CIRM Interim Grants Administration Policy for Clinical Stage Projects

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Preface

This grants administration policy, serves as the terms and conditions of research grants and loans awarded by the California Institute for Regenerative Medicine (CIRM) under CIRM's Clinical Stage Projects, comprising the following Program Announcements: PA 15-01, PA 15-02, or PA 15-03. In addition, it provides guidance to applicants, Grantees and Loan Recipients on their responsibilities as CIRM grantees. 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, Grantees and Loan Recipients may be required to document compliance with any and all provisions set forth in this policy.

This policy applies to all CIRM applicants, Grantees and Loan Recipients who receive CIRM funding through a PA 15-01, PA 15-02, or PA 15-03 Award to any Non-Profit or For-Profit organization. By accepting CIRM funding, the Grantee and Loan Recipients 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, or 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

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

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 funded project or activity, including revisions approved by CIRM and permissible revisions made by the PI or Grantee.
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.
Grantee	An Organization that is the Recipient of an Award and that is legally responsible and accountable for the use of the funds provided and for the performance of the CIRM funded Project or Activity. The Grantee is the entire legal entity even if a particular component is designated in the NGA. Campuses of the University of California shall be considered as separate and individual Grantees.
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.

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 a Grantee'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 Grantee for financial management purposes or $5,000.
Financial Report	A Grantee's periodic report to CIRM detailing expenditures against CIRM funds as specified in the NGA (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, other than a loan, providing money and/or property to an eligible entity to assist the Recipient in carrying out an approved project or activity.
Grant 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 Grantee. CIRM also reconciles and makes any final fiscal adjustments to the Grantee's Award.
Grantee	An Organization that is the Recipient of an Award and that is legally responsible and accountable for the use of the funds provided and for the performance of the CIRM funded Project or Activity. The Grantee is the entire legal entity even if a particular component is designated in the NGA. Campuses of the University of California shall be considered as separate and individual Grantees.
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 a Grantee incurred for common or joint objectives, which cannot be readily and specifically identified with a 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).
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 Grantee and others that an Award has been made, contains or references all terms and conditions of the Award as well as the Grantee'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 a Grantee'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. The 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 Grantee to direct the CIRM-Funded Project or Activity. He or she is responsible and accountable to the Grantee 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	A Grantee's periodic report to CIRM detailing scientific activities and findings in the research project identified in the NGA (see chapter V, section H, part 2).
Project	The total amount of time as stated in an NGA for which CIRM intends

Period	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 Grantee, 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 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 Grantee 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 Grantee 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. Grantee Organization Staff:

a. Authorized Organizational Official (AOO)

The AOO is the designated representative of the Grantee 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 Grantee 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 Grantee to indemnify CIRM as provided in Chapter III, Section B, Liability, and a Grantee's designation of an AOO confers apparent authority to commit the Grantee to such indemnification of CIRM.

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

The PI is the individual, designated by the Grantee, responsible for the scientific or technical aspects of the CIRM-Funded Project or Activity and for its management. The PI and the Grantee are both responsible for ensuring compliance with the financial and administrative aspects of the Award. The PI must work closely with other Grantee 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 grantees 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. The CAPs will report to the Grants Working Group and CIRM on a regular basis regarding the projects' progress CAPs will consider project progress, provide advice and expertise to the project team, and support the team on matters related to the project. The CAP will consider relevant information on the project's progress, such as the project team's quarterly progress report, key data supporting project progress, corrective actions, as needed, plans for the next reporting period and any additional matters relating to the success of the program. Project teams will be required to submit all requested documents to CIRM in advance of the CAP meeting. CAP members may request additional information from the project team as necessary before or during the meeting.

II. GRANT APPLICATION AND REVIEW PROCESS

A. Eligibility

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.

1. 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.

2.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.

A. 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 Candidate Nomination Form (Version 4/2009) (CNF) or Letter of Intent (LOI) 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 your proposal.

B. 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).

C. 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.

D. 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 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 highly meritorious Applications that are recommended for funding to the Application Review Subcommittee of the ICOC.
2. ***Provisionally Recommended for Funding*** (Tier 2)– For meritorious Applications that may require further consideration by the Application Review Subcommittee of the ICOC. 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 not recommended for funding at this time.

E. 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 particular to a given PA or RFA, which general may include the following criteria: 1) Project significance and impact; 2) Rationale; 3) Project design; 4) Feasibility.

