CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

RFA 08-07: CIRM Basic Biology Awards I

I. Purpose

Investigations of the basic mechanisms underlying stem cell biology, cellular plasticity, and cellular differentiation form the foundation for future translational and clinical advances. Despite considerable recent progress, many fundamental issues related to the control of stem cell fate and cellular reprogramming, especially with regard to human cells, remain to be resolved. The purpose of the CIRM Basic Biology Initiative is to support basic research that enables the realization of the full potential of human stem cells and reprogrammed cells for therapies and as tools for biomedical innovation.

II. Objectives

The objective of the CIRM Basic Biology Awards I is to provide funding for cutting-edge stem cell research and to support studies tackling significant, unresolved issues pertinent to understanding the biology of human embryonic stem cells and the control of stem cell fate. Recently, cellular reprogramming has generated great excitement in the stem cell community, and CIRM intends to support research into understanding the basic molecular mechanisms that drive cell fate changes. Furthermore, CIRM sees a strong need to support efforts in elucidating the basic molecular and cellular mechanisms underlying self-renewal of human pluripotent stem cells and the control of their differentiation into functionally mature cell types. With CIRM's overall mission in mind, funding under this initiative will be limited to studies utilizing human cells, except for groundbreaking reprogramming studies, where necessary use of other mammalian systems may be considered.

Specifically, CIRM is seeking proposals in the following areas:

- Mechanisms of cellular reprogramming
  - -Molecular basis for induction of multipotency or pluripotency
  - -Molecular regulation of induced de-differentiation or trans-differentiation
  - -Cellular senescence patterns during reprogramming

- Relationships between reprogramming or self-renewal and oncogenic potential of cultured and transplanted human cells
- Mechanisms that lead to the generation of human cancer stem cells
- Genetic, epigenetic and genomic instability of human pluripotent stem cells (hPSC) in long-term cultures, and the effects of such instability on hPSC differentiation and tumorigenicity
- Contributions of epigenetic memory to cellular plasticity
- Role of the endogenous microenvironment in stem cell fate regulation
- Molecular mechanisms that enable engineered microenvironments to control stem cell fate
- Identification, isolation and characterization of specific precursor populations at intermediate stages of human stem cell differentiation
- Characterization of molecular determinants of stem cell fate decisions during hPSC differentiation
- Differentiation of hPSCs into fully mature, metabolically functional cell types, tissues and mini-organs
- Molecular basis of hPSC self-renewal
- Human stem cell aging

III. Award Information

CIRM is introducing its Basic Biology Initiative in 2009 with two calls for applications. Under this RFA, CIRM Basic Biology Awards I, CIRM intends to commit up to $30 million to support up to 20 awards. Projects will be funded for up to three years, with justifiable direct project costs of up to $300,000 per year.

CIRM Basic Biology Awards II (anticipated release in August 2009) will contain the same scientific content as Basic Biology Award I, and CIRM intends to commit up to an additional $30 million to support up to 20 additional awards. The Initiative was split into two dates to facilitate ease of review. CIRM plans to offer Basic Biology Awards RFAs on a recurring basis. The Basic Biology Awards III RFA is expected to be offered in 2010.

Unlike most previous RFAs released by CIRM, CIRM will not limit the number of submissions from each institution. Instead, CIRM is introducing a new process in which any qualified PI may submit a brief Preliminary Application (Pre-Application, PreApp) for consideration. Applicants submitting the most promising, competitive and responsive proposals will be invited to submit a detailed, full Application. Details of this application procedure are provided in section V below.

IV. Eligibility

A. Institutional Eligibility

All CIRM-supported research must be conducted in California. PIs may apply from non-profit and for-profit research organizations that are, at the time the PreApp is submitted, conducting research at a site in California.

"Non-profit organization" means: (1) a governmental entity of the state of California; or (2) a legal entity that is tax exempt under Internal Revenue Code section 501(c)(3) and California Revenue and Taxation Code section 23701d.

"For-profit organization" means: 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".

B. Principal Investigator (PI) Eligibility

The PI must have an M.D., Ph.D. or equivalent degree, and must be authorized by the applicant institution to conduct the proposed research in California. By the Pre-Application deadline, the PI must:

- be an independent investigator at a non-profit applicant institution, or have an equivalent position and be an employee of a for-profit applicant institution
- have documented authority from the applicant institution to staff the proposed project
- have documented commitment from the applicant institution to provide laboratory space and shared resources sufficient to carry out the proposed research.

