensive documentation regarding compliance with myriad protocols and processes – some CIRM-imposed and others external – the proposed process will rely on certification of compliance by the applicant, with the ability for CIRM to request supporting documentation if cause to do so arises (p. 18).

D. Part IV and V. Award Acceptance; Payment and Use of Funds

Prior to CIRM 2.0, payments to grantees were made primarily based on the calendar – disbursements keyed off the start date of the project and were periodically made based on some given period of time following that date. Under the proposed GAP, however, for clinical stage projects CIRM will shift to a milestone-based payment schedule (pp. 25-27). Thus, this section of the GAP describes the importance of the milestones and how payments on the grant will only be made upon successful completion of the

milestones. Additionally, in many circumstances the grantee will be allowed to keep unspent CIRM funds upon successful completion of the project, to be spent on any other project of the grantee's that is consistent with advancing CIRM's mission. This new process will incentivize grantees to advance the project in the most efficient and shortest time possible, fulfilling CIRM's goal to accelerate such projects.

Another simplification embodied in the new GAP is the section regarding Prior Approval Requirements (pp. 31-33). Because most prior approval requests were routinely granted, and therefore added little value to the process, prior approval requests for rebudgeting and carryforward have been eliminated. We have also eliminated prior approval requests for no-cost extensions because our new CIRM awards will have project end dates that will be extended automatically as needed to complete the final Operational Milestone. CIRM intends to increase the latitude for grantees to pursue their research, while maintaining visibility into and approval of any changes to key components of clinical trials, manufacturing processes, or any other activities that meaningfully impact milestones or suspension events.

Because a CAP will meet with a project team on a quarterly basis to review the team's progress and provide expert advice, progress reports will move to a quarterly basis to enable productive CAP involvement. In addition, because payments are keyed off milestone achievement or suspension events, the grantee will promptly report the occurrence of either (pp. 34-35).

## III. Recommendation

The CIRM Team requests the Science Subcommittee recommend that the ICOC adopt the Interim Grants Administration Policy for Clinical Stage Projects and initiate the rulemaking process to finalize this GAP.

# CIRM Interim Grants Administration Policy for Clinical Stage Projects

# CIRM Interim Grants Administration Policy for Clinical Stage Projects

## Preface

This grants administration policy, serves as the terms and conditions for Clinical Stage Projects funded by the California Institute for Regenerative Medicine (CIRM) pursuant to the following Program Announcements: PA 15-01, PA 15-02, and PA 15-03. In addition, it provides guidance to applicants and Awardees regarding their responsibilities as CIRM awardees. Principal investigators, program directors, and organizational officials with grants management responsibilities are urged to read this document carefully and to refer to relevant sections for answers to questions that arise concerning the administration of CIRM awards. Applicants and Awardees may be required to document compliance with any and all provisions set forth in this policy.

This policy applies to all CIRM applicants and Awardees who receive CIRM funding through PA 15-01, PA 15-02, or PA 15-03. By accepting CIRM funding, the Awardees agree to comply with the provisions set forth in this policy.

This policy may be amended or revised periodically. Any new or amended regulations adopted by the Independent Citizens' Oversight Committee (ICOC), the governing board of CIRM, will be applied to currently active awards under PA 15-01, PA 15-02, and PA 15-03 on the start date of the next Operational Milestone, except as provided in the relevant CIRM Intellectual Property Regulations. CIRM will notify principal investigators, program directors and organizational officials with active CIRM awards of amendments to or revisions of this policy as they are released. Amendments or revisions will be posted on the CIRM website (http://www.cirm.ca.gov).

CIRM's right to enforce this policy shall survive the end of the term of the Project Period, and should CIRM no longer exist, that right may be exercised by the State of California.

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# I. GENERAL INFORMATION

## A. CIRM Background and Mission

The California Institute for Regenerative Medicine (CIRM) is a state agency that was established with the passage of Proposition 71, the California Stem Cell Research and Cures Act, a state ballot initiative approved by 59 percent of California voters on November 2, 2004. Proposition 71 authorizes CIRM to disburse up to $3 billion in state bond funds over a period of 10 years or more in the form of grants, loans and contracts for the purpose of conducting stem cell research and constructing research facilities in the State of California.

CIRM funding will support stem cell research and other vital research opportunities for the development of life-saving regenerative medical treatments and therapies. All research proposals will be peer-reviewed so that the most promising scientific proposals are funded.

Priority for research grant funding is given to stem cell research that meets the criteria established by CIRM and is unlikely to receive federal funding. Under Proposition 71, CIRM is prohibited from funding research on human reproductive cloning.

CIRM is governed by the Independent Citizens' Oversight Committee (ICOC), a 29-member board composed of executive officers from California universities and research institutions, representatives of patient advocacy groups, and experts in the development of medical therapies from the life sciences community. ICOC members are public officials appointed because of their experience in California's leading public universities, non-profit academic and research institutions, patient advocacy groups, and the biotechnology industry.

## B. Abbreviations

CFR – Code of Federal Regulations

CIRM – California Institute for Regenerative Medicine

DHHS – U.S. Department of Health and Human Services

FDA – U.S. Food and Drug Administration

FWA – Federal-Wide Assurance

GMO – Grants Management Office

IACUC – Institutional Animal Care and Use Committee

ICOC – Independent Citizens' Oversight Committee
IDE – Investigational Device Exception

IND – Investigational New Drug

IRB – Institutional Review Board

NGA – Notice of Grant Award

NIH – U. S. National Institutes of Health

NLA – Notice of Loan Award

OHRP – Office for Human Research Protections, DHHS

PHS – Public Health Service, DHHS

PI – Principal Investigator

RFA – Request for Applications

SCRO – Stem Cell Research Oversight Committee

GWG – Scientific and Medical Research Funding Working Group

SPO – Scientific Program Officer

SRO – Scientific Review Officer

**C.** Defined Terms

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| Application | A request for CIRM funding to conduct research; provide services; or construct, lease, or acquire Equipment. An Application shall contain all information upon which approval for funding is based. |
| Approved Budget | The financial expenditure plan for the CIRM-Funded Project or Activity, including revisions approved by CIRM and permissible revisions made by the PI or Awardee. |
| Authorized Organizational Official (AOO) | The individual, named by the applicant organization, who is authorized to act for the applicant organization and to assume the obligations imposed by the laws, regulations, requirements, and conditions that apply to Applications and Awards. |
| Award | CIRM funding in the form of an award, Grant, loan, or contract that is based on an approved Application and budget. |
| Award Close-out | The final stage in the life-cycle of an Award, whether in the form of a grant, loan or contract. During this phase, CIRM ensures that all applicable administrative actions and required work have been completed by the PI and Awardee. CIRM also reconciles and makes any final fiscal adjustments to the Awardee's Award. |
| CIRM-Funded Project or Activity | Those activities specified or described in an Application that are approved by the ICOC for funding and for which CIRM has issued an NGA, regardless of whether CIRM funding constitutes all or only a portion of the financial support necessary to carry them out. |
| Clinical Research | Patient-oriented research; that is, research conducted with Human Subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) in which an investigator (or colleague) directly interacts with Human Subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Included in this definition are: (1)(a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies; (2) epidemiologic and behavioral studies; and (3) outcomes research and health services research. |
| Consultant | An individual who provides professional advice or services related to the proposed project in exchange for a fee. |

