# RFA 13-05: CIRM Tools and Technologies III Awards

## I. Purpose

CIRMs mission is to support stem cell research towards the development of cures to benefit patients. As the stem cell field moves towards and into clinical trials, multiple technical hurdles remain to be addressed. The CIRM Tools and Technology initiative intends to support research that can address regenerative medicine's unique translational challenges. These challenges include bottlenecks in the areas of cell engraftment, preclinical evaluation, cell tracking and cost efficient production of stem cell therapies. Resolving these bottlenecks should help to realize the promise of regenerative medicine.

## II. Objectives

This RFA will support the creation, design and testing of broadly applicable novel tools and technologies and the optimization, improvement, standardization or scale-up of existing tools or technologies for addressing translational bottlenecks to stem cell therapies. Such approaches could include, but are not limited to tissue engineering technologies to enhance cell delivery, survival and integration, the development of biomarkers and assays for stem cell biodistribution, pharmacodynamics and immunological monitoring and stem cell process development advances.

### A. Priorities

In particular, CIRM will prioritize projects addressing the following:

- For indications where large animal modeling is critical; development and testing of:
    - technologies or animal strains that enable long-term (three to six month) xenograft retention of human stem cells in large animal models
    - high purity, therapeutically relevant cell types derived from pluripotent stem cells of large animal model species and comparable to their human counterparts, to enable same species modeling of long term (three to six month) efficacy and/or safety of PSC-derived therapies
- Development and testing of clinically relevant technologies to achieve cell survival, engraftment and integration of human stem cell therapies (e.g., tissue engineering strategies that are suitable for use in humans)

- Methods or reagents/probes to enable the use of clinically compatible imaging modalities for in vivo imaging and tracking of human stem cells at high sensitivity
- Development of xenobiotic-free reagents to improve reproducibility and reduce cost of human stem cell manufacturing processes (e.g., extracellular matrices and chemical replacements for growth factors)
- Methods to expand isolated human HSC and/or generate HSC from human pluripotent stem cells resulting in long term, multilineage engraftment
- Application of clinically compatible nanotechnologies for human stem cell delivery and maintenance in target tissues, for targeted in vivo cell clearance or for in vivo monitoring of cell function, biodistribution and/or cell fate.

Applicants are expected to justify the value of the proposed tool or technology to overcoming a specific bottleneck to stem cell translational research, and to make tools developed under the award accessible to the stem cell community.

To maximize the impact of its funding, CIRM will prioritize projects that benefit from additional non-CIRM funding, from a Collaborative Funding Partner or other source, that increases the likelihood of success and potential impact of the proposed project.

**B. Collaboration**

The development and testing of novel tools and technologies for the translation of potential stem cell therapies is an inherently multidisciplinary effort. Projects may require the collaboration of stem cell biologists and experts in complementary technologies such as biomedical engineering, imaging and animal modeling. CIRM therefore encourages applications from collaborative teams where appropriate. The addition of complementary expertise may be achieved through a variety of mechanisms including:

- collaborations between a California PI and a non-California Partner PI supported by a Collaborative Funding Partner (see Section VI).
- collaboration with a second California investigator, as Co-Principal Investigator (Co-PI). Co-PIs must have a significant project responsibility and expertise distinct from that of the PI.
- collaborations with other investigators from either for profit or not for profit institutions.

**C. Scope**

Responsive projects address the objectives of the RFA, and the CIRM-funded research activities must require the use of human stem cells or their differentiated derivatives. Projects should include proof of concept testing with human stem cells to confirm the utility of the developed technologies to translational stem cell research. In scope activities include development and testing of technologies, both in vitro and in preclinical models. While IND-enabling studies are beyond the scope of this RFA, preclinical evaluation of a technology is appropriate. Clinical trials are

not in the scope of this RFA. Analysis of human subject samples, if directly related to the proposed research, can be funded.