In addition, CIRM, mindful of the urgency of its mission, will only fund PIs who are willing to commit a minimum of 20% effort to the proposed project. During review of the full Application, CIRM will instruct reviewers to give added consideration to the PI's qualifications when the PI commits more than 20% effort to the proposed research.

In extraordinary circumstances, and at the discretion of the President of CIRM, senior research scientists may be permitted to apply as PIs with a commitment of less than 20% effort, if they can demonstrate that doing so will promote the best outcome for the research project. Such exceptions **must** be requested prior to April 9, 2009 (see contact information below) to allow the President of CIRM adequate time to review and to approve or deny the request prior to April 30, 2009, the deadline for submission of a full Application.

In order to broaden the pool of applicants engaged in basic stem cell research, a PI may submit a Pre-Application for either this RFA (RFA 08-07) or the forthcoming Basic Biology Awards II RFA (RFA 09-02), BUT NOT FOR BOTH. It is important to note that the Basic Biology Awards will be re-issued in 2010. Applicants whose proposals are deferred and who are not

invited to submit a full application in 2009 have the opportunity to reapply in the 2010 cycle of the Basic Biology Awards. Additionally, recipients of a CIRM Comprehensive Research Grant (RFA 06-02) or CIRM New Faculty Award (RFA 07-02 and RFA 08-01) are not eligible to participate in either Basic Biology Awards I or Basic Biology Awards II RFAs.

CIRM has recently introduced its Collaborative Funding Program, through which CIRM has partnered with several agencies that fund stem cell research. Through this program, California-based PIs can collaborate with researchers eligible for funding by one of CIRM's partners. If a collaborative funding proposal is approved, CIRM will fund the part of the project that takes place in California, and the funding partner will fund the remainder of the project. Due to time constraints, collaborative funding will not be available as part of the Basic Biology Awards I RFA. Collaborative funding opportunities may be available for the forthcoming Basic Biology Awards II RFA.

V. Application and Evaluation Process

Submission of an application for the CIRM Basic Biology Awards I RFA involves a two-step process. Any qualified applicant may submit a brief Preliminary Application (PreApp). Applicants submitting the most promising, competitive and responsive proposals will be invited to submit a detailed, full Application. All other applicants will be deferred; they may revise their proposals or submit a new proposal for consideration as part of the Basic Biology Awards III RFA.

Applicants may submit PreApps for this RFA or for Basic Biology Awards II, but not both. Applicants who submit a PreApp for the Basic Biology Awards I RFA will not be eligible to submit a PreApp for the Basic Biology Awards II RFA. It is important to note that the Basic Biology Awards RFA will be re-issued in 2010. Applicants whose proposals are deferred and who are not invited to submit a full application in 2009 have the opportunity to reapply in the 2010 cycle of the Basic Biology Awards.

PreApps should emphasize the significance of the proposed work and explain how the proposed research will lead to important advances in stem cell biology or regenerative medicine. PreApps will be evaluated by scientific specialists from outside California who are experts in specific areas of research described in the PreApp and by CIRM scientific staff, based on the scientific review criteria described in section VI below. Applicants whose projects are judged as most promising, competitive, and responsive to the RFA will be invited to submit a full Application. The research project proposed in the full Application must be the same as that described in the PreApp. Full Applications will be evaluated by the CIRM Grants Working Group (GWG), which is composed of fifteen scientific experts from outside California, seven patient advocate members of CIRM's governing board, the Independent Citizen's Oversight committee (ICOC), and the Chair of the ICOC. The membership of the GWG can be found at

http://www.cirm.ca.gov/workgroups/pdf/GrtWkgGpMbr.pdf. The composition of the ICOC can be viewed at http://www.cirm.ca.gov/faq/pdf/Members.pdf. The fifteen scientists on the GWG will review the applications and score them according to scientific and technical merit applying the review criteria described in section VI below. The full membership of the GWG will then review the entire portfolio of applications, taking into consideration the following criteria:

- Appropriate balance among applications addressing various key problems of stem cell biology and cellular plasticity.
- Appropriate balance between risk and feasibility.
- Other considerations from the perspective of patient advocates.