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| Covered Stem Cell Line | A culture-derived, human pluripotent stem cell population that is capable of: (1) sustained propagation in culture; and (2) self-renewal to produce daughter cells with equivalent developmental potential. This definition includes both embryonic and non-embryonic human stem cell lines regardless of the tissue of origin. "Pluripotent" means capable of differentiation into mesoderm, ectoderm, and endoderm. |
| Direct Research Funding Costs | The sum of project costs and facilities costs of a CIRM Award. "Project costs" are those costs that can be specifically identified with a particular CIRM-funded Project or Activity. "Facilities costs" are the operating costs of an Awardee's facilities attributable to housing all elements of the CIRM-funded Project or Activity. |
| Equipment | Non-expendable, free-standing, tangible personal property with a normal life expectancy of one year or more and an acquisition cost which equals or exceeds the lesser of the capitalization level established by the Awardee for financial management purposes or $5,000. |
| Financial Report | An Awardee's periodic report to CIRM detailing expenditures against CIRM funds as specified in the NGA or NLA (see chapter V, section H, part 1). |
| For-profit Organization | A sole-proprietorship, partnership, limited liability company, corporation, or other legal entity that is organized or operated for the profit or financial benefit of its shareholders or other owners. Such organizations also are referred to as "commercial organizations". |
| Grant | A funding mechanism pursuant to which CIRM provides money and/or property to an Awardee on terms set forth in an NGA, in order to assist the Awardee in carrying out approved CIRM-Funded Project or Activity. |
| Human Embryonic Stem Cells | Human embryonic stem cells are immature (i.e., undifferentiated) cells that are derived from a human early stage, preimplantation embryo. Human embryonic stem cells can be cultured in vitro where they self-renew indefinitely and have the potential to develop into any cell type of the body (i.e., they are pluripotent). |
| Human Subject | A living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual or obtains identifiable private information. Regulations governing the use of Human Subjects in research extend to use of human organs, tissues, and body fluids from identifiable individuals as Human Subjects and to graphic, written, or recorded information derived from such individuals. |
| Indirect Costs | Administrative costs of an Awardee incurred for common or joint objectives, which cannot be readily and specifically identified with a |

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| | particular project. |
| Key Personnel | (1) the principal investigator or program director; or (2) any other person, including an independent consultant or an employee of a Subcontractor or Partner, who is expected to contribute to the scientific development or execution of the project in a substantive, measurable way and who is expected to: (a) receive or has been promised income, or anything else of value, of $10,000 or more per year for his or her contribution to the project or (b) contribute one percent (1%) or more effort to the proposed project. "Key Personnel" does not include a person who is expected to be involved in the proposed project but who does not satisfy conditions (1) or (2). |
| Loan | A funding mechanism pursuant to which CIRM loans money and/or property to an Awardee, in exchange for a promise to prepay CIRM pursuant to terms set forth in an NLA, in order to assist the Awardee in carrying out a CIRM-Funded Project or Activity. |
| Non-Profit and Not-for-Profit | Means or refers to either: (a) a governmental entity of the state of California: or (b) a legal entity that is tax exempt under Internal Revenue Code section 501(c)(3) and California Revenue and Taxation Code section 23701d. |
| Notice of Grant Award (NGA) | The document that notifies the Awardee that a Grant has been made, contains or references all terms and conditions of the Grant as well as the Awardee's and PI's agreement to those terms and conditions, and documents the commitment of CIRM funds. |
| Notice of Loan Award | The document that notifies the Awardee that a Loan has been made, contains or references all terms and conditions of the Loan as well as the Awardee's and PI's agreement to those terms and conditions, and documents the commitment of CIRM funds. |
| Operation and Maintenance Expenses | The general operating costs of an Awardee's facilities include expenses normally incurred for such items as janitorial and utility services; repairs and ordinary or normal alterations of buildings, furniture and Equipment; care of grounds; maintenance and operation of buildings and other plant facilities; security; earthquake and disaster preparedness; environmental safety; hazardous waste disposal; property, liability and all other insurance relating to property; space and capital leasing; facility planning and management; and central receiving that are necessary for carrying out the CIRM-Funded Project or Activity(see chapter V, section B, part 3).{check this citation} |
| Operational Milestone | An objective event that is indicative of project progress occurring as proposed in the application. The successful achievement of an Operational Milestone may trigger the disbursement of additional funds under the award as scheduled in the NGA or NLA. The |

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| | intervals between Operational Milestones are used to divide a Project Period for budgetary, funding and reporting purposes. |
| Organization | A generic term used to refer to a Non-Profit, Not-for-Profit or For-Profit Organization or other legal entity which applies for or receives CIRM funding. |
| Other Support | Includes all financial resources – whether federal, non-federal, commercial, or organizational – available in direct support of an investigator's research endeavors, including, but not limited to, research grants, cooperative agreements, contracts, or organizational awards. Other Support does not include training awards, prizes, or gifts. |
| Principal Investigator (PI) or/Program Director (PD) | An individual designated by the Awardee to direct the CIRM-Funded Project or Activity. He or she is responsible and accountable to the Awardee and CIRM for the proper conduct of the project or activity. |
| Prior Approval | Prior written approval from CIRM that is required for specified post-award changes in the Approved Budget or project. Such approval must be obtained before undertaking or spending CIRM funds for the proposed activity. |
| Program Announcement ("PA") | The mechanism for funding opportunities that accept applications on an ongoing basis, rather than a fixed deadline. |
| Progress Report | An Awardee's periodic report to CIRM detailing scientific activities and findings in the research project identified in the NGA or NLA (see chapter V, section H, part 2). |
| Project Period | The total amount of time as stated in an NGA or NLA for which CIRM intends to fund a project or activity and authorizes a PI to conduct the work in the approved Application. For reporting purposes, the Project Period includes all Operational Milestones. |
| Recipient | The Awardee, PI or PD, trainee, Subcontractor, Consultant or any other person or entity that receives CIRM funding pursuant to an Award. |
| Research Patient Care Costs | The same definition as found in the National Institutes of Health Grants Policy Statement, Part II.B.19 "Research Patient Care Costs," effective August 8, 2014, and incorporated herein. Such costs include but are not limited to, routine and ancillary services provided by |

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| | hospitals to individuals participating in research programs. As set forth in Part II.B.19, Research Patient Care Costs do not include: (1) the otherwise allowable items of personal expense reimbursement, such as patient travel or subsistence, consulting physician fees, or any other direct payments related to all classes of individuals, including inpatients, outpatients, subjects, volunteers, and donors, (2) costs of ancillary tests performed in facilities outside the hospital on a fee-for-service basis (e.g., in an independent, privately owned laboratory) or laboratory tests performed at a medical school/university not associated with a hospital routine or ancillary service , (3) recruitment or retention fees or (4) the data management or statistical analysis of clinical research results. |
| Scientific and Medical Research Funding Working Group (GWG) | The advisory body responsible for reviewing the scientific and programmatic content of Applications for research funding and for making funding recommendations to the ICOC. |
| Subcontract/ Subaward | A contract between the Awardee and a third party to perform a portion of research proposed in the Application. |
| Suspension Event | A pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable. |
| Tuition and Fees | Costs charged by the Awardee for the enrollment and instruction of a student. It does not include costs of health insurance for a trainee, which is an allowable cost addressed separately. |

**D.** Types of Support

The objective of clinical stage programs is to create a highly competitive partnering opportunity for promising stem cell-based projects to accelerate the completion of preclinical activities necessary to attain an active IND with the FDA, to initiate start-up activities of the proposed clinical trial, to accelerate the completion of a clinical trial, and support new activities on active projects that will significantly accelerate development of the proposed therapy or increase the likelihood of success.

**E.** Roles and Responsibilities

**1. Awardee Organization Staff:**

**a. Authorized Organizational Official (AOO)**

The AOO is the designated representative of the Awardee organization for matters related to the Award and administration of CIRM funding. This individual's signature on the Application certifies that, should the ICOC approve the Application for funding and should CIRM issue an Award, the Organization will be accountable both for the appropriate use of funds and for the performance of the CIRM-Funded Project or Activity. This individual also certifies to CIRM that the PI and Awardee comply with applicable federal and state laws and regulations, including required certifications and assurances (e.g., IRB, SCRO, IACUC), and CIRM policies, including the terms and conditions of the Award.

A designated AOO must have the legal authority to commit the Awardee to indemnify CIRM as provided in Chapter III, Section B, Liability, and an Awardee's designation of an AOO confers apparent authority to commit the Awardee to such indemnification of CIRM.

**b. Principal Investigator (PI) or Program Director (PD)**

The PI is the individual, designated by the Awardee, responsible for the scientific or technical aspects of the CIRM-Funded Project or Activity and for its management. The PI and the Awardee are both responsible for ensuring compliance with the financial and administrative aspects of the Award. The PI must work closely with other Awardee officials to create and maintain necessary documentation, including both technical and administrative reports; prepare justifications; appropriately acknowledge CIRM support of research findings in publications, announcements, news programs, and other media; and ensure compliance with CIRM, federal, state, and organizational requirements.

