INFRASTRUCTURE

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INFR5: California Cell and Gene Therapy Manufacturing Network

Phase One Awards

REQUEST FOR APPLICATIONS

10.20.22 (revised 11.01.22)

INFR5: California Cell and Gene Therapy Manufacturing Network

Phase One Awards

Objective

The mission of the California Institute for Regenerative Medicine (CIRM) is to *accelerate world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world*.

The manufacturing of cell and gene therapies is a complex, ever-evolving science. Currently, the capacity for and expertise in the many technologies needed for process development and manufacture of cell and gene therapies is limited. These limitations can pose bottlenecks at both early and late stages of cell and gene therapy development.

The expertise and capacity for early process development and early clinical manufacturing of cell and gene therapy candidates is concentrated at academic research institutions with small-scale good manufacturing practice (GMP) manufacturing facilities. The academic GMP manufacturing facilities have varying capabilities and limited capacities, personnel, and resources to meet the growing demand for cell and gene therapy manufacturing. While industry presence with large-scale manufacturing capacity is growing, there are limited partnerships and collaborations between the academic and industry stakeholders to support process development and GMP manufacturing throughout the lifecycle of cell and gene therapy product development and commercialization. In addition, there is an immediate and growing need to build a diverse and highly skilled workforce to support the cell and gene therapy manufacturing demand in the state.

CIRM has developed a unique biphasic funding opportunity for non-profit academic GMP manufacturing facilities to enhance operations, and to establish productive partnerships with industry and non-profit stakeholders to further advance California as the world-class hub of cell and gene therapy manufacturing.

The overall objective of this two-phase funding opportunity is to establish a statewide manufacturing network comprising academic process development and GMP manufacturing facilities as well as industry manufacturing partners that will:

(1) Accelerate and de-risk pathways to commercialization for cell and gene therapies

(2) Advance industry standards and incorporate quality-by-design in cell and gene therapy manufacturing

(3) Build a diverse, highly skilled manufacturing workforce in California

Examples of how the California Cell and Gene Therapy Manufacturing Network may function to meet the goals of this funding opportunity include (but are not limited to):

- Offering world-class expertise and capacity across a range of cell and gene therapy manufacturing and analytical technology platforms

- Implementing innovative manufacturing models that support the delivery of cell and gene therapies for rare diseases
- Operationalizing academic-industry partnerships that accelerate and de-risk late-stage and commercial manufacturing of cell and gene therapies
- Establishing standards and requirements for quality and accreditation of cell and gene therapy manufacturing facilities
- Enabling inclusive workforce entry and advancement opportunities in technical and leadership career pathways

To effectively achieve the program objective, CIRM will issue two phases of awards governed by two separate requests for applications (RFAs). This RFA describes the first phase of awards that will fund California academic GMP facilities to make initial progress toward the three network goals (described above) at their individual facilities. The second phase of awards will operationalize the California Cell and Gene Therapy Manufacturing Network by funding collaborative partnership-driven proposals that effectively scale phase one outcomes across the network. CIRM will coordinate a steering committee composed of awardees, industry partners and external representatives that will bridge the two award phases by driving collaboration, knowledge-sharing and standard-setting between the participating network facilities and collaborators.

Award Information

How is the program structured?

The first phase of the program will fund individual California non-profit GMP manufacturing facilities to address cell and gene therapy manufacturing bottlenecks at their individual facilities, which could include external partnerships where appropriate. The awardees will be expected to implement quality-driven enhancements that de-risk manufacturing of cell and gene therapy projects, to propose and make operational progress on specialization areas of value to the network, and to develop inclusive workforce development programs for technical and leadership career pathways. Successful outcomes of phase one awards may include, but are not limited to, quality-driven improvements on cell and gene therapy manufacturing project execution compared to historical performance, demonstration of competency in specialization areas with execution of pilot project(s), and enrollment of initial trainee cohorts for technical and leadership training programs.

To facilitate achievement of the California Manufacturing Network Goals, CIRM will coordinate a Steering Committee to help drive the formation and function of the network. The Steering Committee will be composed of the Program Directors of the awardee institutions, leaders from California industry stakeholders, external key opinion leaders and CIRM staff. Examples of potential Steering Committee functions include: supporting consistent implementation of industry quality standards, protocols and best practices, developing potential criteria for facility accreditation, facilitating collaborative opportunities between network members for phase two proposals, establishing processes and systems for sharing protocols, resources and operational data, and mitigating capacity and expertise gaps across the network.