The GWG will make funding recommendations to the ICOC, which will make final funding decisions.

VI. Review Criteria

A. Preliminary Application

The goal of the PreApp review process is to identify the most promising, competitive, and responsive proposals. The PreApp will be evaluated in three key areas: Significance and Innovation, Feasibility and Experimental Design, and Responsiveness to the RFA. The quality of appropriate preliminary results is an important factor in assessing feasibility of the proposals. The Basic Biology RFA is limited to studies utilizing human cells, except for groundbreaking reprogramming studies, where necessary use of other mammalian systems may be considered.

1. Significance and Innovation
    A. Major Unsolved Problem: The project addresses a major unsolved problem in stem cell renewal, normal or aberrant cell differentiation, or cellular reprogramming.
    B. Focus on Mechanism: The project is focused on basic molecular or cellular mechanisms.
    C. Innovative Project: The research is innovative such as addressing a new cellular event, pathway, or outcome.
    D. Logical Rationale: The rationale is logical and scientifically sound.
    E. Major Impact: If successful, the project would have a major impact on potential applications of stem cell research and regenerative medicine, rather than incrementally advancing the field.
    F. Creative Approach: The project utilizes a creative approach to solve the problem or addresses an area that is new or neglected by previous research efforts.
2. Feasibility and Experimental Design

A. Sound Approach: The overall experimental approach is sound and likely to produce meaningful results.

B. Logical and Achievable Aims: The specific aims are logical and well organized with achievable milestones or timeline provided for the 3 year timeframe.

C. Compelling Preliminary Results: The scientific evidence and preliminary results (as summarized by the applicant) are well understood, substantive, compelling and supportive of the proposed concepts, hypotheses, and approaches.

3. Responsiveness to the RFA

The proposed research project adequately and appropriately addresses the goals and objectives of the RFA.

B. Full Application

The full Application will be evaluated in three key areas: the significance and innovation of the proposed project, the feasibility and design of the proposed research, and the qualifications of the Principal Investigator and research team. A key component for assessing feasibility will be the quality of the preliminary data. The specific criteria for review of applications (below) are elaborated from the standard review criteria described in the CIRM Grants Administration Policy (GAP, see section X.A of this RFA).

1. Significance and Innovation

A. Major Unsolved Problem: The project addresses a major unsolved problem in stem cell renewal, normal or aberrant cell differentiation, or cellular reprogramming.

B. Focus on Mechanism: The project is focused on basic molecular or cellular mechanisms.

C. Innovative Project: The research is innovative such as addressing a new cellular event, pathway, or outcome.

D. Logical Rationale: The rationale is logical and scientifically sound.

E. Major Impact: If successful, the project would have a major impact on potential applications of stem cell research and regenerative medicine, rather than incrementally advancing the field.

F. Creative Approach: The project utilizes a creative approach to solve the problem or addresses an area that is new or neglected by previous research efforts.

2. Feasibility and Experimental Design

A. Sound Approach: The proposed research is carefully designed to give meaningful results.

B. Logical and Achievable Aims: The specific aims are logical and the research proposal well organized with achievable milestones and timeline provided over the 3 year timeframe.

C. Alternative Plans: Potential difficulties are acknowledged, and alternative plans are provided should the proposed strategies fail.

D. Research Facilities: Appropriate facilities are available to conduct the proposed research.

E. Compelling Preliminary Data: The scientific evidence and preliminary data are well understood, substantive, compelling and supportive of the proposed concepts, hypotheses, and approaches.

3. Principal Investigator (PI) and Research Team

A. Track Record: Evidence of prior success and track record supports the qualification of the PI to conduct the proposed research.

B. PI Commitment: The PI's level of commitment heightens the probability for success of the project.

C. Research Team: The research team has appropriate expertise to conduct the proposed research.

VII. Application Procedure

Applicants must follow these instructions for submission of a PreApp and, if invited, a full Application for the CIRM Basic Biology Award I. Full Applications will only be accepted from applicants who 1) submitted a PreApp and 2) are invited by CIRM to submit a full Application.

A. Preliminary Application Forms

Each applicant must submit a Pre-Application (PreApp) using the PreApp template provided at http://www.cirm.ca.gov/grants/default.asp. The PreApp should emphasize the significance of the work for the field and describe how the proposed research will lead to important advances in stem cell biology and regenerative medicine.