## III. Award Information

Under this Request for Applications (RFA), CIRM intends to commit up to $35 million to support up approximately 20 grants. Projects will be funded for up to three years. CIRM will provide two levels of funding:

- For projects developing and testing *large animal models,* such as pig, sheep or non-human primates with relevant physiology for the indication proposed, total justifiable direct project costs up to $1,200,000.
- For all other projects, total justifiable direct project costs up to $900,000.

CIRM encourages co-funding of projects by Collaborative Funding Partners (see Section VI) and other for profit and not for profit institutions to leverage its investment. For those projects that are funded by other organizations in addition to CIRM, these costs must be justified - and documentation of available funds sufficient to complete the proposed research must be provided as described below in Section X.A.2 and X.C.5.

Given the urgency of CIRM's mission, all approved applications must be initiated (grant start date in issued and signed Notice of Grant Award) within 6 months of approval and authorization for funding by the Independent Citizen's Oversight Committee (ICOC), CIRM's Governing Board.

For all awards, CIRM reserves the right to negotiate funded project activities, success criteria, timelines and budgets prior to issuance of the Notice of Grant Award (NGA), subject to renegotiation annually and/or based on progress. Progress in Tools and Technology projects is important to CIRM. Continued funding is contingent upon timely scientific progress as outlined in the project and timeline established under the NGA. CIRM may also wish to review (for compliance with CIRM's policies and regulations) key contract/agreements that are critical to the success of the project.

## IV. Award Mechanism

CIRM expects to fund approved proposals from non-profit and for-profit institutions (separately or in collaborations), through grants. Institutions will be subject to all terms of CIRM's Intellectual Property and Revenue Sharing Requirements for Non-Profit and For-Profit Grantees (17 Cal. Code Regs. § 100600 et seq.).

## V. Eligibility

### A. Institutional Eligibility

Both non-profit and for-profit organizations are welcome to apply. At the time of the Preliminary Application (PreApp) deadline, the applicant organization must have substantial California operations where the work will be conducted (that is, the organization must have employees who are conducting business or operations at a location in California). If these requirements are not met, CIRM may terminate all further action on the application.

Non-profit and for-profit institutions sponsoring Co-Principal Investigators (Section VII.B, Co-Principal Investigators) are subject to the same eligibility requirements as applicant institutions.

"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".

CIRM encourages collaborative endeavors between non-profit and for-profit 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 PreApp deadline, the PI must:

- Be an independent investigator in California at a Non-profit applicant institution, or have an equivalent position and be an employee in California (at least 50-percent time) 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 order to broaden the pool of applicants engaged in stem cell research and to encourage leveraging of CIRM's investment, CIRM is limiting the number of active CIRM research awards in which an investigator may participate as PI or Co-PI. This RFA is not open to investigators as a PI or Co-PI who are already a PI or Co-PI on 3 or more active CIRM awards as of June 19, 2014 the deadline for submission of the full application.

The limit includes all CIRM awards that have been approved but not yet closed out, with the exception of the following CIRM RFAs/PAs: Shared Research Labs, Major

Facilities, Research Training Awards I & II, Bridges to Stem Cell Research, Tissue Collection for Disease Modeling Awards or Conference Grants.

### C. Co-Principal Investigator (Co-PI) Eligibility

In order to encourage multidisciplinary team-based research, CIRM will allow for a single CIRM-funded Co-Principal Investigator (Co-PI) to be designated. The Co-PI must have an M.D., Ph.D. or equivalent degree and must be sponsored by the institution at which the Co-PI will conduct the proposed research in California.

By the PreApp deadline, the Co-PI must:

- Be an independent investigator in California at a Non-profit applicant institution, or have an equivalent position and be an employee in California (at least 50-percent time) 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.
- Designating Co-PIs is not a requirement. The decision of whether to include Co-PIs (or a Partner PI funded by a CFP, see Section VI) should be guided by the scientific goals of the project.

### D. Percent Effort Requirements

CIRM, mindful of the urgency of its mission, will only fund PIs and Co-PIs who are willing to devote substantial, focused attention to the project. For this RFA, PIs must be willing and able to commit a minimum 20% effort and Co-PIs must commit at least 15% effort.