**2. Clinical Advisory Panel:**

The Clinical Advisory Panels ("CAPs") are expert advisory panels created and appointed by CIRM's President to work closely with each CIRM-funded clinical and pre-clinical project to accelerate the successful development of therapies for patients with unmet medical needs. The CAPs will meet regularly with CIRM awardees to provide scientific, medical, and drug development advice, recommend real-time course correction if warranted, and facilitate a seamless transition from one stage of development to the next. Project teams will be required to submit all requested documents to CIRM in advance of the CAP meeting.

## II. GRANT APPLICATION AND REVIEW PROCESS

### A. Eligibility

#### 1.PI and PD Eligibility

The PI/PD will be subject to a background check to ensure this individual has not been convicted of fraud or other misuse of funds, nor subject to disbarment of federal funds. There are no citizenship requirements for PIs.

#### 2. Organizational Eligibility

An applicant organization must be a legal entity that is accountable for both the performance of the approved project or activity and the appropriate expenditure of funds. In general, Non-profit and For-profit research organizations located and conducting research in California are eligible to apply for and to receive CIRM research funding. Under certain programs, CIRM may limit eligibility to meet the specific goals of a Program Announcement (PA) or Request for Applications (RFA). The determination of eligibility includes verification of the applicant's ability to carry out the proposed project and responsibly manage and account for State funds in the organization's accounting systems, and verification of corporate status .

California Organizations (for-profit and non-profit) may use CIRM funds for eligible project costs incurred both in California and outside California. To qualify as a California organization, the organization must have >50% of its employees located in, and paid in, the state of California, and manage the award activities from the California location.

Non-California organizations may also apply; however, CIRM funding can be used only for allowable expenditures incurred within California. The applicant must demonstrate by the application deadline a commitment of funds from other sources for project activities outside of California.

### 3. Other Requirements

Because eligibility may vary, applicants should carefully review the Program Announcement or RFA for specific eligibility requirements. An applicant may be required to provide proof of eligibility, such as organizational eligibility, PI or PD eligibility.

## B. Application Submission

CIRM funding opportunities will be announced via a PA or RFA, on the CIRM website (http://www.cirm.ca.gov). Each solicitation will specify the objectives and requirements that apply, and the review criteria that will be used to evaluate the merits of Applications submitted in response to the announcement. Information regarding Application forms and instructions for completion and submission of Application materials will be available as part of the funding opportunity announcement. CIRM may require submission of a Letter of Intent (LOI) and/or Communication Plan prior to or as a condition of submission of a full Application. The application will provide an opportunity to declare and exclude up to three individuals and/or organizations the applicant believes could not provide an impartial review of the proposal.

## C. Legal Effect of Signed/Submitted Application

In signing the Application, the AOO warrants to CIRM that all eligibility requirements have been satisfied and agrees that should an Award be issued, the organization will abide by the terms and conditions of the Award, all applicable CIRM regulations, all applicable public policy requirements, and will perform the activities included in the submitted Application as approved by the ICOC (unless Prior Approval is sought and obtained).

## D. Budget Review

Upon submission of an application, an external team of budget professionals will review the proposed budget to provide information to CIRM regarding how the proposed costs compare with established market rates for similar activities (or how well the costs are justified when market rates are not established). When CIRM determines that a proposed budget differs significantly from market rates, adjustments to the budget will be required by CIRM prior to further review of the application. Applicants will be notified of the specific discrepancies and applications will not be forwarded for scientific review until an amended budget has been submitted and approved by CIRM. Additionally, project budgets may be subject to further adjustments prior to issuance of an award based upon assessments of the GWG, the CIRM team or by the Application Review Subcommittee of the ICOC.

## E. Application Review

In accordance with Proposition 71, the Scientific and Medical Research Funding Working Group (Grants Working Group or GWG) makes funding recommendations to the Application Review Subcommittee of the ICOC. The role of the GWG includes consideration of the scientific merit of Applications to support research Facilities.

The membership of the GWG consists of seven patient advocate members of the ICOC, 15 scientists from institutions outside of California, and the chairperson of the ICOC (ex officio).

The GWG conducts its review of Applications in accordance with procedures recommended by the GWG and adopted by the ICOC. For each Application, a recommendation on funding is made by the full GWG and submitted to the Application Review Subcommittee of the ICOC, which makes all funding decisions. The GWG may designate each reviewed Application as one of the following:

1. ***Recommended for Funding*** (Tier 1)– For applications that have exceptional merit and are recommended for funding to the Application Review Subcommittee of the ICOC.
2. ***Not Recommended for Funding at this Time*** (Tier 2)– For applications that do not merit funding at this time but that can be improved and resubmitted for further consideration by the GWG. . The GWG may change the designation as needed to reflect the appropriate communication to the ICOC regarding the merit of the Applications in Tier 2.
3. ***Not Recommended for Funding*** (Tier 3)– For applications that are sufficiently flawed that they do not warrant funding, and the same project should not be resubmitted for review.

## F. Criteria for Review of Research Grant Applications

Pursuant to Proposition 71 (Health and Safety Code section 125290.60), the ICOC has established criteria for the evaluation of Applications by the GWG, each of which may be weighted differently depending on the purpose and goals of a particular PA. The ICOC may also adopt additional or revised review criteria, when appropriate to meet the objectives set forth in a particular PA.

Consistent with Proposition 71, the 15 scientist members of the GWG shall score Applications for scientific merit and base their evaluation on the criteria specified in the PA or RFA.

## G. Appeals of Scientific Review

An appeal of scientific review is limited to demonstrable conflicts of interest as defined in CIRM's Conflict of Interest Policy for Scientific Members of the GWG. Any such appeal shall be filed pursuant to this section.

An applicant may lodge a formal appeal of the review only if the applicant can show that a demonstrable financial, professional, or personal conflict of interest, as defined in the GWG Conflict of Interest Policy, had a negative impact on the review process and resulted in a flawed review. Differences of scientific opinion between or among PIs and reviewers are not grounds for appeal.

To lodge an appeal, the applicant must submit an appeal request in writing to CIRM within 10 days of CIRM's making the review report available to the applicant. The

CIRM team will then assess whether the applicant has established facts constituting a conflict of interest and whether the conflict of interest had a negative impact on the review process and resulted in a flawed review and present a recommendation to the President of CIRM. If the President concludes that the applicant has established facts constituting a conflict of interest and that the conflict of interest had a negative impact on the review process and resulted in a flawed review, the application will be submitted to the GWG for a new review.

## H. Approval for Funding

The GWG is responsible for making recommendations to the ICOC on funding of Applications based on scientific merit and programmatic relevance. The Application Review Subcommittee of the ICOC makes all final funding decisions. In deciding which Applications to fund, the Application Review Subcommittee may consider: (i) programmatic issues, with a focus on portfolio balance, relevance to unmet health need, urgency of timeline, alignment with focus of Proposition 71, alignment with the goals and priorities of the Program Announcement, budget adjustments if necessary, and other stipulations; (ii) recommendations made by CIRM's scientific staff based on their review of the Grants Working Group's recommendations; and (iii) public comment.

## I. Policy on Collection and Use of Personal Information

CIRM values and respects an individual's right to keep personal information private. Likewise, CIRM recognizes the need to collect and use personal information that will enable CIRM to effectively perform the responsibilities for which it was created. All personal information collected about individuals will be kept confidential and in a secure environment. However, information that is not protected from disclosure under the California Public Records Act may be subject to disclosure upon request.

## J. Public Access to Public Records

In the California Public Records Act (Government Code section 6250 *et seq*.), the California Legislature declared that access to information concerning the conduct of the people's business is a fundamental and necessary right of every person in this state. The California Public Records Act requires that public records be generally available to the public upon request (Government Code section 6253(a)) but also contains numerous exceptions.

