CALIFORNIA'S STEM CELL AGENCY

Funding Opportunity Concept Plan

Community Care Centers of Excellence

BACKGROUND

The mission of the California Institute for Regenerative Medicine (CIRM) is to *accelerate world-class science to deliver transformative regenerative medicine treatments equitably to a diverse California and world*. Consistent with this mission, the California Stem Cell Research, Treatments, and Cures Initiative of 2020 (Proposition-14) mandates the establishment of the Community Care Centers of Excellence (CCCE) Program to promote access, across the state, to clinical trials, treatments, and cures arising from CIRM-funded research.[1]

CIRM has performed a state-wide needs assessment[2] and recognizes that making treatments widely available to California patients will require approaches attuned to social determinants that vary both geographically and within defined sub-populations. Further, operational capacities and readiness to support clinical research and make treatments broadly available to California patients also vary across the state. Recognizing this diversity of social determinants and operational readiness, CIRM is funding activities supporting the development of CCCEs commensurate with the variability identified in the needs assessment.

The operational aim of this funding opportunity is to leverage and expand existing organizational and community capacities in California to enable broad awareness and access to regenerative medicine treatments for patients. The CCCEs are designed to serve as a hub for expanding access to clinical trials, regenerative medicine treatments, and CIRM education and training programs. A strategic aim is to provide equitable access to communities and populations that would otherwise have more limited opportunities in the absence of these centers.

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[1] https://www.cirm.ca.gov/sites/default/files/files/about_cirm/Prop-14-full-text.pdf

[2] https://www.cirm.ca.gov/wp-content/uploads/archive/CIRM_CCCE_Workshop_6_22_Background%20%20%281%29.pdf

OBJECTIVE

The objective of CCCE program is to establish geographically diverse and culturally responsive centers of excellence to (1) support access to FDA-authorized clinical trials involving cell, gene and/or approved regenerative medicine treatments, (2) make these treatments broadly available to California patients, and (3) provide workforce career development opportunities. Pursuant to these objectives, the Community Care Centers of Excellence are expected to:

- Operate a licensed and certified healthcare facility[3] with the aim of providing access to regenerative medicine clinical trials and approved products.
- Collaborate with Clinical Trial Stage Projects,[4] Alpha Clinics Network, Patient Support Program, California CGT Manufacturing Network, Education Programs, and other CIRM initiatives.
- Provide career development opportunities for CIRM trainees and health practitioners including physicians, nurses, research coordinators, community health workers, patient navigators, or other medical professionals who are integral to making regenerative medicine clinical trials or treatments accessible.
- Conduct outreach and engagement activities to educate patients, families, healthcare providers, and communities about clinical research opportunities and facilitate access to CIRM programs and resources.
- Leverage existing community-based capacities to support the clinical, career development, outreach, and engagement objectives of this RFA.
- Develop new capacities or capabilities to address needs or gaps that are documented through program implementation and evaluation provided they are consistent with the program objectives.

Core Program Activities:

Applications must have the capacity to perform the core program activities below.

- Clinical Operations: Have licensed and certified healthcare facility[5] with a demonstrated capacity to support human subjects protocols[6] consistent

[3] https://data.chhs.ca.gov/dataset/healthcare-facility-locations
[4] https://www.cirm.ca.gov/researchers/funding-opportunities/clinical-trial-stage-projects/
[5] https://data.chhs.ca.gov/dataset/healthcare-facility-locations
[6] https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html

with FDA guidelines[7] in a health research context. Have current capacity or be in the process of developing capacity to support clinical research protocols involving cell, gene, or regenerative medicine treatments.