### E. Extraordinary Exceptions

The President of CIRM has the discretion to permit exceptions to any eligibility requirement specified in this Section V. The President may permit an exception if he determines, in his individual discretion, that the applicant has demonstrated that the exception would preserve an important research opportunity or make a critical contribution to one of CIRM's mission objectives. Exceptions must be consistent with the objectives of this RFA and the requirements of Proposition 71 as well as California state regulations, including the Grants Administration Policy (see Section XIII.A of this RFA), or they will not be considered.

If CIRM determines that an application does not meet the eligibility requirements, CIRM may terminate all further action on the application. Applicants who will need an exception are strongly encouraged to request it at least 30 days before the relevant application deadline. To request an exception, or for assistance in determining whether one is necessary, contact the CIRM staff listed in Section XII.

## VI. Collaborative Funding Partners

### A. CFP Program

CIRM has established a program with several other agencies that fund stem cell and regenerative medicine research. Through this Collaborative Funding Partner (CFP) program, California-based Principal Investigators (PIs) can collaborate with a Funding Partner PI ("Partner PI") from a Funding Partner applicant institution ("partner applicant institution") eligible for funding from one of CIRM's CFPs to bring important additional resources to the project. If a collaboratively funded proposal is approved (a "CIRM/CFP Award") CIRM will fund all project work done within the State of California and the CFP will fund all project work within its jurisdiction.

For this RFA, applications can include Partner PIs from:

- Australia (supported by NHMRC -- see Appendix A)
- China (supported by MOST -- see Appendix B)
- Germany (supported by BMBF -- see Appendix C)
- NIH intramural investigators (see Appendix D)
- Sao Paulo, Brazil (supported by FAPESP -- see Appendix E)

To apply for a collaboratively funded project involving CIRM and a CFP, applicants must satisfy both the CIRM requirements and any additional requirements put forth by the CFP agency. For more details on these requirements, please see Appendices A, B, C, D or E.

### B. Identifying Collaborators

To assist potential applicants, CIRM and its funding partners have set up an online partnering platform for this RFA. For further information, see Appendix F.

### C. Terms for Collaboratively Funded Awards

Before funding contracts are signed, successful CIRM/CFP applicant teams must have a signed written agreement adequately addressing Intellectual Property (IP) issues relating to the collaborative project. As with all applicants, successful CIRM/CFP applicant teams must obtain all necessary approvals for animal protection, human subject protection, and use of human embryonic stem cells. CIRM and the CFP will monitor compliance with approval procedures required in their respective jurisdictions.

Both CIRM and the CFP may be involved in the management/oversight of the CIRM/CFP Award, by participating in mutually agreed upon joint award administration activities. These activities may include but are not limited to participation in progress monitoring via progress reports.

## VII. Notification Regarding Disclosure Information

All applicants, including those not applying with a Partner PI are hereby notified that CIRM may share Preliminary Applications, full Applications and related information submitted by applicants with a CFP in order to facilitate their participation in this RFA. Information concerning approved CIRM/CFP Awards may also be shared with a CFP. Before receiving any such material, the CFP will agree in writing to hold the materials in strict confidence and to use them solely for purposes directly related to this RFA.

## VIII. Application and Evaluation Process

Submission of an application for this RFA involves a two-step process. Any qualified applicant may submit a brief Preliminary Application (PreApp). Applicants submitting the most promising, competitive and responsive PreApp proposals will be invited to submit a detailed, full Application.

PreApps should emphasize the overall impact of the proposed work and address the review criteria for the PreApp described in Section IX. PreApps will be evaluated by scientific specialists from outside California who are experts in specific areas of research described in the PreApp, based on the scientific review criteria described in Section IX below and by CIRM scientific staff for responsiveness to the RFA (see Section IX). **The research project and Principal Investigator (and Co-PI and/or Partner PI, if applicable) 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 (ICOC), and the Chair of the Governing Board. The list of scientific members who may participate in the GWG review can be found at http://www.cirm.ca.gov/GrantsWkgGrpMembers. The composition of the ICOC can be viewed at http://www.cirm.ca.gov/GoverningBoard.