Proposition 71 (Health and Safety Code section 125290.30(e)) provides that the California Public Records Act shall apply to all records of CIRM but does not require disclosure of the following:

1. Personnel, medical or similar files, the disclosure of which would constitute an unwarranted invasion of privacy;
2. 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 issuer an opportunity to obtain a business advantage over competitors who do not know it or use it; or

3. Pre-publication scientific working papers or research data.

Although Proposition 71 also provides that the California Public Records Act shall not apply to CIRM working groups, including the GWG (Health and Safety Code section 125290.50(f)), the ICOC has decided that the public shall also have access to the records of the working groups except for, among other things: (i) Applications for research, training, and facilities grants, loans, and contracts; (ii) evaluations of such Applications; and (iii) exceptions provided for in the California Public Records Act itself and Health and Safety Code section 125290.30. Subsection (e) of section 125290.30 exempts from public access records containing or reflecting confidential intellectual property and work product, such as that found in invention disclosures to CIRM.

For further information, please see the California Public Records Act and Proposition 71. For details on how CIRM responds to Public Records Act requests, see the CIRM guidelines available at (http://www.cirm.ca.gov/general/pdf/guidelines.pdf).

## III. PRE-AWARD AND AWARD

### A. Pre-Funding Administrative Review (PFAR)

After the approval of funding by the Application Review Subcommittee, applications are then reviewed by the CIRM to ensure that they meet all applicable CIRM funding requirements, including the submission of required public policy assurances. CIRM reviews the Application budget to ensure that all proposed costs are allowable, as specified in this Grants Administration Policy and the pertinent PA. During the administrative review, CIRM reserves the right to revise individual budget items as appropriate.

Issues that arise during administrative review generally must be resolved before CIRM will issue an NGA or NLA. CIRM may, however approve an Application for funding contingent upon the acceptance (by the PI and AOO) of a condition.
An approved awardee must initiate work on the funded project within 45 days of approval and authorization for funding by the Application Review Subcommittee of CIRM's governing board.

### B. Liability

CIRM is not responsible for the conduct of CIRM-funded research or for the acts or omissions of Recipients of CIRM funding, because such conduct is under the direction and control of the Awardee and subject to its organizational policies. Further, Awardee organization personnel compensated in whole or in part with CIRM funds are not considered employees of CIRM.

Awardees shall indemnify or insure and hold CIRM harmless against any and all losses, claims, damages, expenses, or liabilities, including attorneys' fees, arising from research conducted by the Awardee pursuant to the award, and/or, in the alternative, Awardees shall name CIRM as an additional insured and submit proof of such insurance. (Health and Safety Code section 125290.45, subd. (a)(2).). If the Awardee chooses only to insure, such insurance must provide coverage in amounts appropriate and proportional to cover the risks described in the previous sentence. Awardees that fail to provide evidence of such insurance prior to issuance of the NGA will be deemed to have agreed to indemnify and hold CIRM harmless.

In all cases, the Awardee will maintain, or cause to be maintained, in full force and effect, insurance or a self-insurance program that provides for general liability coverage that is (a) applicable to the CIRM-Funded Project or Activity, (b) in an amount not less than $1 million per occurrence, $3 million aggregate and (c) that is comparable to coverage held by institutions of similar size and nature. Upon request, the Awardee shall provide CIRM with certificates of insurance evidencing such coverage.

## C. Public Policy Requirements

Organizations and individuals that receive support from CIRM shall comply with, and where applicable provide evidence of compliance with, the following public policies. Initial funding or continued funding of any CIRM-Funded Project or Activity is contingent upon compliance with these requirements. Documentation that certifies or verifies compliance generally may be required to be submitted before CIRM will issue an NGA or NLA. In cases where research requiring public policy assurances will be conducted at a later phase of the funded research, CIRM may issue an NGA or NLA imposing a condition or restriction on the use of funds until documentation of required assurances is submitted.

The Awardee shall retain records and supporting documentation that demonstrate compliance with public policy requirements for a minimum five years from the date of submission of the final expenditure report for the Award. If related audit findings have not been resolved, documentation must be maintained for longer than five years, until such findings are resolved. Records and supporting documentation may be audited by CIRM or other appropriate state agencies, including the Office of the Attorney General of California.

### 1. Conduct of Research

**a.** "Research misconduct" means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. "Fabrication" means making up data or results and recording or reporting them. "Falsification" means manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. "Plagiarism" means the appropriation of another person's ideas, processes, results, or words without

giving appropriate credit. Research misconduct does not include honest error or differences of opinion.

**b.** Awardees and Recipients must conduct all research in accordance with the highest medical and ethical standards for scientific research and all applicable laws. The Awardee bears the ultimate responsibility for preventing, detecting and imposing sanctions for research misconduct. Awardees must adopt, maintain and ensure compliance with written policies and procedures for inquiry, investigation, and adjudication of allegations of research misconduct. An acceptable standard for such policies and procedures, for example, is found in the *Public Health Service Policies on Research Misconduct* (42 CFR Part 93)(effective May 17, 2005).

**c.** Within 30 days of concluding an investigation of research misconduct, Awardees shall notify CIRM in writing of any finding of research misconduct against a Recipient of CIRM funding and of any related proposed corrective actions.

**d.** The administrative actions imposed by CIRM for research misconduct may include, but are not limited to, the following: correction of the scientific literature; special plan of supervision to ensure integrity of the scientific research; certification of the accuracy of the scientific data; certification of the accuracy of sources and contributions for scientific ideas and writings; disqualification of the Awardee or Recipient from eligibility for CIRM funds; termination of the Award, and/or return of CIRM funds. The duration of these actions will depend on the nature and seriousness of the misconduct. Additional actions that CIRM may take are described in chapter V, section J, *Failure of Compliance and Award Termination.*

**2. Conflict of Interest**

Awardees must establish safeguards to prevent employees, Consultants, contractors, collaborators, and members of governing bodies who may be involved in the CIRM-Funded Project or Activities from participating in or in any way attempting to use their position to influence those activities in which they know or have reason to know they have a financial interest.

Awardees must enforce within their institutions all such applicable safeguards. If the Awardee uses contractors or collaborators to conduct CIRM-funded research, the Awardee must take reasonable steps to ensure that such contractors or collaborators comply with the Awardee's safeguards. An acceptable standard for such a policy, for example, may be found in 42 CFR Part 50, Subpart F (R*esponsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding Is Sought*)(effective October 1, 2000). The Awardee must promptly notify CIRM if and when it takes a suspension or separation action involving a financial conflict of interest against a PI or other Recipient of CIRM Funding.

**3. Administrative Actions**

The Awardee promptly shall promptly notify CIRM of the results of any investigation and any administrative, civil, or other action taken by any funding agency, the Office of Research Integrity, the Office of Laboratory Animal Welfare, the Office for Human Research Protections (OHRP), the Awardee itself, any other institution, or any law enforcement agency concerning a charge of research misconduct made against an Awardee concerning the Awardee's research activities.

**4. Use of Human Stem Cell Lines**

Awardees shall abide by the CIRM Medical and Ethical Standards (commencing with Title 17, California Code of Regulations, section 100010) developed by the CIRM Scientific and Medical Accountability Standards Working Group (Standards Working Group or SWG) and adopted by the ICOC for the use of "Covered Stem Cell Lines" or use of human oocytes or embryos. This requirement includes use and derivation of Human Embryonic Stem Cells. Consequences of failure to comply with CIRM regulations governing medical and ethical standards are described in chapter V, section J, *Failure of Compliance and Award Termination*. All CIRM-funded research involving "Covered Stem Cell Lines" must comply with CIRM regulations relating to SCRO committee review or notification as described in Title 17, California Code of Regulations, section 100070.CIRM will not issue an NGA or continue payment on active Awards without current certification of compliance with section 100070 as required or without imposing limiting conditions. In addition to the certification of compliance, CIRM may request documentation of the approval or notification required by section 100070. The documentation must include the name of the organization hosting the SCRO, the name of the committee, the name of the PI, the name of the Awardee, the CIRM Application number, the specific Covered Stem Cell Lines approved, the project title, and the period for which approval has been granted or expiration date of the approval. *(see chapter III, section D, Just-in-Time Procedures).*

**5. Use of Human Fetal Tissue**

When using human fetal tissue in research, CIRM Awardees shall abide by Title 17, California Code of Regulations, section 100085. Unless otherwise required by CIRM, the certifying statement required pursuant to Section 100085 (c) shall be provided just-in-time for approved Applications prior to issuance of the NGA (see Chapter III, Section D, *Just-in-Time Procedures*).Consequences of failure to comply with the CIRM regulations are described in chapter V, section J, *Failure of Compliance and Award Termination*.