- Career Development: Have a demonstrated capacity to support education, training, and career development of physicians, nurses, research coordinators, community health workers, or other health/medical professionals.
- Outreach and Engagement: Have a demonstrated track record of conducting or coordinating health education, research, and engagement activities.
- Community-Based Partnerships: Community-Based Organizations (CBOs) can play an important role in supporting populations that are underrepresented in clinical research. Partnerships should be proposed to support patient education, career development, and community engagement, activities.
- New Capacities: Implement evidence-based approaches for evaluating the effectiveness of proposed clinical, career development, and education/engagement programs. Drawing on this evidence centers should propose new community-centered capacities, consistent with CCCE program objectives, to improve program effectiveness.

Clinical Operations:

CIRM will fund clinical operations that provide one of two core functions under an award:

1. **Support Site Only**: A Support Site will offer patients access to FDA-regulated regenerative medicine clinical trials or approved products available at partnering institutions such as an Alpha Clinic site.
2. **Support and Delivery Site**: In addition to offering access to regenerative medicine clinical trials or approved products, these sites will deliver onsite treatments to patients under an FDA-regulated clinical trial or for an approved regenerative medicine product.

Support Sites:

Sites should perform a variety of clinical support activities vital for facilitating patient access to regenerative medicine clinical trials or

[7] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trials-guidance-documents

approved products. These activities include:

- Clinical trial cohort identification, outreach, and engagement
- Patient navigation including referrals to CIRM's Patient Support Program, the Alpha Clinics Network, or CCCE Support and Delivery sites.
- Clinical research support including screening, enrollment, pretreatment evaluation, workup, or post-intervention follow-up and monitoring, and evaluation of outcomes (Real World Evidence).

Optimally, Support sites will enhance access to research and approved products by enabling the delivery of clinical protocols in a community care setting that is responsive to the needs of the populations being served.

Support and Delivery Sites:

Support and Delivery sites should (a) perform the clinical support activities described above in addition to (b) initiating clinical trials with the capacity to deliver investigational or approved regenerative medicine products. These additional activities include:

- Clinical trial initiation including working with sponsors to create clinical trial agreements and contracts.
- Developing operations and management systems to address the unique technical needs of regenerative medicine clinical trials including product manufacturing, processing, and delivery.
- Enrolling and providing coordinated care to patients in clinical trials or the delivery of approved products.

Career Development:

CCCEs should propose career development programs to advance the knowledge of physicians, nurses, research coordinators, community health workers or other health care professionals that are integral to education, navigation or the delivery of regenerative medicine clinical trials or treatments. Programs may include educational seminars intended to provide healthcare providers with information related to the delivery of regenerative medicine clinical trials and treatments. Centers are encouraged to collaborate with the Alpha Clinics or CIRM Education

programs to adapt, expand, or otherwise utilize established training opportunities. Applicants should propose fellowship programs for trainees participating in CIRM-funded Education Programs.

Applicants should consider how health education or delivery occurs among underserved populations in their catchment area and propose activities that facilitate or otherwise support workforce education, training or certification to support broad access. Partnerships with established Community-Based Organizations (CBOs) are encouraged as a means of engaging underserved populations.

Outreach and Engagement:

CCCEs should develop outreach and engagement programs intended to enable awareness and informed access to clinical trials and regenerative medicine treatments. Programs should be adapted to the needs of different populations and serve to support the successful attainment of DEI objectives in CIRM Clinical Stage Applications.[8] The program should include the capacity to inform patients about clinical trials being conducted in the Alpha Clinics or Community Care Centers of Excellence Network. In addition, programs should facilitate the utilization of other CIRM resources including but not limited to the Patient Support Program and other CIRM engagement programs.

Community Based Partnerships:

Making treatments widely available to California patients will require approaches attuned to social determinants that vary both geographically and within sub-populations. Community-Based Organizations (CBOs) provide an efficient and effective (e.g., socio-culturally appropriate) means of engaging stakeholders. Community-based partnerships may be proposed to satisfy or complement the core program actives above.