The PreApp for the Basic Biology Awards I consists of the following sections:

1. *Cover Page*

   Identification information about the PI and Institutional Official.

2. *Title of Proposed Project (limited to 90 characters)*

3. *Specific Aims of Proposed Research (limited to 1500 characters)*

   Describe concisely the goal and specific aims to be achieved by the proposed project.

4. *Preliminary Results (limited to 3800 characters)*

   Summarize concisely the preliminary data that support the proposed study. Figures or Tables cannot be included in the PreApp.

5. *Experimental Approach and Design (limited to 2900 characters)*

   Describe concisely the experimental approaches proposed for accomplishing the project goals within 3 years including appropriate milestones or timeline. Highlight novelty or creative use of approaches and methods.

6. *Significance of Proposed Research (limited to 2800 characters)*

   Describe the importance of the proposed research for stem cell biology and regenerative medicine. Identify the major unsolved problem addressed by the proposed research and, most importantly, describe how proposed experiments will overcome existing hurdles and significantly advance the field.

7. *Project Keywords*

   Select all of the keywords (from the list provided) that apply to the proposed research. If appropriate, supply additional keywords that are central to the proposed project

In addition to the PreApp form, applicants from for-profit institutions must submit a Related Business Entities Disclosure Form (Adobe PDF template provided at http://www.cirm.ca.gov/grants/default.asp). The information in this form is required for compliance with the Conflict of Interest policy under which CIRM operates. The Related Business Entities Disclosure Form should be submitted electronically as a distinct attachment together with the PreApp form.

B. Preliminary Application Submission Instructions

Each applicant may submit only a single PreApp for either this RFA or for the forthcoming Basic Biology Awards II RFA, not both. The completed PreApp form (less the Official signature) and the Related Business Entities Disclosure Form (if applicable) must be sent as interactive pdf documents (the original document format) as email attachments to BasicBiologyPreApp@CIRM.ca.gov and must be received by CIRM no later than 5:00 pm (PST) on January 27, 2009.

Additionally, a hard copy of the cover (first) page of the PreApp, signed by an institutional official authorized to sign on behalf of the applicant's organization, must be received by CIRM no later than 5:00 pm (PST), on January 27, 2009. No exceptions will be made.

Send the signed cover page of the PreApp to:

Basic Biology I PreApp
California Institute for Regenerative Medicine
210 King Street
San Francisco, CA 94107

C. Full Application Forms

Full Applications for the CIRM Basic Biology Awards I may be submitted only by applicants who 1) submitted a PreApp (as described above) and 2) are invited by CIRM to submit a full Application. Application forms will be available on the CIRM website (http://www.cirm.ca.gov/grants/default.asp) by March 20, 2009.

The full Application for the CIRM Basic Biology Awards I consists of four parts:

Part A: Application Information Form (Adobe PDF template provided at

http://www.cirm.ca.gov/grants/default.asp). Part A includes: Abstract, Public Abstract, Statement of Benefit to California, Key Personnel, and Budget (section numbers 1-5 below).

Part B: Basic Biology Award Research Proposal (MS Word template provided at http://www.cirm.ca.gov/grants/default.asp). Part B includes: Rationale and Significance, Specific Aims, Preliminary Data, Research Design and Methods, Project Timeline, References, and Environment including Laboratory Facilities and Major Equipment (section numbers 6-12 below).

Part C: Biographical Sketches for Key Personnel (MS Word template provided at http://www.cirm.ca.gov/grants/default.asp) and letters of collaboration.

Part D: Related Business Entities (Adobe PDF template provided at http://www.cirm.ca.gov/grants/default.asp). In order to comply with the Conflict of Interest policies under which CIRM operates, Part D must be submitted to indicate whether the application would, if awarded, fund a for-profit organization that is either: 1) the applicant organization; 2) a subcontractor; or 3) the employer of a co-investigator, consultant or subcontractor (section number 13 below).

The application for Basic Biology Awards I includes the following sections:

1. Abstract (up to 3000 characters in Part A)

State the goals of the proposal. Summarize the overall plans of the proposed research and how these will meet the stated objectives of the RFA. Summarize the rationale for the studies and techniques employed to pursue these goals.