**6. Research Involving Human Subjects**

**a.** An organization is engaged in research involving Human Subjects when its

employees or agents (1) intervene or interact with living individuals to obtain data for research purposes, or (2) obtain individually identifiable private information for research purposes.

**b.** Awardee organizations must apply California Health and Safety Code 24170-24179.5 to all CIRM-funded human biomedical or clinical subjects research. Compliance with this requirement may be demonstrated through written institutional policies or through provisions or full accreditation through the Association for the Accreditation of Human Research Protection Programs. In addition, the Awardee and any collaborating organizations (within the United States) must be covered by a Federal-Wide Assurance (FWA) approved by the OHRP, or an IND or IDE approved by the U.S. Food and Drug Administration (FDA).

**c.** The Awardee must appoint and maintain an Institutional Review Board (IRB) to provide oversight of research involving human subjects.

**d.** The Awardee bears ultimate responsibility for protecting Human Subjects involved in CIRM-funded research, including Human Subjects at all participating and collaborating sites. PIs and Awardees engaged in CIRM-funded research involving Human Subjects must certify that the research has been reviewed and approved by an IRB and will be subject to continuing review by the IRB. At CIRM's request, the prospective Awardee must provide the following documentation regarding itself and each collaborating site to CIRM:

- **i.** Documentation of IRB review and approval specifying the name of the PI, the name of the Awardee and any collaborating organization or site, the CIRM Application number, the project title, and inclusive dates for which IRB approval has been granted;
- **ii.** Sample human subject (patient) information and informed consent documents;
- **iii.** Documentation of human research subject education of Key Personnel;
- **iv.** For clinical trials, a data safety monitoring plan;
- **v.** Institutional assurance that the research is conducted in accordance with relevant national, state, and local laws; and
- **vi.** A copy of the FDA-IND or IDE letter, where applicable when a clinical investigation involves the use of any drugs or devices.

Prior to the issuance of an NGA or NLA and during annual Progress Reports (see chapter V, section H, *Reporting Requirements*), an Awardee shall certify to CIRM that any IRB approval required to conduct the CIRM-Funded Project or Activity is obtained or will be obtained before CIRM funding is spent on such activities. (see section D, *Just-in-Time Procedures*).CIRM will not authorize continued funding of active Awards without current certification for Human Subjects research.

**e.** Serious Adverse Event Reporting. In the case of an adverse event occurring during a CIRM-funded clinical trial or program that is both serious and unexpected, the PI must notify CIRM of such an event at the same time that the IRB and Awardee are notified. Prior to issuance of a NGA/NLA the Awardee shall agree to a Communication Plan that addresses the process and timelines for notifying CIRM in the event of a Serious Adverse Event or other crisis issue or occurrence that may impact the conduct of a trial.

**f.** Consequences of failure to comply with required Human Subjects research assurance are described in chapter V, section J, *Failure of Compliance and Award Termination*. The AOO shall promptly inform CIRM of any investigation or administrative action by OHRP or by the Awardee concerning Recipients of CIRM funding and their use of Human Subjects in research.

**g.** Women and members of minority groups must be included in all CIRM-funded Clinical Research, unless a clear and compelling rationale and justification establishes to the satisfaction of CIRM that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. This policy applies to research subjects regardless of age in all CIRM-funded Clinical Research studies.

**i.** Since a primary aim of research is to provide scientific evidence leading to a change in health policy or standard of care, it is imperative to determine whether the intervention or therapy being studied affects women or men or members of minority groups and their subpopulations differently. This requirement ensures that all CIRM-funded clinical research will be carried out in a manner sufficient to elicit information about individuals of both sexes/genders and diverse racial and ethnic groups and, particularly in clinical trials, to examine differential effects on such groups.

**ii.** PIs must include in their annual Progress Report the cumulative subject accrual and progress in conducting analyses for sex/gender and race/ethnicity differences (see chapter V, section H, Reporting Requirements).

**7. Animal Subjects**

**a.** The PI, Awardee and any collaborating sites are responsible for the humane care and treatment of animals involved in research activities and must establish appropriate policies and procedures that are based on the standards set forth in the *Guide for the Care and Use of Laboratory Animals* prepared by the National Academy of Sciences and released January 2, 1996.

**b.** The PI, Awardee and any collaborating sites conducting CIRM-funded

research that involves the use of vertebrate animals shall comply with all applicable federal, state, and local laws. Sites where CIRM-funded animal research is conducted must be accredited or seeking accreditation by the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

**c.** The Awardee must appoint and maintain an Institutional Animal Care and Use Committee (IACUC) to provide oversight of research involving vertebrate animals.

**d.** The prospective Awardee must provide certification of IACUC review and approval of research involving the use of live vertebrate animal subjects. Prior to the issuance of an NGA or NLA, a prospective Awardee shall certify to CIRM that any IACUC approval required to conduct the CIRM-Funded Project or Activity will be obtained before CIRM funding is spent on such activities. CIRM may request documentation of IACUC approval at any time upon request. The documentation must include the name of the PI, the name of the Awardee, the name of the organization hosting the committee, the CIRM Application number, the project title and inclusive dates for which approval has been granted. (see section D, *Just-in-Time Procedure*s).

**e.** Certification of updated IACUC approvals must be submitted with the annual Progress Report (see chapter V, section H, *Reporting Requirements*). CIRM will not authorize continued funding of active Awards without current certification of such approval.

**f.** Consequences of failure to comply with required animal subjects research assurance are described in chapter V, section J, *Failure of Compliance and Award Termination*.

**8. Biosafety**

The Awardee must ensure that any approval required by the Awardee and/or federal or state law for the proposed use of biohazardous materials, radioisotopes, and/or controlled substances is current and in effect. The applicant must also ensure all research personnel will obtain appropriate training and authorization for the use of biohazardous materials, radioisotopes, and/or controlled substances prior to their commencing work on the proposed project or activity. A prospective Awardee shall provide documentation that verifies such organizational approvals upon request. Awardees are also responsible for meeting applicable federal, state, and local health and safety standards, and for establishing and implementing necessary measures to minimize their employees' risk of injury or illness in conducting CIRM-funded research.

**9. Sharing of Intellectual Property:**

PIs and Awardees may have obligations to share the results of CIRM-funded

research, as required by regulations adopted by the ICOC. For further information, PIs and Awardees should consult Title 17, California Code of Regulations sections 100600-100612.

### 10. Preference for California Suppliers

It is a goal of Proposition 71 that more than 50 percent of the goods and services used in CIRM-supported research is purchased from California Suppliers (Health and Safety Code section 125290.30, subpart (i); Title 17, California Code of Regulations section 100502). To achieve this goal, CIRM expects the Awardee to purchase from California Suppliers, to the extent reasonably possible, the goods and services it uses in its CIRM-supported research. The PI and Awardee must provide a clear and compelling explanation in the Progress Report for not purchasing more than 50 percent of its goods and services from California Suppliers. Please see chapter V, section H, part 2, *Progress Report*.

## D. Just-in-Time Policy

Just-in-time procedures allow CIRM to defer review of certain required information until after an Application is approved for funding by the ICOC and prior to issuance of an NGA. When the required information is requested of the prospective Awardee, the information is to be submitted to CIRM. Just-in-time information includes, but is not limited to the following:

### 1. Certification

CIRM requires certification from the Awardee that the Awardee has or will obtain appropriate IRB, SCRO and/or IACUC approval or notification for CIRM-funded Activity requiring such approvals before CIRM funding is spent on such activities.

### 2. Other Support

As part of the just-in-time procedures, the PI and Awardee shall provide information on all other active and pending support. Before an NGA is issued, CIRM will review this information to ensure the following:

PIs, PDs (and other Key Personnel when requested) are not committed beyond a total effort of 100% for all active and other approved but not yet funded projects, whether or not salary support is requested in the Application.

There is no scientific or budgetary overlap. Scientific overlap occurs when substantially the same research, or a specific research aim, proposed in the approved Application is funded over any part of the Project Period by another source. Budgetary overlap occurs when funds from more than one source are used to cover the same item or the same part of a budgetary item (e.g., Equipment, salaries) and may be evident when duplicate or equivalent budgetary items are requested in an Application but are already funded by another source.