Applicants should propose at least one partnership with a Community-Based Organization (CBO) or organizations to support clinical research, career development or engagement. Emphasis should be placed on supporting populations that are underrepresented in clinical research and would benefit from engagement intended to address informational, economic, or social determinants impacting access to or participation in research.[9] Program implementation will include research ethics training for

[8] https://www.cirm.ca.gov/wp-content/uploads/archive/files/about_stemcells/CLIN2_PA_08_08_22_1.pdf
[9] The engagement initiative may be proposed as part of a Workforce, Community Partnership.

community partners consistent with requirements for clinical and social science research.

New Capacities:

CCCEs should propose structured / evidence-based approaches for evaluating the effectiveness of proposed clinical, career development, and education/engagement programs. Evaluation instruments should aim to capture clinical, informational, economic, and social determinants that may impact the efficacy of the CCCEs or other CIRM programs. Evaluative studies should include a data-sharing and dissemination plan. Based on the findings of evaluative studies, CCCEs may propose new capacities, consistent with CCCE program objectives, to improve overall performance.

AWARD INFORMATION

What activities will CIRM fund?

CIRM funds will support the following activities under this opportunity:

- Creation of teams necessary to support clinical trials involving cell, gene, and/or regenerative medicine treatments.
- Development of systems or deployment of technologies integral to supporting the clinical, career development, or engagement and outreach objectives of this program.
- Contracts with existing CIRM programs or other service providers to support the implementation of clinical, career development, engagement, and outreach programs.
- Partnerships with Community-Based Organizations (CBOs).

Facilities Funding:

Applicants may request facilities funds. Funds may be utilized for renovating existing facilities or acquiring equipping integral to the operation of a Community Care Center of Excellence. Applicants are required to demonstrate that facilities funds are essential for creating or expanding their capacity to support clinical research protocols involving cell, gene or regenerative medicine treatments. Expenditure may include but not be limited to:

- Acquisition of equipment or renovation of facilities necessary for the delivery

of investigational products to patients in clinical trials.

- Acquisition or deployment of equipment or renovation of facilities necessary for the delivery of approved regenerative medicine products to patients.

- Acquisition or deployment of equipment or renovation of facilities necessary to navigate, screen or follow up with patients who are participating in clinical trials.

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

- Cost associated with the operation of individual clinical trials[4]
- Activities already budgeted or paid for under a prior, existing, or future CIRM award.

What is the award amount and duration?

The CIRM Governing Board has allocated $60.2 million for funding the CCCE program to support (1) core operations, (2) community partnerships, (3) building renovation, and equipping facilities for a five-year duration. The total budget proposal is an estimate assuming the following distribution of awards:

- Three “Support and Delivery” awards at $10.054 million per award.
- Four “Support” awards at $7.5 million per award.

Pursuant to Proposition 14, CIRM shall prioritize applications for the Community Care Centers of Excellence that offer matching funds or verified in-kind support, consistent with the highest medical standards, as established by the CIRM governing board.

How will funds be awarded?

Awards will be made in the form of a grant. 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.

ELIGIBILITY

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following eligibility requirements.

(1) Must be ready to initiate work on the funded project within 120 days of approval.

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 120 days of approval and authorization for funding by the Application Review Subcommittee of the Independent Citizens' Oversight Committee.

(2) Non-profit organization with 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 the appropriate hospital/clinics and facilities accreditations and operational medical 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 human subjects research in health research context

Have licensed and certified healthcare facility[10] with a demonstrated capacity to support human subjects protocols[11] consistent with FDA guidelines[12] in a health research context. Applicants can demonstrate this capacity by describing research protocols performed by the organization. Descriptions should include the research aims and findings, a description of the participant population, and how review and oversight of the study was performed (e.g., IRB or other required review and oversight).

(4) Must have the capacity to support career development, accreditation or certification programs

Applicant organizations must have the capacity to administer and support the career development of health workers and other trainees. This capacity may be developed in partnership with established training or accreditation programs. Proposed partnerships should be described in memorandum of understanding.

(5) Patient Protections

[10] https://data.chhs.ca.gov/dataset/healthcare-facility-locations
[11] https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html
[12] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trials-guidance-documents

The applicant organization must **not** provide direct-to-consumer fee for service interventions involving "stem cell therapies"[13] subject to the notice requirements of CA Bus & Prof Code § 684 (2018).