The fifteen participating scientists on the GWG will review the applications and score them according to scientific and technical merit applying the review criteria described in Section IX. The entire GWG will make funding recommendations based on scientific merit. The Board's Application Review Subcommittee will make funding decisions based on the GWG recommendations, any staff recommendations and a programmatic review.

CIRM's confidentiality and conflict screening rules will apply to everyone who will have access to applications or who will attend the review meeting, including CIRM staff, external reviewers, and representatives of Collaborative Funding Partner Agencies.

## IX. Review Criteria

CIRM intends the Tools and Technology III Research Awards to support research to resolve key translational bottlenecks to the development of stem cell therapies. As part of this effort, the GWG and CIRM will give special consideration to promising proposals addressing the RFA priorities listed in Section II.A above.

### 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 four key areas: rationale and significance, feasibility and design, qualifications of the PI (Co-PI and Partner PI, if applicable) and responsiveness.

**Rationale and Significance**

- The rationale for the tool or technology and its potential for use in translation of human stem cell therapies is logical and scientifically sound
- The proposed tool or technology offers advantages over other technologies or could significantly improve an existing technology.
- The proposal addresses a major unsolved bottleneck to the translation of human stem cell therapies.
- If successful, the project would have a significant impact upon the field of human stem cell translation.

**Feasibility and Design**

- The scientific evidence and preliminary results are substantive, compelling and support the feasibility of the proposed research.
- The proposed research is carefully designed with a logical plan that is likely to achieve meaningful results. The aims and the timeline are appropriate and achievable within the proposed timeframe.
- The experimental plan includes proof of concept testing with human stem cells.

**Qualification of PI (Co-PI and/or Partner PI, if applicable)**

- The PI has the appropriate expertise and track record to lead the proposed program.
- Where applicable, the Co-PI and/or Partner PI provide critical complementary expertise.

**Responsiveness**

- The proposal addresses the RFA's goal to resolve bottlenecks to the translation of stem cells.
- The proposal addresses an RFA priority.
- Collaborations bring critical intellectual, technical or infrastructure resources to the project.

- Human stem cells or their differentiated derivatives are required for the project, or, for projects developing differentiated derivatives of large animal PSC, the proposal includes demonstration of their pluripotency and functional comparability of the derivatives to their human counterparts.

## B. Full Application

The full Application will be evaluated in four key areas: significance and rationale, feasibility and experimental design, qualifications of PI and Team and responsiveness. Preliminary data will be a key component of the feasibility assessment. The specific criteria for review of applications are elaborated below. The specific criteria for review of applications are based upon the standard review criteria described in the CIRM Grants Administration Policy (GAP, see Section XIII.A).

### Significance and Rationale

- The proposal addresses a significant bottleneck to the translation of human stem cell therapies. The proposal addresses a bottleneck identified as a priority (see Section II.A).
- The rationale for the tool or technology and its use in translation of human stem cell therapies is logical and scientifically sound.
- If successful, the project would have a major impact upon the field of human stem cell translation.
- The proposed tool or technology offers advantages over other technologies or could significantly improve an existing technology.
- The applicants present convincing rationale for the tools ultimate uptake/use by the stem cell community.
- Technology development involving a proposed large animal model is adequately justified.

### Feasibility and Experimental Design

- The scientific evidence and preliminary data provided are compelling and supportive of the proposed research.
- The aims of the research are logical and can be reasonably achieved within the proposed timeline. Success criteria provide scientifically meaningful quantitative measures to determine if the aims and objective(s) of the proposal have been achieved.
- The proposed research is carefully designed with a logical plan that will achieve meaningful results. Vulnerabilities in the plan are noted and alternative plans are provided.
- The experimental plan includes proof of concept testing with human stem cells (and/or in vivo testing where appropriate).
- The investigators have access to the necessary reagents, methodologies and technologies to execute the research plan.

- Appropriate facilities are available to conduct the proposed research. The scientific environment is beneficial and conducive to project success.
- Any proposed collaborative efforts are appropriate, complementary, and enhance the likelihood of achieving the aims of the overall project.