F. 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 has 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 has 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.

G. 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.

H. 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.

I. 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. CIRM may, however approve an Application for funding contingent upon the acceptance (by the PI and AOO) of a condition.
An approved grantee 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 Grantee and subject to its organizational policies. Further, Grantee organization personnel compensated in whole or in part with CIRM funds are not considered employees of CIRM.

Grantees 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 Grantee pursuant to the award, and/or, in the alternative, Grantees 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 Grantee chooses only to insure, such insurance must provide coverage in amounts appropriate and proportional to cover the risks described in the previous sentence. Grantees 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 Grantee 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 Grantee 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. In cases where research requiring public policy assurances will be conducted at a later phase of the funded research, CIRM may issue an NGA imposing a condition or restriction on the use of funds until documentation of required assurances is submitted.

The Grantee 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. Grantees and Recipients must conduct all research in accordance with the highest medical and ethical standards for scientific research and all applicable laws. The Grantee bears the ultimate responsibility for preventing, detecting and imposing sanctions for research misconduct. Grantees 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, Grantees 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 Grantee or Recipient from eligibility for CIRM funds; 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

Grantees 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.

Grantees must enforce within their institutions all such applicable safeguards. If the Grantee uses contractors or collaborators to conduct CIRM-funded research, the Grantee must take reasonable steps to ensure that such contractors or collaborators comply with the Grantee'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 Grantee 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 Grantee 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 Grantee itself, any other institution, or any law enforcement agency concerning a charge of research misconduct made against a Recipient of CIRM-funding concerning the Recipient's research activities.

4. Use of Human Stem Cell Lines

Grantees 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 Grantee, 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 Grantees 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. PIs and Grantees 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. In addition, the Grantee 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. Grantee 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.

d. The Grantee bears ultimate responsibility for protecting Human Subjects involved in CIRM-funded research, including Human Subjects at all participating and collaborating sites. At CIRM's request, the prospective Grantee 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 Grantee 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, a prospective Grantee shall certify to CIRM that any IRB approval required to conduct the CIRM-Funded Project or Activity will be obtained before CIRM funding is spent on such activities. (see section D, *Just-in-Time Procedures*).

e. Certification or evidence of updated IRB approvals and related documents may be requested with the annual Progress Report (see chapter V, section H, *Reporting Requirements*). CIRM will not authorize continued funding of active Awards without current certification for Human Subjects research.

f. 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 Grantee are notified.

g. 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 Grantee concerning Recipients of CIRM funding and their use of Human Subjects in research.

h. 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, Grantee 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, Grantee 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 Grantee must appoint and maintain an Institutional Animal Care and Use Committee (IACUC) to provide oversight of research involving vertebrate animals.

d. The prospective Grantee 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, a prospective Grantee 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 Grantee, 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 Grantee must ensure that any approval required by the Grantee 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 Grantee shall provide documentation that verifies such organizational approvals upon request. Grantees 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 Grantees may have obligations to share the results of CIRM-funded research, as required by regulations adopted by the ICOC. For further information, PIs and Grantees 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 Grantee to purchase from California Suppliers, to the extent reasonably possible, the goods and services it uses in its CIRM-supported research. The PI and Grantee 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 Grantee, 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 Grantee that the Grantee 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 Grantee shall provide information on all other active and pending support. Before an NGA is issued, CIRM will review this information to ensure the following:

a. 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.

b. 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 ther 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 will be sent to the AOO designated in the Application. The NGA 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 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 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 is signed by the PI and AOO, and returned to and received by CIRM. In accepting an Award, the PI and Grantee assure CIRM that any funds expended under the Award will be for the purposes set forth in the approved Application. Further, the PI and Grantee agree to comply with terms and conditions of all applicable CIRM regulations, including this Grants Administration Policy. The NGA 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 Grantee 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.

Urgency is one of the component values of CIRM's mission. Therefore, the prospective Grantee is required to certify that they are able to initiate the award 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 Grantee 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, Grantee 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, Grantee will demonstrate to CIRM's reasonable but sole satisfaction that the Grantee 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 Grantee's co-funding requirement. Provision by the Grantee 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 ICOC approval and no later than the final Operational Milestone) will qualify toward the co-funding requirement.