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What activities will CIRM fund? Or what activities must be performed?

Applications are expected to be responsive to all three categories of activities defined below but the scope of proposed activities in each category and the respective budget allocations are at the discretion of the applicant.

- Implementation of quality-driven enhancements that de-risk and accelerate early **and** late-stage process development and GMP manufacturing of cell and gene therapies. Potential enhancements could include but are not limited to:
    - Implementation of, and staff training in, industry quality standards and quality-by-design principles
    - Facilitation of project transition to manufacturing partners for late-stage manufacturing support
    - Mitigation of project delays and long lead-times resulting from capacity or expertise gaps at applicant facility
    - Development of electronic records systems and technology transfer package templates
    - Enhancement and implementation of in-house or partnered analytical capabilities
    - Implementation of in-house or partnered services to support sponsors in process development, analytical assay development, technology transfer, quality-by-design, etc.

- Specialization in one or more functional areas that overcome bottlenecks in the development and delivery of cell and gene therapies. Specialization areas could include but are not limited to:
    - Current and emerging cell and gene therapy technology platforms
    - Innovative manufacturing models for cell and gene therapies for rare diseases
    - Application of quality-by-design in deep product characterization, identification of critical quality attributes and critical process parameters, and process control strategies
    - Development of data capture systems and analytics to support correlation of product characteristics to clinical outcomes
    - Systems for sharing manufacturing protocols, data, and analytics
    - Development of novel manufacturing process analytical technologies and manufacturing technologies

- Workforce development programs for technical and leadership positions, preferably in partnership with CIRM EDUC-funded programs, California cell and gene therapy industry stakeholders, and California academic institutions. Workforce development activities include but are not limited to:
    - Development of paid training and/or certification programs for technical positions

- Recruitment, technical training and leadership mentoring programs for facility leadership positions
- Partnering with other California GMP manufacturing facilities and industry partners for cross-functional training, job placement and other coordinated activities

CIRM funds cannot be used to support the following activities under this opportunity:

- Costs associated with process development or manufacturing activities for individual projects
- Workforce development activities located outside of California
- Construction or renovation of physical facilities
- Activities already budgeted or paid for under a prior, existing or future CIRM award
- Equipment costs exceeding 5% of the direct project costs

What is the award amount and duration?

The CIRM Governing Board has allocated $80 million to support the funding opportunity. CIRM has allocated $20 million for funding of phase one awards. Phase one awards will provide up to $2.0 million in total funding over a 2-year period. CIRM will not fund indirect costs for awards issued under this funding opportunity.

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Award (NOA) and based on operational milestones. **Costs resulting from a delay or failure to meet an operational milestone will be the sole responsibility of the recipient.** Successful applicants will have thoughtfully accounted for foreseeable project risks and developed contingency plans that **do not** require additional funding from CIRM. Continued funding is contingent upon timely progress, and, when applicable, the ongoing ability of the applicant to fund its operations and to satisfy its co-funding commitment.

Eligibility

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

(1) Must be ready to initiate work on the funded project within 90 days of approval

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 90 days of approval and authorization for funding by the Application Review Subcommittee of CIRM's governing board, the Independent Citizens' Oversight Committee ("ICOC").

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(2) Must have a California operating location

Only non-profit organizations are eligible to apply. At the time of the application deadline, the applicant organization must be located in California and must have appropriate cell and gene therapy process development and GMP manufacturing facilities in California. If these requirements are not met, CIRM may terminate all further action on the application.

(3) Must have demonstrated ability to perform process development and/or GMP manufacturing for cell or gene therapy development projects

The applicant organization must demonstrate a track record of performing GMP manufacturing activities for cell and gene therapy candidates, having supplied at least one cell or gene therapy clinical trial. Applicants will be required to identify cell and gene therapy process development or GMP manufacturing projects that are either active or would be initiated in the first year of the award periods, which they will execute in order to demonstrate achievement of applicable award objectives.

(4) Application must be accurate and complete

All required components of the application must be completed and may not contain false or inaccurate information.

(5) Applicant must be in "good standing"

In Applicants must certify that they are in good standing, as follows:

- The applicant's Chief Executive Officer, Chief Financial Officer, and Program Director must not have been convicted of, or currently under investigation for, crimes involving fraud/misappropriation;
- The applicant must have accounting systems in place that are capable of tracking CIRM funds; and
- The Program Director or key personnel named in the application must not be currently under investigation for research misconduct by the applicant institution or a funding agency and must not be currently debarred by HHS Office of Research Integrity.