**Qualifications of PI and Team**

- The PI (and Co-PI and/or Partner PI, if applicable) has evidence of prior success and the track record, training and experience to support his/her qualification to successfully lead proposed project.
- The PI's (and Co-PI's and/or Partner PI's, if applicable) level of commitment to lead the proposed project heightens its probability of success.
- An appropriate team has been assembled to enable both development of the technology and proof of concept testing of the technology with stem cells.
- Proposed collaborations have been secured and are critical to the success of the proposed project.
- The budget is appropriate for the research proposed. The project addresses the RFA's priority of bringing additional funding (see Section II.A). If the project will require funds beyond those provided by CIRM and its partners, the applicant has provided documentation assuring that these additional funds are committed and will be made available to support the project (in Part C, letters of support).

**Responsiveness**

- The proposal addresses the RFA's objective to resolve bottlenecks to the translation of stem cells.
- The applicant has provided a plan describing how the technology, if successfully developed, will be made accessible to the stem cell community.
- Human stem cells or their differentiated derivatives are required for the project or, for projects developing differentiated derivatives of large animal PSC, pluripotency and functional comparability of the derivatives to their human counterparts will be established.

## X. Application Procedure

Applicants must follow these instructions for submission of a PreApp and, if invited, a full Application for the CIRM Tools and Technology III Research Awards. 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 PreApp using the forms and instructions provided in the Grants Management Portal at https://grants.cirm.ca.gov

The PreApp consists of the following sections:

***1. Principal Investigator (Co-PI and Partner-PI)***
Provide identification information about the PI and Authorized Organizational Official (and Co-PI and Co-PI applicant organization, if applicable). For CIRM/CFP collaborations, include the name of the Partner PI and the Partner applicant institution.

Briefly describe the qualifications of the PI (Co-PI and/or Partner PI, if applicable) to lead the proposed program and, where applicable, highlight the complementary expertise provided by critical collaborations.

***2. Additional Co-Funders***
If your proposed project will be co-funded by sources other than CIRM and its Collaborative Funding Partners, please specify these funding sources here.

***3. Title of Proposed Project (limited to 300 characters)***

***4. Specific Aims of Proposed Research (limited to 1500 characters)***
Describe concisely the goal and specific aims to be achieved by the proposed project. Where applicable, delineate the aims to be completed by the PI, Co-PI or Partner PI.

***5. Large Animal Model Certification***
Project funding levels are described in Section III. Complete the checkbox to certify whether or not the program entails development and testing of a large animal model(s).

***6. Significance and Rationale (limited to 3000 characters)***
Identify the significant translational bottleneck addressed by the proposed research. Describe the proposed research to overcome this bottleneck and address how it will significantly advance stem cell therapy. Explain how the tool or technology is appropriate for use in stem cell translation. Comment on the potential breadth of use of the tool or technology, if successfully developed. If the project is co-funded, explain how the additional funding will increase the potential impact and success of the project.

***7. Preliminary Results (limited to 3500 characters)***
Summarize concisely the scientific evidence and preliminary results that support the concepts and approaches of the proposed study. Figures or Tables cannot be included in the PreApp.

***8. Experimental Approach and Design (limited to 3500 characters)***
Describe concisely the experimental approaches proposed for accomplishing the project aims within 3 years including an appropriate timeline. Describe how your team will demonstrate feasibility of applying the proposed technology in

translational stem cell research by proof of concept testing. Where applicable, clearly delineate the studies to be completed by the PI, Co-PI or partner PI.

***9. Project Keywords***
Select keyword(s) in each category that best describes the proposed research (from the lists provided). If appropriate, supply additional keywords that are central to the proposed project.

***10. Related Business Entities Disclosure***
Applicants must complete the Related Business Entities Disclosure section when applicable (see instructions at https://grants.cirm.ca.gov). Applicants (PIs) from for-profit institutions (including Partner PIs from a for-profit institution to be funded by the Funding Partner) must complete the disclosure by listing all related business entities. The information in this form is required for compliance with the Conflict of Interest policy under which CIRM operates.