### 3. For-Profit Applicants – Certification and Verification.

The PI, CEO and CFO of a For-Profit Applicant will certify at the time of application that none of these individuals have been convicted of a felony involving fraud or the misappropriation of funds, and that no such charges are pending. In addition, these individuals will certify that none have ever been barred by any federal or state agency from applying for a grant or other funding. In the event the application is awarded funding by the ICOC, the applicant will be required to engage a third party to conduct the necessary background evaluation to verify this information.

For-Profit applicants will also undergo a financial stability assessment to assess the risk of insolvency due to, for example, bankruptcy or risk of litigation.

## E. Award Notice

Once CIRM funding requirements are fully met, an NGA or NLA will be sent to the AOO designated in the Application. The NGA or NLA specifies the Project Period (start and end dates of the project or program) as well as the monetary allocations (itemized Direct Research Funding Costs (including Facilities costs) and an amount allocated for Indirect Costs). The NGA or NLA also incorporates this Grants Administration Policy and all other applicable CIRM regulations by reference and specifies any special terms and conditions of the Award. During the active award period, the NGA or NLA may be amended in response to Prior Approval Requests, failure to meet Operational Milestones, and/or occurrence of Suspension Events.

# IV. AWARD ACCEPTANCE AND TERMS

## A. Award Acceptance

An Award is accepted when an NGA or NLA is signed by the PI and AOO, and returned to and received by CIRM. In accepting an Award, the PI and Awardee assure CIRM that any funds expended under the Award will be for the purposes set forth in the approved Application. Further, the PI and Awardee agree to comply with terms and conditions of all applicable CIRM regulations, including this Grants Administration Policy. The NGA/NLA must be signed and returned to CIRM within 45 days (or more, if extended in writing by CIRM) of issuance. Payment will not be issued until then Award is accepted. If the PI or Awardee cannot accept the Award, including the legal obligation to perform in accordance with its provisions, they shall so notify CIRM in writing immediately upon receipt of the NGA/NLA.

Urgency is one of the component values of CIRM's mission. Therefore, the prospective Awardee is required to certify that they are able to initiate work on the funded project within 45 days of ICOC approval, unless this provision is waived in writing by the President.

## B. Terms

**1.** FDA Meetings: CIRM has the right to attend key FDA meetings regarding the funded project, including but not limited to any clinical milestone meeting, or clinical hold meeting (FDA Meetings). CIRM also has the right to review any data package(s) or other information, including confidential and/or proprietary information, provided by Awardee to the FDA in connection with such FDA Meetings, as well as any FDA Meeting minutes, and to share such information with CIRM's confidential advisers. To facilitate CIRM's participation in FDA Meetings, Awardee shall notify CIRM as soon as practicable after it has scheduled an FDA Meeting, and shall, upon request, provide CIRM a copy of any data package or other information it intends to provide or has provided to the FDA, as well as any FDA Meeting minutes.

**2.** Co-Funding Requirement: Upon completion of an Operational Milestone, Awardee will demonstrate to CIRM's reasonable but sole satisfaction that the Awardee has from either its own assets, from an industry partner, or from other funding sources arranged by the applicant, expended an amount that is equal to or greater than the total co-funding requirement set forth in Appendix A for that Operational Milestone. Only funds expensed to cover Allowable Project Costs shall count toward Awardee's co-funding requirement. Provision by the Awardee of "in-kind" or similar types of support shall not be counted toward the match requirement. Also, only funds spent concurrently with CIRM funds (no sooner than Application Review Subcommittee approval and no later than the final Operational Milestone) will qualify toward the co-funding requirement.

**3.** Operational Milestone: CIRM will disburse funds based on achievement of specific Operational Milestones established by CIRM. An "Operational Milestone" is an objective event that is indicative of project progress occurring as proposed in the application. CIRM establishes Operational Milestones for inclusion in the NGA/NLA based upon information provided in the Application. Upon issuance of the award, funds budgeted to achieve the initial Operational Milestone will be disbursed. Upon the successful completion of the initial Operational Milestone and each successive milestone, additional funds will be disbursed. If funds allocated to a specific Operational Milestone (including both CIRM funds and the required applicant co-funds) are exhausted prior to achievement of that milestone, the Awardee will be responsible for covering any remaining costs. CIRM expects that the applicant's contingency plan will identify the project timeline and budget risks and will provide details for covering such costs, including the source of funding. CIRM reserves the right to make adjustments to the timeline for inclusion in the NGA/NLA to ensure that funds are appropriately dispersed across Operational Milestones.

If CIRM determines, in its sole discretion, that Awardee has not satisfied an Operational Milestone as set forth in Appendix A to the NGA/NLA, CIRM may suspend disbursements until such time as Awardee satisfies the

Operational Milestone. Upon suspending disbursements, CIRM may permanently cease disbursements if Awardee does not satisfy the Operational Milestone within four months of the date that the Operational Milestone was scheduled to have been satisfied, or if the delay is not addressed to CIRM's satisfaction, as determined by CIRM in its sole discretion.

4. The Awardee shall have 30 days from the date of occurrence of a Suspension Event to submit a plan to cure the cause of the Suspension Event. The Awardee may continue to use CIRM funds for project-related allowable costs during these 30 days but not beyond, pending CIRM agreement that the Suspension Event has been cured. If CIRM determines, in its sole discretion, that the Suspension Event cannot be cured, or will not be cured by the Awardee's proposed plan, CIRM may, in its sole discretion, terminate the Award.

## V. PAYMENT AND USE OF FUNDS

### A. Payment

The schedule of payments will be based on Operational Milestones established by CIRM prior to issuance of an NGA/NLA. Once CIRM has a fully-executed NGA/NLA, it may initiate payment for activities leading up to the first Operational Milestone. Payments for each subsequent Operational Milestone are contingent on the receipt and acceptance by CIRM of documentation demonstrating achievement of the prior Operational Milestone as well as submission of the financial and progress reports due. Costs resulting from the delay or failure to meet an Operational Milestone will be the sole responsibility of the Awardee to be covered by the Awardee's financial contingency plan.

The timing of the distribution of funds pursuant to this Grant shall be contingent upon the availability of funds in the California Stem Cell Research and Cures Fund in the State Treasury, as determined by CIRM in its sole discretion.

### B. Costs and Activities

During the Project Period, CIRM funds shall only be used for allowable project costs and activities. Specific allowable or unallowable costs may be described in the PA or the NGA/NLA. In accordance with Proposition 71, Direct Research Funding Costs include scientific and medical funding for an approved research project and the general operating costs of Facilities for conducting the approved project.

#### 3. Pre-Award Costs

An Awardee may, at its own risk and without Prior Approval, incur obligations and expenditures to cover costs between the Application Review Subcommittee approval date and the award start date up to a maximum of 45 days, if such costs are necessary to conduct the project and are allowable CIRM costs and activities. If specific expenditures or activities would

otherwise require Prior Approval, the Awardee must obtain CIRM approval before incurring the cost. An Awardee's decision to incur pre-award costs in anticipation of an Award imposes no obligation on CIRM either to make the Award or to increase the amount of the Approved Budget if an Award is made for less than the amount anticipated and is inadequate to cover pre-award costs incurred. Awardees are on notice that a decision to incur pre-award costs is a decision to borrow against future support and that such borrowing must not impair the Awardee's ability to accomplish the project objectives or in any way adversely affect the conduct of the CIRM-funded Project.

**4. Allowable Project Costs and Activities**

Project costs are those costs that can be specifically identified with a CIRM-Funded Project or Activity. Unless otherwise specified in a PA or NGA, allowable project costs can include but are not limited to salary for personnel (detailed below), fringe benefits, itemized supplies, Tuition and Fees, research animal costs, Consultants, itemized clinical study costs (including Research Patient Care Costs), travel-related expenses (detailed below), itemized project-related Equipment (as approved), publication costs, service contracts, Subcontracts, and specific, identifiable administrative costs where required to carry out the approved project. When not otherwise specified by CIRM regulations, CIRM applies the Office of Management and Budget cost allocation principles of reasonableness, allocability, consistency, and allowability in determining whether costs under specific scenarios are allowable as a direct charge to a CIRM research grant.