(6) Application must be accurate and complete

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

(7) Applicant must be in "good standing"

In order to be eligible to apply for CIRM funding, an applicant must certify that it is in good standing, as follows:

a. Organizations in existence for less than five years:
   (i) The applicant's Chief Executive Officer, Chief Financial Officer, and Program Director must not have been convicted of, or are currently under investigation for, crimes involving fraud/misappropriation.

   (ii) The applicant must have accounting systems in place that are capable of tracking CIRM funds.

b. All Applicants:
   The Program Director or key personnel must not be currently under investigation for research misconduct by the applicant institution or a funding agency and must not be currently debarred by the HHS Office of Research Integrity.

Who can apply?

California Organizations

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:

[13] "Stem cell therapy" means a therapy involving the use of human cells, tissues, or cellular or tissue-based products, but shall not include a therapy involving human cells, tissues, or cellular or tissue-based products that meets the criteria set out in Section 1271.10 of Title 21 of the Code of Federal Regulations, as amended May 25, 2004, as published in the Federal Register (69 Fed. Reg. 29829), or that qualifies for any of the exceptions described in Section 1271.15 of Title 21 of the Code of Federal Regulations, as amended May 25, 2004, as published in the Federal Register (69 Fed. Reg. 29829).

- Must be an employee of the applicant organization(s) 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. Any effort for which salary from CIRM is claimed must be expended in California.
- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PD.
- 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.

Addressing the Needs of Underserved Communities in CIRM-Funded Projects

All applicants for the Community Care Center of Excellence program will be required to provide a statement describing:

1. How their Community Care Center of Excellence will support and facilitate outreach and study participation by underserved and disproportionately affected populations in the clinical trials they serve.

2. How the assembled site team and collaborators will bring diverse and inclusive perspectives and experience to the implementation of proposed activities.

3. How the research team demonstrates a successful track record for promoting and valuing diversity, equity, and inclusion (DEI).

Knowledge Sharing Plan

Knowledge sharing has contributed to the success of CIRM Infrastructure Programs and is vital to advancing the field of regenerative medicine. Data or Knowledge Sharing Plans are required in all CIRM awards. Such plans include the collection, curation, and preservation of data resulting from the conduct of the award. In the context of the CCCE award, applicants should develop plans intended to capture operational information vital to evaluating or replicating the (1) center's core competencies, (2) training programs, and (3) outreach and engagement efforts. Applicants should propose how this information can be made available to CIRM partners and the broader scientific community.

Applicants should describe their experience, resources, and capacities to support

data collection and integration with established platforms such as registries, repositories, or other platforms in accordance with system standards such as the FAIR Principles of findable, assessable, interoperable, and reusable data. CIRM expects applicants to facilitate the sharing of knowledge to maximize the impact of CIRM-funded programs.

A 5-year strategic CIRM goal is to build knowledge networks that foster and advance novel research approaches to generate a healthy culture of team science. Applicants should describe how their proposed CCCE will contribute to this strategic goal. Applicants are encouraged to allocate funds in their proposed budget for personnel and/or activities related to managing and sharing knowledge.

Organizational Integration Plan

In the application proposal, individual sites will be expected to describe, in the form of a Business and Organizational Integration plan, how they aim to leverage their capabilities, so they become integral to clinical operations beyond the award period. In addition, the plan should describe operational synergies between the Alpha Network site and other CIRM Infrastructure and Research Programs. For example, the plan may discuss how proposed offerings may be supported by budgets from clinical trial awards or contracts.

SCHEDULE AND DEADLINES

Applications Due	June 2024
Grants Working Group (GWG) Review	Approximately 60 days post submission
ICOC Review and Approval	Approximately 90 days post submission
Award Start	Must start within 120 days of award approval (i.e., approximately 205 days post submission)