***11. Collaborative Funding Partner Requested Information (limited to ~3000 characters)***
A Partner PI may use this section, in addition to those above, in order to comply with the specific Funding Partner's requirements. Please see relevant Funding Partner Appendix.

**B. Preliminary Application Submission Instructions**

PreApps must be submitted online using the CIRM Grants Management Portal at https://grants.cirm.ca.gov. A PI may submit only a single PreApp for this RFA and it must be received by CIRM no later than 5:00 pm (PST) on January 7, 2014.

**C. Full Application Forms**

Full Applications for this RFA 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 via the Grants Management Portal at https://grants.cirm.ca.gov on January 18th, 2014.

The application for the Tools and Techology III RFA consists of **three parts**:

**Part A: Application Information Form** (Web-based form)
**Part B: Proposal** (MS Word template)
**Part C: Biographical Sketches and Letters of Support** (MS Word template)

The full Application includes the following sections:

***1. Abstract (up to 1500 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 1500 characters in Part A)***
In lay language, briefly describe the proposed research and how it will overcome a major unsolved bottleneck to the translation of human stem cell therapies. This Public Abstract will become public information and will be posted on the CIRM website; therefore, do not include proprietary or confidential information or information that could identify the applicant (e.g., PI name, applicant institution name or location).

***3. Statement of Benefit to California (up to 1500 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 and will be posted on the CIRM website; therefore, do not include proprietary or confidential information or information that could identify the applicant (e.g., PI name, applicant institution name or location).

***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. Key personnel who are neither part of the applicant organization nor funded by a CFP should be listed in the subcontract section of the application.

Personnel that are not key, such as technical support staff, may be supported by award funds but need not be listed. A minimum of one percent effort is required for each key person, except the PI and Co-PI, if applicable, who are required to commit a minimum of 20% and 15% effort, respectively.

For each key person (except for technical staff and students) listed, provide a two-page biographical sketch using the template provided under Part C. The sketch should highlight prior relevant research experience, accomplishments and/or special skills related to the proposed research. Include relevant publications and/or patents or patent applications. Following biosketches for the PI and, if applicable, the Co-PI and Partner PI, include all remaining biographical sketches in alphabetical order.

***5. Budget (included in Part A)***
Provide all budget information requested in the budget section of Part A. Budgets must be justified in detail, including all subcontracts and consulting fees. For applications that designate a Co-PI, the PI and the Co-PI will each be responsible for an individual budget (composed of CIRM Direct Project Costs,

CIRM Direct Facilities Costs and CIRM Indirect Costs) for that portion of the total project performed under their authority. For CIRM/CFP collaborations, the funding requested from the CFP (total and per year requested, Part A) must be indicated and justified in sufficient detail (in the Part A section "Budget Justification") for reviewers to assess the appropriateness of the non-California research budget.

If, to achieve the objective of the project described in Part B, the applicant will require funding from sources other than CIRM and, if applicable, its Funding Partner, then the applicant must specify the portion of the project to be completed with CIRM (or CFP) funding as well as identify and justify the added cost and identify the additional funding source(s) that will enable conduct of the project (in the "Budget Justification" section). Provide letters documenting commitment of additional funding (excluding any CFP funding) in Part C.

All allowable costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy (GAP, see Section XIII.A of this RFA). For CIRM/CFP teams, allowable costs for research funded by the Collaborative Funding Partner may differ. Guidance will be provided separately by NHMRC, MOST, BMBF, NIH and FAPESP please see Appendices A, B, C, D or E, respectively.

Under this RFA, CIRM-funded 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, each of whom must perform the subject work in California, based on percent of full time effort commensurate with the established salary structure of the applicant institution. The total salary requested must be based on a full-time, 12-month staff appointment or the full time annual salary for employees of a for-profit institution. Institutions may request stipend, health insurance and allowable tuition and fees as costs for trainees. Administrative support salaries should be covered exclusively by allowed Indirect Costs.