Salaries for all personnel shall not exceed an annual rate of $230,000. CIRM will adjust this limitation biennially beginning July 1, 2014 as follows: (a) the base dollar amount of $230,000 shall be increased or decreased by the cumulative percentage change in the annual average California Consumer Price Index for All Urban Consumers from 2010 to the end of the calendar year immediately preceding the year in which the adjustment will take effect and (b) the dollar amount obtained by Application of the calculation set forth in subdivision (a) shall be rounded to the nearest $1,000. The resulting figure shall be the adjusted maximum annual salary in effect until June 30 of the next even-numbered year. Biennial adjustments will be posted at www.cirm.ca.gov.

Allowable travel-related expenses for both domestic and international travel include costs for transportation, lodging, subsistence, and related items incurred by all personnel on project-related business. Reimbursement for transportation expenses shall be based on the most economical mode of transportation (e.g., coach fare) and the most commonly traveled route consistent with the authorized purpose of the trip. Reimbursed lodging and subsistence expenses must be ordinary and necessary to accomplish the official business purpose of the trip.

## 5. Unallowable Project Costs and Activities

Unallowable project costs and activities cannot be charged to CIRM funding nor accounted for as part of the Awardee's co-funding requirement and include but are not limited to visa expenses for foreign nationals, malpractice insurance, membership dues, furniture, telephone equipment, personnel recruitment, receptions, and cost of food or meals unrelated to allowable travel expenses, and construction or renovation of physical infrastructure.

## 6. Allowable Facilities Costs

Facilities costs cover general operating costs of the Awardee's facilities attributable to housing all elements of the CIRM-Funded Project or Activity. Non-profit Awardees may request two categories of facilities costs: (a) costs based on the Awardee's current, federally negotiated rates for Operation and Maintenance Expenses, and for Library Expenses; and (b)(1) costs based on the Awardee's current, federally negotiated rates for depreciation or use allowances on buildings, capital improvements, and Equipment, and for interest on capital debt, as a proxy for a market lease rate of reimbursement (Health and Safety Code section 125292.10, subdivision (u)); or (b)(2) the actual out-of-pocket lease cost incurred by a Awardee if the Awardee leases space to conduct approved research; this cost must be reported in the Annual Financial Report (see chapter V, section H, part 1, *Annual Financial Report*). Non-profit Awardees may request both categories (a) and (b) as allowable facilities costs. Facilities costs for for-profit Awardees are limited to 35% of direct project costs. Total facilities rates shall be applied to the total allowable project costs exclusive of costs of Equipment, Tuition and Fees, Research Patient Care Costs, and the total cost of each service contract, Subcontract and Consultant agreement in excess of $25,000.

## 7. Unallowable Facilities Costs (Major Facilities)

Beginning on the date of occupancy projected in the NGA for a CIRM Major Facilities Grant (i.e., a facility Grant subject to 17 Cal. Code Regs. § 100701), on a going-forward basis, CIRM will not fund the facilities costs for category (b) ("Facilities Part B") noted above for any currently active or subsequently funded CIRM research Grant located in a CIRM Major Facility.

CIRM will calculate on an annual basis the cumulative amount of the Facilities Part B reductions for all research grants to an institution or members of a consortium or facilities collaboration. Once this cumulative reduction equals the amount funded under the CIRM Major Facilities Grant (adjusted for the annual cost of funds) to an institution, consortium or facilities collaboration, Facilities Part B funding will be restored to all CIRM funded research grants to those institutions.

### 8. Indirect Costs

The specific indirect cost percentage allowable for a PA or RFA will be stipulated in the PA or RFA but are generally limited to a maximum of 20 percent of allowable Direct Research Funding Costs for non-profit Awardees and 10 percent of allowable Direct Research Funding Costs for for-profit Awardees, exclusive of the costs of Equipment, Tuition and Fees, Research Patient Care Costs, and the total cost of each service contract, Subcontract and Consultant agreement in excess of $25,000.

### 9. Post-Project Allowable Costs

If the Awardee has remaining CIRM funds following the completion of the CIRM-Funded Project or Activity, those funds may be used to either (1) reduce co-funding to an amount no lower than originally required by the Award, or (2) for projects at the Awardee organization that further CIRM's mission, subject to CIRM regulations and audit. The Awardee will be required to obtain CIRM's Prior Approval of its intentions for use of the funds and certification that those funds will be appropriately accounted for.

## C. Budgetary Overlap

CIRM funds cannot be combined with the operating budgets of the Awardees and may not be used for any fiscal year-end expenditures or deficits not directly related to the Award. Budgetary overlap, defined as using funds from more than one source to cover the same item or the same part of a budgetary item (e.g., salary, Equipment), is prohibited.

## D. Prior Approval Requirements

PIs and Awardees must perform project activities as described in the approved Application. A PI and Awardee must request and obtain prior written approval for pre- award or post-award changes described below by submitting such requests in writing together with appropriate justification for the proposed change. Such approval will be granted in the form of an amendment to the NGA/NLA and must be obtained before expending CIRM funds for the proposed activity. The following changes require CIRM Prior Approval:

### 1. Change in Research Plan:

The PI and Awardee must obtain Prior Approval in writing via an amendment to the NGA/NLA for any change that constitutes a significant deviation from the aims, objectives, experimental design, or purposes of the approved Application (hereafter "change in scope"). Any savings due to the elimination of activities will result in a reduction to the Award unless CIRM approves use of those funds for the additional activities. When considering such a change, the PI should consult with CIRM. Examples of actions likely to be considered a change in scope requiring Prior Approval include but are not limited to:

**a.** A change in a clinical trial that requires a Protocol Amendment;
**b.** A change in patient enrollment criteria in a clinical trial;
**c.** A change in a manufacturing process or release specifications;
**d.** Removal or addition of substantive activities described in the Application;
**e.** Any change that impacts activities described in Milestones or Suspension Events.

## 2. Relinquishment of Award and Award Transfer

An Awardee may at any time relinquish an Award or Application approved for funding by the ICOC by submitting a relinquishing statement that includes a) a statement of reasons for relinquishing the award; b) an estimate of the unexpected balance of any funds paid to the Awardee; c) and an assurance that all unexpended balance of any funds will be returned to CIRM within 90 days of the date of relinquishment. In the case of a transfer, the relinquishing Awardee may be required to transfer CIRM-funded equipment purchased with the Award.

With Prior Approval, an Award may be transferred to another eligible organization when a PI transfers from an Awardee to that organization. CIRM approval will be contingent upon the Awardee relinquishing rights to the Award among other considerations.

The transferee Awardee must submit to CIRM a letter that states its intention to assume responsibility for the Award based on the approved Application, and that encloses the following items:

**a.** A new Application with original signatures;
**b.** Description of how the PI will ensure the project will be able to accomplish its goals, potential length of delays in project progress due to the transition and mitigation plans to minimize project delays.
**c.** Detailed budget(s) for the remaining Project Period (including the estimated unexpended balance from the relinquishing Awardee). The originally approved budget prevails when an award is transferred. CIRM does not have authority to increase the award amount without approval by the Application Review Subcommittee;
**d.** Biographical sketches for new Key Personnel;
**e.** Description of facilities and resources; and
**f.** Certification to public policy assurances (e.g., Human Subjects, animal, biohazard), where applicable.

If the President determines that the proposed transferee Awardee is eligible and can fulfill the responsibilities of the relinquishing Awardee, CIRM will approve the transfer by cancelling the original NGA/NLA and issuing a new NGA/NLA to the transferee Awardee. Transfer of the Award will be effective when CIRM receives the new NGA/NLA executed by the PI and the AOO of the transferee Awardee. Payment will not be issued until the Award transfer is

effective.

### 3. Change in PI Status or Percent Effort

Prior Approval is required for the PI to decrease his/her percent effort on the approved project below the level required by the RFA or PA.