(6) Must include a project manager

The project team must include a project manager with experience in GMP manufacturing facility operations and be able to devote at least 50% effort to the project.

(7) Must demonstrate co-funding support

CIRM will require all applicants to co-fund at least 20% of the total "Allowable Project Costs". Allowable Project Costs are those costs permitted under CIRM policies and regulations and include direct and facilities costs. Indirect costs are not supported by this funding opportunity. The sum of CIRM funds requested plus the co-funding contribution by the applicant make up the total Allowable Project Cost. The co-funding may come from any funding source arranged by the applicant.

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Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided at the time of application submission.

Who can apply?

Only California Organizations are eligible to apply for this opportunity.

California Organizations 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 must direct and control the award activities from the California location.

Who can serve as the Program Director (PD)?

To be eligible, the PD must satisfy the following requirements:

- Must be the Director of the GMP manufacturing facility of the applicant organization or must hold an equivalent position
- Must be an employee of the applicant organization or be accountable for the conduct of the proposed project to the applicant organization through a formal contract
- Must propose a level of effort on the project consistent with achieving the project's aims and not less than 30% on average over the project period (note: "project" includes both the CIRM-funded, applicant co-funded components and steering committee participation). Any effort for which salary from CIRM is claimed must be expended in California
- Must be authorized by the applicant organization to conduct the proposed activities and assume the responsibilities of the PD
- Must be authorized by the applicant organization, and be able to commit the level of effort required, to participate in the California Manufacturing Network Steering Committee
- Must not currently have another application pending review or approval under this funding opportunity
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.

Additional requirements

Addressing the Needs of Underserved Communities in CIRM-Funded Projects

All applicants for the California Cell and Gene Therapy Manufacturing Network will be required to provide a statement describing:

- How the proposed project activities will improve access to cell and gene therapies by underserved and disproportionately affected populations

- How the project team will bring diverse and inclusive perspectives and experience to the implementation of proposed activities
- How well the project team demonstrates a successful track record for promoting and valuing diversity, equity and inclusion (DEI)
- How any proposed workforce development programs will increase workforce participation by underserved and disproportionately affected populations in California

Knowledge Sharing Plan

The CIRM 2022-2027 strategic plan prioritizes knowledge sharing and collaborative approaches to the discovery, development and commercialization of regenerative medicine therapies. Applicants should describe how they will contribute to knowledge sharing in the California Cell and Gene Therapy Manufacturing Network. Applicants are encouraged to allocate funds in their proposed budget for personnel and/or activities related to managing and sharing knowledge.

Applicants should develop plans intended to capture and disseminate within the network any operational data, protocols, processes, expertise, guidance or other information vital to achieving the three goals of the California Cell and Gene Therapy Manufacturing network. The knowledge sharing plan may also include the ability to support CIRM TRAN and CLIN awardees that may utilize the Manufacturing Network in meeting their own CIRM data sharing requirements.

Organizational Business Plan

In the application proposal, applicants will be required to describe their plans for maintaining sustainability beyond the immediate project period of any proposed operational enhancements, quality-based improvements, specialization areas and training programs that will be developed, implemented and/or scaled up as part of these funding opportunities.

Schedule And Deadlines

Applications Due	2:00 pm (PST/PDT), January 24, 2023
Grants Working Group (GWG) Review	Approximately 90 days post submission
ICOC Review and Approval	Approximately 120 days post submission
Award Start	Must start within 90 days of award approval (i.e., approximately 210 days post submission)

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Application Review Information

What is the process for evaluating an application?

Pre-submission Consultation

In accordance with CIRM's mission, the agency is committed to helping develop promising stem cell and gene therapy-based technologies by partnering with world-class investigators. Therefore, prospective applicants are encouraged to contact CIRM before applying with questions or to discuss their project's eligibility, scientific, or budget considerations.

Eligibility Review

CIRM will assess whether the proposed project meets eligibility requirements sought under this program. If CIRM determines, in its sole discretion, that an application does not meet the eligibility requirements of the program, CIRM will notify the applicant of its decision and terminate all further action on the application.