- ***Supplies***
  Grant funds will support supplies, including specialized reagents and animal costs. Minor 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 Tools and Technology III are encouraged to attend a 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 XIII.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 and justified. Under this RFA, no more than 5% of total direct project costs can be used for equipment. Under special circumstances, with sufficient rationale, CIRM may allow a higher percentage of direct project costs for equipment. Equipment costs should not be included as allowable direct costs in indirect cost calculations.

***• Consultants/Subcontracts***
Grantees that subcontract CIRM-funded work should note that CIRM-funded **research** must generally be conducted in California. Examples of such research include study design; analysis and interpretation of data; development of new methods.

Aside from small consulting contracts, Grantees may not use CIRM funds to contract for research to be performed outside of California. Consulting contracts for out-of-state research are limited to $15,000 per year for a single contract, and $25,000 per year in aggregate. (CIRM may allow modest increases to these limits in exceptional circumstances.)

For activities **other than research**, Grantees may subcontract outside California, but must make a good faith effort to use California suppliers for more than half of their contracts and purchases in accordance with CIRM's California Supplier regulation (Cal. Code Regs., tit. 17, § 100502).

***• 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. Applicants may use lower Indirect cost rates and use up to 100% of the awarded funds for direct research purposes. The Indirect cost rate budgeted is to be applied to the entire award project period.

See Appendices A-E for details concerning specific CFP allowable costs.

***6. Related Business Entities (included in Part A)***
All applicants (including, if applicable, a Co-PI and/or a Funding Partner applicant institution) 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, Partner PI, consultant or subcontractor. 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).

### *7. Tools and Technology Award Research Proposal*

***Significance and Rationale (up to 1 page in Part B)***
Summarize the context and background of the application and the specific rationale for the work proposed. Identify the significant translational bottleneck addressed by the proposed research. Describe the proposed research to overcome this bottleneck and address how it will significantly advance stem cell therapy, if successful. Explain how the tool is appropriate for use in stem cell translation. Comment on the potential breadth of use of the tool or technology, if successfully developed.

***Preliminary Data (up to 3 pages in Part B)***
Provide preliminary data and other data (e.g. published) to support feasibility of the proposed research. Present preliminary data for successful application of the technologies and methodologies proposed. Clearly indicate data generated by the applicant PI and, if applicable, by a Co-PI or Partner PI. Clearly distinguish technologies/methodologies used by the applicant PI and, if applicable, by the Co-PI or Partner PI.

***Research Plan (up to 5 pages in Part B)***
Describe concisely but in sufficient detail, the experimental design, methods and techniques to be employed to achieve the specific aims within three years. Provide measurable, quantifiable success criteria for each specific aim. For proposals including Co-PIs or Partner PIs clearly indicate proposed activities to be conducted by the applicant PI, Co-PI or Partner PI during the course of the integrated project. Identify novel or risky aspects of the research, anticipated pitfalls and describe alternative approaches should the initial approaches fail. Assuming success, describe plans to make the developed technology accessible to the stem cell community.

***Timeline (up to 1 page in Part B)***
Provide a realistic timetable for completing each specific aim proposed.

***References (up to 2 pages in Part B)***
List all references used in the body of the proposal.

***Collaborations, Resources and Environment (up to 2 pages in Part B)***
Successful collaborations are those that bring critical intellectual, technical or infrastructure resources to the project. When collaborations (intra- or inter-institutional), including collaborations with a Co-PI or with a Partner PI funded by CFP are part of the research plan, describe the nature of the collaboration and

explain why it is integral to the success of the project. For projects that include matching or additional funding beyond that to be provided by CIRM and it's CFPs, provide letters of commitment for the additional funds that will be dedicated to the proposed project in Part C. Discuss how the PI will ensure communication, coordination and collaboration among the team members. If advisors, consultants or subcontractors will provide expertise or resources critical to the success of the project, summarize their credentials and relevant track records.

Provide a short description of the facilities, core services and environment(s) in which the research 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 environment(s).

Provide evidence of institutional support for the PI (the Co-PI and the Partner PI, if applicable) and the proposed research.