2. Public Abstract (up to 3000 characters in Part A)

In lay language, briefly describe the proposed research and how it will contribute to the advancement of stem cell biology and regenerative medicine. This Public Abstract will become public information; therefore, do not include proprietary or confidential information or information that could identify the candidate and applicant institution.

3. Statement of Benefit to California (up to 3000 characters in Part A)

Describe in a few sentences how the proposed research will benefit the State of California and its citizens. This Statement of Benefit will become public information; therefore, do not include proprietary or confidential information or information that could identify the candidate and applicant institution.

4. Key Personnel (included in Part A and C)

List all key personnel and their roles on the project. Key personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not they receive salaries or compensation under the grant. Key personnel may include any technical staff, trainees, co-investigators (collaborators), or consultants who meet this definition. A minimum of one percent effort is required for each key person, except the PI, who is required to commit a minimum of twenty percent (20%) effort. For each key personnel (except for technical staff and students) listed, provide a two-page biographical sketch using the template provided. The sketch should highlight prior relevant research experience, accomplishment and/or special skills related to the proposed research. Include relevant publications and/or patents or patent applications.

5. Budget (included in Part A)

Provide all budget information requested in the budget section of the Application Information Form. All allowable costs for research grants are detailed in the CIRM Grants Administration Policy (GAP, see section X.A of this RFA). Under this RFA, allowable costs include the following:

• Salaries for Key Personnel

  Salaries for Key Personnel may include the Principal Investigator, Co-Investigators, Research Associates, and technical support staff (all of whom must work in California) based on percent of full time effort commensurate with the established salary structure of the applicant institution. The total salary requested by the PI must be based on a full-time, 12-month staff appointment. Institutions may request stipend, health insurance and allowable tuition and fees as costs for trainees. Administrative support salaries are expected to be covered exclusively by allowed Indirect Costs.

• Supplies

Grant funds will support supplies, including specialized reagents and animal costs. Small equipment purchases (less than $5,000 per item) are considered supplies and may be included as direct costs in the budget.

• Travel

Recipients (PIs) of CIRM Basic Biology Awards I are required to attend an annual CIRM-organized grantee meeting in California and should include travel costs for this meeting in the budget. Travel costs associated with collaborations necessary to the grant are allowable. Details of allowable travel costs can be found in the GAP (see section X.A of this RFA).

• Equipment

Major equipment (more than $5,000 per item) necessary for conducting the proposed research at the applicant institution should be itemized. Equipment costs should not be included as allowable direct costs in indirect cost calculations.

• Indirect Costs

Indirect costs will be limited to 20 percent of allowable direct research funding costs awarded by CIRM (i.e., project costs and facilities costs), exclusive of the costs of equipment, tuition and fees, and subcontract amounts in excess of $25,000.

6. Rationale and Significance (up to 1 page in Part B)

Summarize the context and background of the application and the specific rationale for the work proposed. Specifically identify the gaps in the current knowledge base that the project is intended to fill. If the aims of the application are achieved, state how the findings will make a critical contribution to the field of stem cell biology or regenerative medicine.

7. Specific Aims (up to 1 page in Part B)

Explain the goal of the specific research proposed. Identify and enumerate each specific aim of the proposal in a concise and step-wise fashion, and describe how each aim will support the goal of this research.

8. Preliminary Results (up to 4 pages in Part B)

Provide preliminary data to support the concepts, hypotheses and/or approaches proposed in the application.

9. Research Design and Methods (up to 4 pages in Part B)

Describe concisely, but in sufficient detail to permit evaluation of the merit of the research, the experimental design, methods and techniques to be employed to achieve the goals specified in the

proposal. Identify the new or risky aspects of the research, anticipated pitfalls, and plans to overcome or circumvent difficulties that may arise. Describe the methods of analysis of results, including criteria for success of the proposed studies. If collaboration is integral to the success of the project, describe how the collaborations will be managed.

10. Project Timeline (up to 1/2 page in Part B)

Provide a realistic timetable for completing each proposed specific aim of the project; where appropriate, provide specific milestones for evaluating the achievement of each specific aim.

11. References (up to 2 pages in Part B)

List all references used in the body of the proposal.