Budget Review

CIRM will review the proposed budget to assess how the proposed costs compare with established market rates for similar activities, how well the costs are justified when market rates are not established and to confirm that costs designated as Allowable Project Costs comply with CIRM policies. When a proposed budget differs significantly from market rates, is not well justified or does not comply with Allowable Project Cost policy, 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.

Scientific Review

The scientific merit of each application will be assessed by the GWG, which is composed of fifteen subject matter experts from outside California, seven patient advocate or nurse members of the ICOC, and the Chair of the ICOC. The list of scientific members who may participate in the GWG review can be found at http://www.cirm.ca.gov/WorkingGroup_GrantsReview. The composition of the ICOC can be viewed at http://www.cirm.ca.gov/GoverningBoard.

The fifteen participating scientists on the GWG will evaluate the applications and score them according to scientific and technical merit, applying the review criteria described below. The GWG will score each application and make one of the following specific recommendations to the ICOC's Application Review Subcommittee: 1) fund the project based on the proposal's exceptional merit; 2) do not fund the project but may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants Working Group's review; or 3) do not fund the project and do not allow resubmission.

The ICOC's Application Review Subcommittee will make final funding decisions giving consideration to the GWG recommendations and any CIRM team recommendations.

Consideration of Related CIRM Award Information (If Applicable)

The GWG may consider information from a previously funded and related CIRM award as part of its review. CIRM will provide the GWG with objective information regarding a related award that CIRM, in its sole discretion, deems relevant, including but not limited to achievement of specific milestones, data, and outcomes for a related CIRM award or awards.

A "related CIRM award" includes: (1) an award for which the applicant PD served as the PD/PI, a co-PD/PI, a co-investigator, or otherwise substantially participated in the conduct of the award; (2) an award involving the same research project or product; or (3) an award that includes overlapping team members.

Confidentiality

CIRM's confidentiality and conflict screening rules apply to everyone who will have access to applications or who will attend any review meeting in which confidential information is discussed, including but not limited to CIRM team members, reviewers and members of the ICOC. (Per Gov. Code §6254.5(e) non-public records may be disclosed to government agencies under confidentiality agreements).

How will the scientific merit of an application be evaluated?

Scientific members of the GWG will evaluate and score applications based on the following key questions:

1. Does the project offer a significant value proposition that would contribute to the creation of a California Cell and Gene Therapy Network capable of accelerating manufacturing development, advancing industry standards in manufacturing and building an inclusive manufacturing workforce?

Do the proposed operational enhancements, specializations and workforce development programs address critical manufacturing and analytical bottlenecks for cell and gene therapies? Does the proposal demonstrate an organizational commitment to sustainability of the operational enhancements, specializations and workforce development programs beyond the project period? Does the proposal leverage collaboration opportunities with appropriate partners such as CIRM Alpha Clinics, CIRM Education programs, other manufacturing facilities or industry partners? Does the proposal position the facility for scaling its operational enhancements, specializations and training programs across the manufacturing network in phase two of this funding opportunity?

2. Is the project well planned and designed?

Are the proposed operational enhancements adequate to de-risk early-stage process development and manufacturing of cell and gene therapies at the applicant facility and to accelerate project transition to late-stage manufacturing? Are the proposed outcome criteria adequate to measure the impact of the operational enhancements? Are the proposed activities and the proposed pilot project likely to demonstrate the facility's progress toward competency in the specialization areas? Would the

proposed workforce development program create technical and leadership career entry and advancement opportunities in manufacturing for underserved California populations?

3. Is the project feasible?

Is the proposed plan feasible and likely to be implemented within the proposed timeline? Is the proposed team appropriately staffed and qualified to execute the project plan? Does the project have access to the necessary facilities and resources to execute the project plan? Does the applicant have an adequate project pipeline to support demonstration of operational enhancements and progress toward competency in specialization areas?

4. Does the project effectively serve the needs of underserved and disproportionately affected communities?

Will the proposed activities improve access to cell and gene therapies for underserved and disproportionately affected populations? Will proposed workforce development programs increase workforce participation from underserved and disproportionately affected populations in California? Does the project team bring diverse and inclusive perspectives and experience to the implementation of proposed activities? Does the project team demonstrate a successful track record for promoting and valuing diversity, equity and inclusion (DEI)?

Application Components and Submission

How does one apply?

Applications must be completed and submitted online using the CIRM Grants Management Portal at https://grants.cirm.ca.gov. Any prospective PD must create a login in the system to access application materials and apply. Applications are available in the system only to the PD. A PD may submit only a single application in a given review cycle and may not submit additional applications during the review period.