3. Operational Milestone: CIRM funds under an award will be disbursed 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 Grant or Loan Agreement 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 Grantee 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 Grant or Loan Agreement to ensure that funds are appropriately dispersed across Operational Milestones.

If CIRM determines, in its sole discretion, that Grantee has not satisfied an Operational Milestone as set forth in Appendix A to this NGA, CIRM may suspend disbursements until such time as Grantee satisfies the Operational Milestone. Upon suspending disbursements, CIRM may permanently cease disbursements if Grantee 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 Grantee shall have 30 days from the date of occurrence to submit a plan to cure the cause of the Suspension Event. The Grantee 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 Grantee's proposed plan, the Award may be terminated.

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. Once CIRM has a fully-executed NGA, 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. 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.

1.Pre-Award Costs

A Grantee may, at its own risk and without Prior Approval, incur obligations and expenditures to cover costs between the ICOC 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 Grantee must obtain CIRM approval before incurring the cost. A Grantee'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. Grantees 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 Grantee's ability to accomplish the project objectives or in any way adversely affect the conduct of the CIRM-funded Project.

2. 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.

3. Unallowable Project Costs and Activities

Unallowable project costs and activities cannot be charged to CIRM funding nor accounted for as part of the Grantee'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.

4. Allowable Facilities Costs

Facilities costs cover general operating costs of the Grantee's facilities attributable to housing all elements of the CIRM-Funded Project or Activity. Grantees may request two categories of facilities costs: (a) costs based on the Grantee's current, federally negotiated rates for Operation and Maintenance Expenses, and for Library Expenses; and (b)(1) costs based on the Grantee'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 Grantee if the Grantee 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*). Grantees may request both categories (a) and (b) as allowable facilities costs. Rates from both categories 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 .

5.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.

6.Indirect Costs

The specific percentage allowable for a PA or RFA will be stipulated in the PA or RFA. Per Proposition 71, Indirect Costs are limited to a maximum of 25 percent of allowable Direct Research Funding Costs, 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.

7.Post-Project Allowable Costs

If the Grantee has remaining CIRM funds, those funds may be used to either (1) reduce co-funding no lower than originally required by the Award, or (2) for projects at the Grantee organization that further CIRM's mission, subject to CIRM regulations and audit. The Grantee 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 Grantees 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 not permitted.

D. Prior Approval Requirements

PIs and Grantees must perform project activities as described in the approved Application. A PI and Grantee 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 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 Grantee must obtain Prior Approval in writing via an amendment to the NGA 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 deletion 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

A Grantee 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 Grantee; 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 Grantee 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 a Grantee to that organization. CIRM approval will be contingent upon the Grantee relinquishing rights to the Award among other considerations.

The transferee Grantee 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 Grantee). The originally approved budget prevails when an award is transferred. CIRM does not have authority to increase the award amount without ICOC approval;

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 Grantee is eligible and can fulfill the responsibilities of the relinquishing Grantee, CIRM will approve the transfer by cancelling the original NGA and issuing a new NGA to the transferee Grantee. Transfer of the Award will be effective when CIRM receives the new NGA executed by the PI and the AOO of the transferee Grantee. 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.

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

a. The PI's status at the Grantee 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. Grantee or the criteria in the RFA) 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 Grantee. The Grantee 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 Grantee 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 Grantee 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 Grantee 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 Grantee 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 Grantee 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 a Grantee to commission an independent audit of Award accounting records at the Grantee'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 Grantee practice that is inconsistent with sound fiscal,

business or research practices or that results in an unnecessary cost to CIRM.

Grantees 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 Grantee (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, Grantee 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

Grantees 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 Grantee 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 Grantee 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 a 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; 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 Grantee shall promptly inform CIRM in writing of the occurrence of any Suspension Event, as detailed in the NGA.

4.Other Reports

PIs and Grantees 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 Grantee have submitted all required reports, and reconciliation of amounts due the Grantee or CIRM. CIRM may withhold funds for future or concurrent Awards if a Grantee is delinquent in submitting reports.

Close-out of an Award does not extinguish requirements for property accountability, record retention, or financial accountability, or requirements associated with regulation of medical and ethical standards of 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 Grantee or PI violates one or more terms and conditions of the Award, including this policy and any applicable CIRM regulations; (2) the Grantee 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 Grantee 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 Grantee (or PI as appropriate) from eligibility for future
6. Awards for a specified period; Disqualifying the Grantee (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.