12. Environment Including Laboratory Facilities and Major Equipment (up to 1 page in Part B)

Provide a short description of the facilities and environment in which the work will be done, and the major equipment and resources available for conducting the proposed research. Discuss ways in which the proposed studies will benefit from unique features of the scientific environment or employ useful collaborative arrangements where applicable.

13. Related Business Entities (Part D)

All applicants must provide information on related business entities for any application that, if awarded, would fund a for-profit organization either as: 1) the applicant organization; 2) a subcontractor or 3) the employer of a co-investigator, consultant or subcontractor. If the application does not seek funding for any such for-profit organizations, indicate that on Part D and submit the form. If for-profit funding is sought, include the following for each for-profit organization to be funded:

• A list of any parent organization that owns 50% or more of the for-profit's voting shares;

• A list of all subsidiaries in which the for-profit owns 50% or more of the voting shares; and

• A list of all other related business entities (i.e., entities with which the for-profit shares management and control, or shares a controlling owner).

D. Full Application Submission Instructions

Full Applications will only be accepted from applicants who 1) submitted a PreApp and 2) are invited by CIRM to submit a full Application.

The full Application consists of four parts: Part A: Application Information Form, Part B: Basic Biology Award Research Proposal, Part C: Biographical Sketches for Key Personnel, and Part D: Related Business Entities. **All four parts of the full application for CIRM Basic Biology Awards I must be submitted together and received by CIRM no later than 5:00 pm (PDT) on April 30, 2009, in both electronic form and in hard copy (a signed original and five copies)**. **No exceptions will be made.** Send electronic copies of all parts of the application as attachments in a single email to BasicBiologyAwards@cirm.ca.gov. In addition to the electronic submission, candidates must submit an original copy of the application (consisting of Parts A-D) signed by both the applicant and the institution's Authorized Organizational Official (AOO), plus 5 copies of the full application (preferably double-sided) to:

Basic Biology Awards I Application
California Institute for Regenerative Medicine
210 King Street
San Francisco, CA 94107

VIII. Schedule of Deadlines and Reviews

Pre-Applications due	5:00 pm (PST), January 27, 2009
Invitations for full Applications sent out by CIRM	Last week of March, 2009
Full Applications due	5:00 pm (PDT), April 30, 2009
Review of full Applications by Grants Working Group (GWG)	June, 2009
Review and Approval by ICOC	August, 2009
Earliest Funding of Awards	Fall, 2009

IX. Contacts

For information about this RFA or the review process:

Gilberto R. Sambrano, Ph.D.
Senior Review Officer
California Institute for Regenerative Medicine
Email: gsambrano@cirm.ca.gov
Phone: (415) 396-9103

X. CIRM Regulations

Grant awards made through this RFA will be subject to CIRM regulations. These regulations can be found on CIRM's website at http://www.cirm.ca.gov/reg/default.asp.

A. CIRM Grants Administration Policy

CIRM's Grants Administration Policy (GAP) for Academic and Non-Profit Institutions (Non-Profit GAP) and the Interim GAP for For-Profit Institutions (For-Profit GAP) serve as the standard terms and conditions of grant awards issued by CIRM. All research conducted under this award must comply with the stated policy. Progress reports of research, as required by the GAP, are important to CIRM: Funding from year to year will depend on adequate scientific progress as outlined in the grant application timeline.

B. Intellectual Property Regulations

CIRM has adopted intellectual property and revenue sharing regulations for non-profit and for-profit organizations.

C. Human Stem Cell Research Regulations

CIRM has adopted medical and ethical standards for human stem cell research (Title 17, California Code of Regulations, sections 100010-100110). All research conducted under this award will be expected to comply with these standards. While these regulations prohibit donors of gametes, embryos, somatic cells or human tissue from receiving valuable consideration for their donation, they do allow for reimbursement for permissible expenses as determined by an Institutional Review Board (IRB) (Title 17, California Code of Regulations, section 100080). "Permissible Expenses" means necessary and reasonable costs directly incurred as a result of donor participation in research activities and may include costs such as those associated with travel, housing, child care, medical care, health insurance and actual lost wages. For research activities proposing to obtain gametes, embryos, somatic cell or tissue from human subjects, CIRM requires the candidate to submit, at the time of application, their reimbursement policy describing how they intend to calculate permissible expenses.