Applications are due by 2:00pm (Pacific Time) on January 24, 2023.

What components does an application include?

CIRM's online application is designed to collect information for CIRM staff to assess eligibility, for Grants Working Group reviewers to evaluate the project, and for CIRM to rapidly initiate an award if the project is approved for funding.

It includes overview sections characterizing the proposed team, the applicant institution, the proposed project, and major planned activities, a detailed budget and budget justification, and an application uploads section that includes the Project Proposal and reference documentation including Key Personnel Biosketches, Letters of Support and Other Support.

What are the contents of the Proposal?

Project Summary: High-level summary of the project.

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Facility Profile: Description of the facility's track record of supporting development of cell and gene therapies, breakdown of internal and external project support, description and utilization of current differentiated offerings, and existing integration with clinical facilities, CIRM Alpha Clinics and CIRM Education programs.

Project Value Proposition: Description of how the proposed activities will enhance the overall value proposition of the facility, add value to the California Cell and Gene Therapy Manufacturing Network and position it competitively for the phase two funding opportunity.

Project Plan: Description of all proposed activities detailing how the objective of the RFA will be met.

Organizational Business Plan: Brief description of the facility's plans to sustain beyond the immediate project period any operational enhancements, specialization areas and training programs that will be developed, implemented and/or scaled up as part of the proposed project.

Gantt-Like Project Timeline: Timeline for all proposed activities.

Team Organization: Description of the qualifications and staffing of the team that will be responsible for executing the proposed project. Description of the facility's organizational structure, training plan and communications plan.

Organizational Capacity and Resources: Description of the facility's capacity, suites, process development labs, analytical testing labs, floor plan, equipment and quality system. Description of any other institutional facilities and resources, and partners' facilities and resources that will be utilized for the project.

Addressing the Needs of Underserved Communities: Description of how the proposed project will improve access to cell and gene therapies by underserved and disproportionately affected patient populations, how proposed workforce development programs will increase workforce participation by underserved California populations, description of proposed or completed activities to bring diverse and inclusive perspectives and experience to the project, and how the team demonstrates a successful track record for promoting and valuing diversity, equity, and inclusion.

Knowledge Sharing Plan: Description of plans and processes intended to capture and disseminate within the network any operational data, protocols, processes, expertise, guidance or other information vital to achieving the proposed project objectives. Description of any planning enhancements to the facility's data management systems and processes that support the ability of any CIRM Translational and CIRM Clinical awardees utilizing the facility's services in meeting their respective CIRM data sharing requirements. Description of any funds allocated in the application budget for personnel and/or activities related to managing and sharing knowledge.

Plans for Risk Mitigation & Financial Contingency: Potential risks, mitigation strategies, associated costs, and non-CIRM sources of contingency funding.

References: Listing of all references used in the body of the proposal.

Who are Key Personnel?

In the application, we ask you to identify by name pertinent Key Personnel and their specific roles on the project. Key Personnel are defined as (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,

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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).

Individuals who do not meet the definition of Key Personnel may be supported with CIRM funds, but should not be identified by name in the application. Such unnamed personnel may be referenced indirectly by their role on the project (e.g., technician). The budget includes a line item for requesting support for unnamed personnel.

What should one know before preparing the budget?

A specific and well-justified budget must be provided that clearly outlines the total costs of the project, including those costs not proposed to be funded by CIRM. The corresponding budget justification should provide enough detail to allow budget professionals to determine the appropriateness of the costs in relation to the activities being performed. Allowable Project Costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy. Generally, project costs for personnel, supplies, travel, equipment, and subcontracts may be claimed. Limits for specific cost categories must be observed.

What are the rules for spending CIRM funds outside of California?

California non-profit organizations may use CIRM funds for Allowable Project Activities conducted both in California and outside of California. "Allowable Project Activities" means those activities that are conducted in California, and for activities outside of California, those activities over which the California organization exercises direction, supervision and control, including activities performed by a wholly owned subsidiary of the California organization outside of California. It does not include activities undertaken by a separate organization outside of California that retains intellectual property or publication rights in connection with the performance of those activities, including a research collaboration in which the research is conducted outside of California.

What are Direct Facilities Costs?