In addition, Awardees must notify CIRM immediately if any of the following changes in PI status occur:

**a.** The PI's status at the Awardee organization changes (e.g., from full-time to part-time appointment, from paid to an unpaid position or from employee to a non-employee position).
**b.** The PI withdraws from the project, takes a leave of absence, or is expected not to be involved in the day-to-day conduct of the approved project for a continuous period exceeding 90 days. This includes requests for sabbaticals.
**c.** The PI is no longer eligible (under either the standards of the
**d.** Awardee or the criteria in the RFA/PA) to serve as a PI.

If CIRM determines that a PI's change in status will adversely impact the conduct of the CIRM-funded Project as described in the approved Application, CIRM will so notify the Awardee. The Awardee may respond to such notification by seeking approval to substitute an eligible PI that is satisfactory to CIRM. CIRM may terminate the Award if no request is made or if the proposed substitute PI is not satisfactory. The Awardee shall return to CIRM all unexpended funds within 120 days of termination of the Award.

### 4. Submitting Prior Approval Requests

Prior Approval requests must be submitted in writing to CIRM and must be signed by the PI and the AOO. All such requests shall identify the proposed action requiring CIRM Prior Approval and include a justification. Approval by CIRM shall not be effective unless in writing and signed by the President of CIRM, or his/her delegee.

## E. Equipment Management

The Awardee must have a property management system for Equipment that includes the following:

**1.** Records that adequately identify items of Equipment purchased with CIRM funds;
**2.** Control procedures and safeguards to prevent loss, damage, and theft;
**3.** Adequate maintenance procedures to keep the Equipment in good condition; and
**4.** Proper procedures to dispose of, sell, or transfer Equipment purchased with CIRM funds when authorized by CIRM.

## F. Accounting Records, Documentation, Access to Records and Audits

### 1. Accounting Records

The Awardee shall maintain an accounting system and supporting fiscal records to assure that CIRM funds awarded are used solely for the purpose outlined in the approved Application and for allowable costs and activities.

### 2. Document Retention

The Awardee shall retain accounting records and supporting documentation for five years from the date of submission of the final expenditure report for the entire Project Period. All records must be maintained in excess of this minimum time period if audit findings have not been resolved.

### 3. Access to Records

The Awardee shall allow CIRM, the Bureau of State Audits access to its accounting records and supporting documentation the California State Controller, or any other appropriate state agency with reasonable notice.

### 4. Audits

Accounting records and supporting documentation may be audited at the direction of appropriate state agencies, including the Bureau of State Audits, the State Controller's Office and CIRM. In addition, CIRM may require an Awardee to commission an independent audit of Award accounting records at the Awardee's expense as a condition of further funding eligibility.

## G. Misuse of Funds

Misuse of funds means fraud or abuse of public funds. Fraud means an intentional deception or misrepresentation made by a person who knows or should have known that the deception could result in some unauthorized benefit to that person or some other person. It includes any act that constitutes fraud under applicable state or federal statutes. Abuse means any Awardee practice that is inconsistent with sound fiscal, business or research practices or that results in an unnecessary cost to CIRM.

Awardees shall report to CIRM cases of real or apparent fraud, or abuse of CIRM funding immediately upon knowledge thereof. Examples of fraud, and abuse that must be reported include, but are not limited to: embezzlement of CIRM funds, misuse or misappropriation of CIRM funds or property; and false statements regarding the use of CIRM funds, whether by organizations or individuals. This includes personal use of CIRM funds; using funds for non-approved purposes; theft of CIRM-funded property or property acquired or leased with CIRM funds; charging CIRM for services of "ghost" individuals; submitting false financial reports; and submitting false financial data in bids submitted to the Awardee (for eventual payment by CIRM).

Fraud, or abuse can result in any of the administrative and other actions described in section J, *Failure of Compliance and Award Termination*. In addition, any PI, Awardee or Recipient of CIRM funds suspected of misuse of funds may be referred for investigation to state and/or local law enforcement authorities.

## H. Reporting Requirements

Awardees must report financial and scientific progress to CIRM quarterly and upon achievement of an Operational Milestone.

The requested information is required for effective grant management by CIRM and for meeting specific reporting requirements of the California State Legislature. CIRM also is responsible for disseminating the outcomes of funded research to interested constituencies, as well as to the general public.

### 1. Financial Report

The Awardee shall submit to the GMO a financial report within 15 days after each quarter of the Award and within 60 days after each Operational Milestone as stated in the NGA, unless CIRM requires more frequent reports. The financial report must include all cumulative actual costs incurred against CIRM funds and any co-funding. If CIRM requires co-funding, the minimum percentage of co-funding is required to be maintained at each Operational Milestone, hence if upon completion of an Operational Milestone the co-funding is any less than the required minimum in proportion to the CIRM funds disbursed for that Operational Milestone, CIRM will reduce the next payment by the amount the co-funding was short the requirement. CIRM will also check to ensure the Awardee has access to the co-funding necessary to get to each subsequent Operational Milestone. The failure to provide evidence of access to the co-funding required for each subsequent Operational Milestone will result in a Suspension Event.

### 2. Progress Report

The Awardee shall submit to CIRM a quarterly Progress Report detailing scientific progress, outcomes and activities during the previous quarter and an Operational Milestone Progress Report upon achievement of an Operational Milestone.

Quarterly Progress Reports shall include a summary of scientific and operational progress; a cumulative subject accrual and progress in conducting analyses for sex/gender and race/ethnicity differences in clinical trials. Operational Milestone Progress Reports shall include the same items as quarterly Progress Reports as well as a public summary of progress; an updated budget, budget narrative and Gantt chart; award outcomes; updated list of personnel who participated in the project; an updated list of Other Support for the PI; and a statement of the percentage of goods and services purchased with

CIRM funds from California suppliers; and certification of applicable public policy assurances (e.g., ESCRO, IRB, IACUC). An Operational Milestone Progress Report may substitute for a quarterly Progress Report when submitted within 45 days of the next quarterly Progress Report due date.

**3. Suspension Events (Report)**

The Awardee shall promptly inform CIRM in writing of the occurrence of any Suspension Event, as detailed in the NGA.

**4. Other Reports**

PIs and Awardees are also required to report to CIRM publications, inventions, patent applications, licensing and invention utilization activities that result from CIRM-funded research. Specific reporting requirements related to these areas may be found in regulations adopted by the ICOC governing intellectual property.

**5. Overdue Reports**

Failure to submit complete financial, progress, or other required reports in a timely fashion may result in reduction, delay or suspension of payments. Further, if a report is delinquent for more than 30 days, CIRM may take action as described in section *J, Failure of Compliance and Award Termination.*

## I. Grant Close-Out

CIRM will close out an Award after conclusion of the authorized Project Period end date after the PI and Awardee have submitted all required reports, and reconciliation of amounts due the Awardee or CIRM. CIRM may withhold funds for future or concurrent Awards if an Awardee is delinquent in submitting reports.

Close-out of an Award does not extinguish requirements for property accountability, record retention, financial accountability, or requirements associated with regulation of medical and ethical standards or intellectual property. Following close- out, CIRM may recover amounts based on the results of an audit covering any part of the funding period.

## J. Failure Compliance and Award Termination

CIRM, in its sole discretion, may take one or more of the actions specified below if: (1) the Awardee or PI violates one or more terms and conditions of the Award, including this policy and any applicable CIRM regulations; (2) the Awardee or PI engages in research misconduct; or (3) the occurrence of a Suspension Event which CIRM determines, in its sole discretion, cannot be cured.

CIRM will afford the Awardee an opportunity to correct any deficiency before taking action unless public health or welfare concerns require immediate action or prompt action is necessary to protect CIRM's interests. (See also chapter III,

section C, part 1, *Research Conduct.*)

Depending on the nature of the deficiency, CIRM actions may include, but are not limited to the following:

**1.** Temporary withholding of payment;
**2.** Placing special conditions on Awards;
**3.** Conversion to a reimbursement payment method;
**4.** Termination of the Award
**5.** Disqualifying the Awardee (or PI as appropriate) from eligibility for future Awards for a specified period;
**6.** Disqualifying the Awardee (or PI as appropriate) from receipt of further CIRM funds;
**7.** Recovery of previously awarded funds;
**8.** Civil action and/or referral to the Office of the Attorney General of California for criminal investigation and enforcement;
**9.** Other available legal remedies.