***Assets*** *(up to 1 page in Part B)*
Discuss relevant assets such as intellectual property (patent applications, patents) and licenses that are available to the project. In addition, provide a list of any third-party intellectual property (e.g., non-licensed patents or materials) currently known to the Investigator to be necessary for research and/or commercialization purposes. Intellectual property assets are important for proposed technologies that must be commercialized to bring benefit to patients. When proprietary cell lines, small molecules, antibodies or other critical materials that are not readily available are required for the project (e.g. are the potential/proposed development candidate), provide appropriate material transfer agreements (MTAs) for their use. If MTAs are not available, provide appropriate letters of commitment from the asset owner.

***Biographical Sketches and Letters of Commitment*** *(Part C)*
Provide biographical sketches for all key personnel as described above in Section X.C.4 above. In addition, include letters of support, letters of collaboration and letters documenting additional funds available to the project, if applicable, as described above in Section X.C.5 here.

## 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.

**All three parts of the Tools and Technology III application must be submitted together and received by CIRM no later than 5:00PM PDT on June 19, 2014 via the Grants Management Portal (https://grants.cirm.ca.gov). It is the applicant's responsibility to meet this deadline; no exceptions will be made.**

### E. Submission of Supplemental Information

If necessary, the PI may submit limited supplemental materials that provide critical new information related to their research proposal after the application deadline but not later than 5:00pm PDT on May 8, 2014. Supplementary materials will not be accepted after this deadline. CIRM will accept a one-time-only submission of materials from the PI only if it meets the submission deadline and conforms to the requirements described herein. Accepted submissions will be forwarded to reviewers for their consideration.

The submission should be in the form of a one-page letter addressed to the Associate Director, Review and submitted via email to gsambrano@cirm.ca.gov. The body of the letter may not exceed 500 words and should briefly describe the type of information submitted and when the information became available. The following materials qualify for submissions of supplemental materials.

Within the one-page letter:

- Provide specific citation(s) to journal publications related to the proposed project that were published or accepted for publication since the application submission deadline. You may briefly describe the significance of the publication(s) to the proposal in the cover letter.

- Confirmation of funding secured from other sources.

- Regulatory (e.g., IND, IDE) filings or approvals acquired since the application submission deadline.

- Notice of patent application(s) filed, notice of allowance received or patent(s) issued, or notice of license(s) to relevant intellectual property (granted or received) since the application submission deadline.

The letter may not be used to describe any additional data or experiments. Changes in scope, experimental approach, or research design are not allowed.

## XI. Schedule of Deadlines and Reviews

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|---|---|
| Pre-Applications due | 5:00 pm (PST), January 7, 2014 |
| Invitations for full Applications sent out by CIRM | Mid April, 2014 |
| Full Applications due | 5:00 pm (PDT), June 19, 2014 |
| Review of full Applications by Grants Working Group (GWG) | Mid September, 2014 |
| Review and Approval by ICOC | December 2014 |

| | |
|---|---|
| Earliest Funding of Awards | Winter, 2015 |

## XII. Contacts

For information about this RFA or the review process:

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

## XIII. 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 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. CIRM's GAP is available at http://www.cirm.ca.gov/our-funding/our-regulations/stem-cell-regulations-governing-cirm-grants#GAP

### B. Intellectual Property Regulations

CIRM has adopted intellectual property and revenue sharing regulations for non-profit and for-profit organizations. By accepting a CIRM Grant, the Grantee agrees to comply with all such applicable regulations.

### C. Human Stem Cell Research Regulations

As reflected in CIRM's GAP, CIRM has adopted medical and ethical standards for human stem cell research (Title 17, California Code of Regulations, sections 100010-100110 available at http://www.cirm.ca.gov/our-funding/our-regulations/stem-cell-regulations-governing-cirm-grants#standards). All research conducted under this award will be expected to comply with these standards. This information can be found on the CIRM website.

### D. California Supplier Regulation

CIRM has adopted a regulation to implement the requirement in Proposition 71 that grant and loan recipients make a good faith effort to achieve a goal of purchasing more than 50% of their goods and services from California suppliers (Title 17,California Code of Regulations, section 100502). Grant and loan recipients are required to comply with this standard.