Direct Facilities Costs are the general operating costs of the Awardee's facilities attributable to housing all elements of the CIRM-funded project or activity. Facilities costs for non-profit applicant organizations are limited to the current applicable, federally negotiated rates for the organization as defined by the Office of Management and Budget (OMB) Circular A-21 or A-122. Facilities rates for for-profit applicant organizations are limited to 35% of the direct project costs. Facilities rates are applied to direct project costs exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of $25,000. The facilities cost rates approved and in place at the time of the application are to be applied to the entire award project period.

How much can an applicant claim for indirect costs?

Indirect Costs will not be funded by this RFA.

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Award Administration

Issuance of Award

A CIRM award is issued via a Grant or Loan Agreement, which is the formal contract that defines the terms and conditions of an award and documents the commitment of funds from CIRM.

Operational Milestones and Payment

CIRM funds under the 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 Awardee will be responsible for covering any remaining costs. CIRM expects that the applicant’s contingency plan will identify 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 Notice of Award to ensure that funds are appropriately dispersed across Operational Milestones.

If CIRM determines, in its sole discretion, that an awardee has failed to satisfy an Operational Milestone within four months of the date that the Operational Milestone was scheduled to have been completed, or if the delay is not addressed to CIRM's satisfaction, CIRM may permanently cease disbursements and terminate the award.

Suspension Events

CIRM reserves the right to hold or terminate disbursements if CIRM determines, in its sole discretion, that a Suspension Event has occurred. A “Suspension Event” means a pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable. Following a Suspension Event, the Awardee is expected to provide CIRM with a plan to resolve the issue that triggered the Suspension Event. CIRM establishes Suspension Events for inclusion in the Notice of Award based on information provided in the Application.

Reporting

Grantees will be required to provide periodic written progress and financial reports to CIRM.

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Other Requirements

CIRM Regulations

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

Change in Status

Applicants are required to notify CIRM of any material change in status while the application is pending review, e.g., the applicant has commenced the trial that is the subject of the award, the applicant no longer qualifies as a California Organization, etc.

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Contacts

For information about this RFA:

Shyam Patel, Ph.D.
Director of Business Development
California Institute for Regenerative Medicine
Email: spatel@cirm.ca.gov

For information about the application and review process:

Gilberto R. Sambrano, Ph.D.
VP of Portfolio Development and Review
California Institute for Regenerative Medicine
Email: gsambrano@cirm.ca.gov

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Definitions

"California organization" means an entity, regardless of profit status, that has >50% of its employees located in, and paid in, the state of California, and conducts the award activities from the California location.

"Critical Quality Attribute" means a property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality.

"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".

"Good Manufacturing Practice (GMP)" per the FDA are regulations enforced by the FDA referring to systems that assure proper design, monitoring, and control of manufacturing processes and facilities. Adherence to current GMP regulations assures the identity, strength, quality, and purity of drug products by requiring that manufacturers of medications adequately control manufacturing operations. https://www.fda.gov/drugs/pharmaceutical-quality-resources/facts-about-current-good-manufacturing-practices-cgmps

"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.

"Operational Milestone" means an objective event that is indicative of project progress occurring as proposed in the application.

"Partner" means an organization that, in exchange for the right to the opportunity for a future financial return, has (1) agreed to provide matching funds for the proposed project or (2) entered into an agreement with the applicant organization relating to the commercialization of the proposed project.

"Process Analytical Technology" means a system for designing, analyzing, and controlling manufacturing through timely measurements (i.e. during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality.

"Quality" means the suitability of either a drug substance or drug product for its intended use.

"Quality by Design" means a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management.

Reference Documents:

International Conference on Harmonization (ICH) Q8(R2): Pharmaceutical Development - Guidance for Industry. November 2009: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q8r2-pharmaceutical-development

Project A-Cell: https://alliancerm.org/wp-content/uploads/2022/09/PROJECT-A-CELL-V2.pdf

Project A-Gene: https://alliancerm.org/wp-content/uploads/2021/06/ALL-PROJECT-A-GENE-V6-FINAL.pdf

"Rare disease" as defined by the Orphan Drug Act means a disease or condition that affects less than 200,000 people in the United States.

"Subcontractor" means an organization (other than the applicant organization) that is expected to: (a) contribute to the scientific development or execution of the project in a substantive, measurable way *and* (b) receive $50,000 or more through the proposed project. "Subcontractor" does not include suppliers of widely available goods.

"Suspension Event" means a pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable.

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Revisions

Revision Date	List of Changes
11/01/22	• Application deadline date changed to January 24, 2023